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TeamLEAD: Educating Students beyond Duke-NUS

Duke-NUS' hallmark team-based learning approach, TeamLEAD, is making its mark outside of the graduate medical school, benefitting local mainstream schools and elevating the way students learn.

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The Deans on 2014

Duke-NUS Deans give their take on the past year and share their thoughts on 2014.

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Understanding the Flu

Influenza, or the "flu" for short, remains one of the most common infectious diseases in the world. The diversity of the different viral strains and their ability to adapt and evolve and even jump the species barrier makes the disease one of the most challenging infections to study, prevent and treat.

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Duke-NUS Researcher Studies "the Architecture of Life"

Professor Karl Tryggvason did not set out to

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Duke-NUS Clinician Scientists

be a world-renowned physician scientist. Instead he started his illustrious career as an architecture student at the University of Oulu in Finland.

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Produced by the Cognitive Neuroscience Lab

Teaching to Learn

Third-year student Petty Chen shares why she initiated a peer tutoring group to help juniors who were struggling to keep up with the rigorous Duke-NUS curriculum.

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VITAL SCIENCE

This e-communications update is produced by the Office of Communications, Development and Alumni Relations
Produced by: Janice Tan (Editor), Dharshini Subbiah and Sheralyn Tay

Our banner story: TeamLEAD: Educating Students beyond Duke-NUS. Read the story here.

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DUKE NUS GRADUATE MEDICAL SCHOOL SINGAPORE

TeamLEAD: Educating Students beyond Duke-NUS

Duke-NUS' hallmark team-based learning approach, TeamLEAD, is making its mark outside of the graduate medical school, benefitting local mainstream schools and elevating the way students learn.

Duke-NUS has extended the teaching and learning of medicine in more ways than one. Apart from being Singapore's first graduate-entry medical school, it has also successfully implemented its innovative team-based learning pedagogy called TeamLEAD. This is an active learning approach that incorporates principles such as the development of clearly defined learning goals, the provision of resources for self-directed learning, and individual and team-based testing. The process promotes learning via peer engagement, theory application and development of critical thinking skills.

Duke-NUS has gone on to take the novel teaching and learning approach beyond its campus. For instance, the Fellowship in Team-Based Learning (FTBL) program – a structured program that teaches the full range of team-based learning skills so participants can develop and run modules in their respective institutions – has benefited over 40 educators from across the globe since its launch in 2012.

A new way to teach and learn math

Closer to home, TeamLEAD has also made its mark. Mr. Christopher Chee, a teacher formerly with Christchurch Secondary School (and now with Spectra Secondary School) has adapted the method in his mathematics class at both schools, with good results. The senior teacher was intrigued and inspired by the rich and extensive possibilities of TeamLEAD after reading the series of commentaries on cognitive learning and education in the *TODAY* newspaper and contacted the author, Professor Ranga Krishnan, Dean of Duke-NUS. With guidance from Dr. Robert Kamei, Dr. Sandy Cook and Dr. Frank Starmer, the schools experimented with the pedagogic model and adapted it for use early in late 2013.

Dr. Starmer shared that one of the challenges in the adaptation process was in identifying appropriate resources. The Khan Academy was eventually selected as the best source for self-directed, pre-class learning resources, assessment tools and testing materials. The Duke-NUS team also assisted Mr. Chee in converting some of his own learning videos into voice annotated presentations (VAPs). VAPs, which combine audio files and lecture slides, are a key element of the self-directed learning approach, allowing students to view lessons at their own pace and 'rewind' the lesson as needed. Under this teaching and learning model, students have not only improved

Profs. Ranga Krishnan and Frank Starmer

their grades, but learnt to support each other in the learning process as well [see box story below: Team-based Learning for a more engaged classroom].

Dr. Starmer reflected, “The partnership between Mr. Christopher Chee and Dean Krishnan, Dr. Kamei, Dr. Cook and I has been quite productive. Mr. Christopher Chee's work has provided Duke-NUS with an important data point demonstrating that knowledge acquisition of medical students learning via TeamLEAD can be successfully applied to a secondary school setting, producing significant results that promote learning outcomes.”

Dean Krishnan, whose series of commentaries in *TODAY's* ‘The Way We Learn’ was the catalyst for all this, was gratified to see TeamLEAD adapted into a mainstream secondary school. He observed, “The active and interactive approach is suitable for children; children by their very nature play, interact and learn from each other. The team-based learning method feels natural and the children learn from each other at their own pace.”

Sharing TeamLEAD with others

Hoping to further the positive impact of TeamLEAD amongst the schools locally and abroad, and in response to growing interest in the subject, Duke-NUS has organized distinguished lectures, customized school visits, half-day workshops and the FTBL program.

The next FTBL program – the third intake to date – will see participants from the Ministry of Education (MOE) in Singapore. This illustrates a recent “overwhelming” interest in TeamLEAD, said Dr. Cook. In 2013 alone, Duke-NUS hosted 104 educator participants, including leaders from 42 secondary schools, 48 tertiary institutions and 14 representatives from the Ministry of Education, SingHealth, Singapore General Hospital, GlaxoSmithKline, Academy of Principals (Singapore) and Academy of Singapore Teachers.

Dean Krishnan also delivered a keynote speech, ‘Learning in the 21st century’, to over 200 teachers at Seng Kang Secondary’s Learning Festival in November, while Dr. Starmer held an interactive session with 31 teachers to demonstrate TeamLEAD. Earlier in the year, at the Academy of Principals (Singapore)'s Asia-Pacific Assessment conference in September, Dr. Cook’s hosted a session on team-based learning which was also well received.

Prof. Robert Kamei and Dr. Sandy Cook sharing the merits of team-based learning at various events

Said participant, Mrs. Belinda Charles, Dean, Academy of Principals (Singapore), “What was exciting for me was to see how good design and well-posited questions are able to make students think further and deeper about a topic regardless of how superficial had been their acquaintance with the topic earlier.” She was also impressed with the way students worked with each other, “Students [were] able to genuinely interact with each other's contribution, not just relying on the teacher as the source. This will really help to build that culture of mutual learning and mutual respect that should be at the heart of any learning community.”

Similar positive feedback was gained at a recent presentation on TeamLEAD at National Junior College on January 3, 2014. Biology teacher, Nah Hong Leong, wrote in to Duke-NUS to commend Dean Krishnan on his keynote speech on the effectiveness of team-based learning. He said teachers found it to be the best sessions they had attended in terms of relevance and engagement. “The lecture provided them with a different perspective on education and they were able to connect with you,” he shared, adding that the presentation has sparked interest among teachers to visit classes at Duke-NUS to better understand how to carry out team-based learning in their own classrooms.

Dr. Cook said, “We believe that TeamLEAD represents not only a new way of educating physicians, it can be successfully used in the public school systems in Singapore. It offers a paradigm shift that values teamwork, communication skills and thinking, rather than rote memorization. We hope that our school can be a positive influence on Singapore education and are pleased at the interest in TeamLEAD.”

Team-based Learning for a more engaged classroom

Education Minister Heng Swee Keat presents Dean Krishnan with a token of appreciation for the advice and assistance to Spectra Secondary School

At Spectra Secondary School, a pilot program that started in 2013 involves students ‘teaching’ themselves. Adapting Duke-NUS’ TeamLEAD approach, normal technical students attend class *after* already viewing video lessons at home or in school. Class time is reserved for asking questions, seeking clarification or doing individual or team tests.

Though the concept is unique to Singapore, students have not only accepted the new lesson format, but have improved grades and formed better teacher-student and student-student relationships. Mr. Christopher Chee, who worked with Duke-NUS faculty to develop the customized math curriculum shared: “The secondary 3 normal-technical class has readily accepted this approach and now work as a team; the better-abled students guide the weaker ones in their learning, as they attempt class assignments. Those that taught their peers have gained confidence while students taught by their peers have improved their grades.” Significantly, all the students involved in the pilot have found greater meaning in their participation in class. “Our teachers, having witnessed the transformation in the students, are themselves transformed and now would have it in no other way when conducting their lessons.”

Mr. Chee further reflected that unlike the conventional ‘one-size-fits-all’ teacher-directed method, team-based learning is more student-centric. “It allows students to take charge of their learning. He added, “Traditionally students learn in isolation, whereas in this approach, students work collaboratively and build on their communication skills. Intuitively, the students help each other and not compete with each other.” All this goes towards not just building academic competence, but essential life skills (team work, communication and, leadership etc.) as well. In short, highly-empowered students.

Minister Heng later observed a demonstration of Spectra's learning approach involving a group of visiting students. Spectra based their apporach on Duke-NUS' model of team-based learning

In a recent Facebook post (January 26, 2014), Singapore Education Minister Heng Swee Keat said he appreciated Mr. Chee’s gumption to innovate his teaching methods, following Duke-NUS’ success with its own medical students. Minister Heng added that he is “excited for the great learning opportunities that will open up for our children.”

Duke-NUS' other educational and technological innovation:

Voice-Annotated Presentations (VAPs)

Voice-annotated presentations (VAPs) are recorded power point presentations. Each slide of the presentation is annotated and indexed into a playlist. This allows the listener to return to or skip to any slide within the presentation. These VAPs are converted to small portable files and made available online to ease streaming over any compute/mobile device (e.g. iPads, smartphones, laptops etc.). VAPs facilitate flexible learning: students can access lectures anywhere and at any time; VAPs also allow students to learn at their own pace to enable more effective self-directed learning.

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The Deans On 2014

Duke-NUS Deans give their take on the past year and share their thoughts on 2014.

Prof. Ranga Krishnan

Prof. Ranga Krishnan, Dean

2013 has been the year of Academic Medicine. The Academic Clinical Programs (ACPs) are in place and the two institutes - AM•EI and AMRI - are highly productive and well ahead of expectations in meeting their objectives.

2013 was terrific for Duke-NUS. Many of our faculty received numerous awards and honors.

Our education approach has been well-recognized this year and the Education Minister Mr. Heng Swee Keat, has commended our approach in his speech during the annual MOE Work Plan Seminar last September. The TeamLEAD method is now being tested and implemented in some of the secondary schools in Singapore. Dr. Sandy Cook, Prof. Robert Kamei and Prof. Frank Starmer are in demand for demonstrating the method they built to numerous teachers and educators both from Singapore and globally.

Our research has produced major breakthroughs that has the potential to improve patient lives.

Faculty	Achievement	Date
Prof Wang Linfa *Emerging Infectious Diseases Program*	Discovered that genes regulating the immune systems in two distant bat species undergo the most rapid changes and published the findings in *Science*. Reported by *Reuters* and a number of international news sources	25 January 2013
Assoc Prof Antonius Van Dongen & Dr Mark Dranias *Neuroscience and Behavioral Disorders Program*	Found that neuronal networks formed for cells in culture have short-term memory processes similar to those found in intact brains and published the study in the *Journal of Neuroscience.*	30 January 2013

Prof Teh Bin Tean *Cancer and Stem Cell Biology Program*	Identified a new type of deadly intestinal lymphoma that is particularly common in Asia and published the findings in *Leukemia*.	12 February 2013
Prof David Matchar *Health Services and Systems Research Program*	Developed a modeling methodology of System Dynamics for the long-term care in Singapore projecting the burden expected to be borne by family caregivers over the coming years and published the model in *Health Services Research.*	April 2013
Professor Patrick Tan *Cancer and Stem Cell Biology Program*	Human Genome Organisation's (HUGO) Chen New Investigator Award	18 Apr 2013
Assoc Prof Ong Sin Tiong *Cancer and Stem Cell Biology Program*	Identified a new drugable target called MNK-eIF4E in chronic myeloid leukemia (CML) and published the results in *Proceedings of the National Academy of Sciences* (*PNAS*).	July 2013
Adjunct Assoc Prof Terrance Chua *Cardiovascular and Metabolic Disorders Program*	National Medical Excellence Awards (NMEA)'s National Outstanding Clinician Award	24 Jul 2013
Professor David Virshup *Cancer and Stem Cell Biology Program*	Elected a Fellow to the American Association for the Advancement of Science (AAAS)	25 Nov 2013
Assoc Prof Ong Sin Tiong *Cancer and Stem Cell Biology Program* Assoc Prof Paul Yen *Cardiovascular and Metabolic Disorders Program* Assoc Prof Koh Woon Puay *Office of Clinical Sciences*	Clinician Scientist Award / Clinician Scientist Investigator Award (Singapore) **CSA (Senior Investigator)**	2013
Asst Prof Mei Wang *Cancer and Stem Cell Biology Program* Assoc Prof Marcus Ong Eng Hock *Office of Clinical Sciences* Assoc Prof Christopher Ang *Academic Clinical Program for Neuroscience*	Clinician Scientist Award / Clinician Scientist Investigator Award (Singapore) **CSA (Investigator)**	2013
Prof Michael Chee *Neuroscience and Behavioral Disorders Program* Prof David Virshup *Cancer and Stem Cell Biology Program* Prof Antonio Bertoletti *Emerging Infectious Diseases Program* Prof Tan Eng King *Neuroscience and Behavioral Disorders*	Singapore Translational Research (STaR) Investigator Award (Singapore)	2013

Program		
Prof Salvatore Albani *Office of Research*		
Prof Wong Tien Yin *Office of Clinical Sciences and Academic Medicine Research Institute*		
Adjunct Asst Prof Sng Ban Leong *Office of Clinical and Academic Faculty Affairs*	Transition Award (Singapore)	2013
Adjunct Asst Prof Zhou Zhidong *Neuroscience and Behavioral Disorders Program*		
Asst Prof Andrea Kwa *Emerging Infectious Diseases Program*		
Dr Joanne Ngeow Yuen Yie *Academic Clinical Program for Oncology*		

We are thankful to each and every one of you in working together with and at Duke-NUS in making patients' lives better through research and by training the next generation. I am very proud of what you have done and I look forward to an equally fulfilling 2014.

Prof. Patrick Casey, Senior Vice Dean, Research

Looking back at 2013, I believe that one of the key words to describe the year from the viewpoint of the Office of Research is "impact".

The commitment of Duke-NUS faculty and staff to making a real impact in health sciences research and education, as well as public healthcare policy, enhances our special relationship with stakeholder institutions and ministries.

There is no doubt that our ability to deliver impactful findings will only strengthen in 2014, particularly as our Academic Medicine partnership with SingHealth matures.

Prof. Patrick Casey

Prof. Robert Kamei, Vice Dean, Education

Education at Duke-NUS continues to do well with our third batch of students graduating and matching into residency training programs. The students' academic performance on all of our measures remain high, a tribute to the hard

Prof. Robert Kamei

work of both students and faculty.

Our novel method of education, TeamLEAD has been gaining interest from the local schools across all levels, with some teachers successfully using the technique for their secondary school students. Prof. Krishnan, Starmer, Cook and I have educated over a thousand teachers and administrators from MOE at various lectures and workshops over the past year. We also continue to receive visit requests to Duke-NUS from institutions globally to learn about this teaching methodology.

Our new education deans, Dr. Mara McAdams (Student Life), Assoc. Prof. Lim Soon Thye (Career Advising) and Dr. Shiva Sharraf-Yazdi (Admissions and Recruitment) have already made significant impact on our academic programs. New initiatives in Student Wellness programs, re-organizing the Student College system for improved student advising and a more comprehensive career mentoring program are just a few of the improvements planned by the new deans.

The Academic Medicine Education Institute (AM•EI) now in place for slightly over a year, already has over 1,000 members. It is a globally unique institution with its inclusive and interdisciplinary participation of faculty to improve education offering throughout the SingHealth system. Besides faculty development, the AM•EI is one of the key drivers of innovation in all our educational offerings.

Plans for 2014 include a major “re-look” at how we educate our students in the first clinical year. Traditionally this program takes place in the hospital wards, but we know that most patient care occurs in the outpatient clinics and in the community. Along with this, we want to further leverage on our advanced educational technology to enhance the efficiency of faculty and student learning.

Prof. Tan Kok Hian, Senior Associate Dean, Academic Medicine

With the partnership in Academic Medicine between Duke-NUS and SingHealth, we now have a good eco-system of learning and discovery, advancing medicine and improving lives. It has been fulfilling to see our students graduate and do well in SingHealth Residency programs. Having new and younger faculty passionate about teaching spurs new research collaborations that would ultimately translate to better outcomes and care for patients.

In 2014, we will further strengthen our Academic Clinical Programs (ACPs) and forge even stronger collaborations across the various specialties with the Signature Research Programs, AMRI and AM•EI. It will be exciting as we have many new plans, and our success will grow rapidly in tandem as SingHealth and Duke-NUS work and advance together in this strong Academic Medicine partnership.

Prof. Tan Kok Hian

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Understanding the Flu

Influenza, or the "flu" for short, remains one of the most common infectious diseases in the world. The diversity of the different viral strains and their ability to adapt and evolve and even jump the species barrier makes the disease one of the most challenging infections to study, prevent and treat.

Many types of influenza, such as Influenza A, originate from birds and other animals such as pigs. There are many types of influenza because the virus mutates readily when it comes into contact with other influenza viruses or the human immune systems. This helps influenza virus adapt to become more resistant or to gain the ability to transmit more effectively between hosts, be it between animals, from animal to humans or from human to human. Associate Professor Gavin Smith also pointed out that increased air travel and intensification of farming and urbanization that brings human environments closer to natural ones, have also led to the increased spread of the disease.

Flu fighters: Asst. Prof. Vijay Dhanasekaran and Assoc. Prof. Gavin Smith

At Duke-NUS, the Emerging Infectious Diseases (EID) Program collates and analyzes data on influenza and other infectious diseases to gain better insights into understanding their ecology. Disease ecology, explains Assistant Professor Vijaykrishna Dhanasekaran, is the study of how pathogens interact with their human or animal hosts and the impact of this on the transmission of diseases. "Every now and then, viruses that circulate in animals jump from animals to humans. This inter-species transmission can cause a major epidemic or in some cases, a global pandemic because we don't have any immune protection against these viruses. This is one reason we need to understand the ecology of infectious diseases not just in humans, but in animals as well."

Dr. Gavin Smith, who runs the Laboratory of Virus Evolution elaborated, "Understanding where those contact points (between animals and humans) exist is important to stop any transmission; because if you understand where transmission happens, why it happens and the probability of transmission, then you can remove the source."

These factors make influenza a challenging pathogen to study, he explained, but it also presents an opportunity for researchers. "Because of its properties, influenza spreads easily, has a relative high mortality, and a high level of interest, a lot of information is being collected globally all the time. This makes it a good model virus to study." The high mutation rate also means there is a lot of information to work with.

Areas of research

Making sense of this wealth of information plays an important role in understanding the fundamental behavior of influenza. “When a new pathogen emerges, the response is necessarily reactive because we don’t know what it is, where it comes from and how it will spread. The general idea is to gain a better understanding,” said Dr. Smith. The work is akin to doing the “homework” beforehand. Surveillance in the absence of disease, the study of at animal populations and analyzing data on influenza patterns all help researchers make better predictions. “What we are trying to do is to learn from past events and currently circulating viruses to then try and understand what the possible scenarios are if something new emerges,” he explained. That information also helps develop mathematical modeling about different control scenarios for pandemic preparedness plans. “In the event of a pandemic, it sets out what to do and whether there are enough antivirals, how effective an antiviral is or how long it will take to develop a vaccine.”

For instance, the Laboratory of Virus Evolution at Duke-NUS helps to fill in the existing gaps in global influenza data. “While surveillance in North America and parts of Europe are highly-represented, surveillance in South East Asia, South Asia and Africa are not so established. One of the things we want to do is to fill these gaps,” explained Dr. Dhanasekaran. Thus far, the lab has established surveillance in three different countries and works with four of the six WHO centers that compile influenza data.

Other areas of research include studying the global movements of the virus (called epidemiology), analyzing adaptations in the inter-species transmission to try and understand why some viruses are more successful than others, risk assessment and tracing the origins of pathogens. This involves collaborative research with different teams around the world. Recently, Dr. Dhanasekaran was part of a team that discovered that certain populations, namely indigenous Australian and Alaskan people, are more vulnerable to H7N9 than others due to an absence of preexisting antibodies. All this, explains Dr. Smith, goes into enabling better pandemic preparedness plans.

The lab also contributes to the development of the biannual influenza vaccine by working with collaborating centers and training people in disease ecology analysis. “We help these centers to analyze big data sets on flu surveillance,” said Dr. Smith, “The information plays a role in the global vaccine strategy”. (See box story: Creating the flu vaccine).

Creating the flu vaccine

The constant mutations in influenza viruses means vaccine formulas too have to be adjusted every six months to ensure they remain effective. The WHO's Global Influenza Surveillance and Response System works with a wide network of National Influenza Centres who monitor and compile information on the types of influenza viruses circulating in humans. Every six months, the WHO meets to review the data and uses the information to develop a vaccine that targets the most virulent strains in circulation.

Influenza rising

While a flu epidemic strike occasionally – with numbers rising during the annual ‘flu seasons’, there have officially been four major pandemics in the last century.

1918: The infamous ‘Spanish Flu’ that affected large swathes of the globe and killed an estimated 40 million, many of whom were healthy young adults

1957: A pandemic of Influenza A that affected large parts of Asia

1968: The Hong Kong influenza

2009: The H1N1 virus, originating from pigs, affected parts of the United States and Mexico and resulted in almost 17,000 deaths in the latter country. While these emerging influenza strains are of concern, the common established influenza strains are still significant.

According to the WHO, influenza epidemics affects five to 15 per cent of the global population, causing three to five million severe cases of illness and between 250,000 and 500,000 deaths annually.

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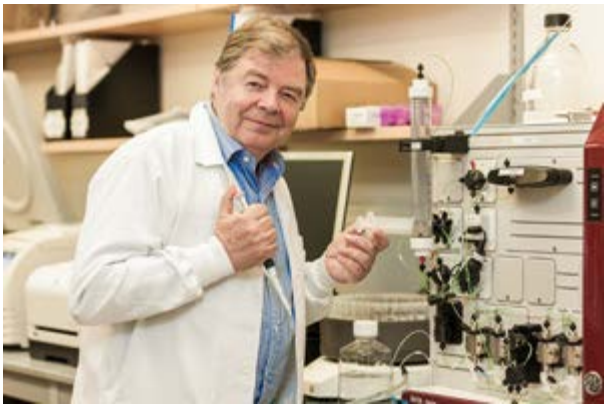
Duke-NUS Researcher Studies "the Architecture of Life"

Professor Karl Tryggvason, from the Cardiovascular and Metabolic Diseases Program at Duke-NUS, did not set out to be a world-renowned physician scientist. Instead he started his illustrious career as an architecture student at the University of Oulu in Finland. Halfway through, he switched to study medicine, which turned out to be his calling. Today, his research involves the molecular components, biology and diseases of a special part of the connective tissues: basement membranes (BM). BMs are located closest to most cell types in the body and, as their name suggests, form the base of the biological structure in the body.

Pretty fitting research concentration for an almost architect.

Using his BM expertise, Dr. Tryggvason and his team at Karolinska Institutet in Sweden (where he also holds an appointment) recently discovered a method of generating human embryonic stem (hES) cells without destroying any human embryos. Their findings were published recently in the journal, *Nature Communications*.



Prof. Karl Tryggvason is the Tanoto Foundation Professor in Diabetes Research and a Professor in the Cardiovascular & Metabolic Diseases Program at Duke-NUS

The two main hurdles for hES cell applications have been ethical and technical. The ethical concern is that it is generally believed that one cannot generate hES cell lines without destroying human life, which is why it is so difficult to get approval for the generation of hES cell lines in the United States. Using a standard IVF procedure, Dr. Tryggvason and his team demonstrated that it is indeed possible to clonally derive new hES lines without destroying an embryo. The technical issue was that until now, there hasn't been a chemically defined, xeno-free method for deriving and expanding hES cells. The researchers solved this by using the human xeno-free laminin substrate (LN-521) and adhesion molecule found to be associated with pluripotent stem cells in the early human embryo. Dr. Tryggvason's team produced this protein in the laboratory and isolated it for culturing the hES cells. "It is my hope that the results of this study will help soften up negative attitudes toward the establishment and use of hES cells for the development of cell therapy in regenerative medicine," said Dr. Tryggvason.

A central part of the discoveries has to do with use of laminins -- a family of base proteins. Early in his career, the first laminin protein was isolated at the National Institute of Health in the United States, where Dr. Tryggvason was a postdoc. Realizing later that there are at least 16 in the body, he questioned why there were so many. He presumed they were important or phenotypically specific to the specific cell types and organs they supported. He was right.

Dr. Tryggvason has a large body of data showing that specific laminins support cellular phenotypes. Using this knowledge, he created in vitro environments that mimic those in vivo and it helped to develop better protocols for cell differentiation and phenotype stability, especially in the case of the hES cell generation.

"Our findings enable the robust expansion of hES cells and allow us to envision the establishment of a hES cell bank that could represent most tissue antigen classes is possible. A stem cell bank could mean that in the future, these cells that are representative of different tissue antigens, etc., could be stored for use," Dr. Tryggvason said. "Imagine the limitless possibilities of their use in regenerative medicine." The study was supported by the National Research Foundation, under its Singapore Translational Investigator (STaR) Award and was administered by the Singapore Ministry of Health National Medical Research Council (NMRC), and by Swedish grants.

This article first appeared on Duke Today.

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Teaching to Learn

Third-year student Petty Chen shares why she initiated a peer tutoring group to help juniors who were struggling to keep up with the rigorous Duke-NUS curriculum.

Medical school is tough. In the midst of our first year, my classmates and I felt inadequate and overwhelmed, even disconnected from what we started out to do. During the *Normal Body* course especially, many of us forgot that we were there to learn about medicine and apply the knowledge to a real patient as it was a tough module. How come things that seemed easy to our professors were so difficult to understand, let alone remember? Some of us had difficulty adjusting to the fast-paced introduction of our medical careers and breakdowns, anxiety, and burnout seemed like a routine that never stopped.

Taking the initiative: Petty Chen, MS3

Back then, my notes were full of questions I was afraid to ask in class because I did not want to appear dumb. After a year of clinical rotations, I realized the key to learning efficiently was to learn bit by bit. Brute memorization will only get you 30 per cent of the knowledge required, but understanding how everything works and its importance will help with the rest. Memorization was inevitable as it helped form a skeleton to build our knowledge on. My fellow tutors and I wanted to reinforce concepts that were essential and reduce the number of items that got lost in translation. We wanted an avenue where it was okay to make mistakes and ask questions. We should never forget that we are students and we are here to learn.

With this mindset, I decided to start a peer tutoring group to ease the transition and enhance our juniors' academic experience with less anxiety, and more learning. My own experiences of adjusting to different education systems having lived in Taiwan and the US helped me realized that Asians tend to learn everything and were discouraged from asking questions beyond the curriculum. Yet in the US, I was taught that the sky is the limit. Elements from these contrasting styles should be combined instead to maximize their individual merits. This is exactly what I aimed to achieve in the peer-tutoring program - to learn in a structured and efficient manner while maintaining the innate curiosity we have as students.

It was not easy when we first started because in our third year, we concentrated on research. The only way to remain proficient was to use the knowledge and sometimes, the tutors did not feel like they knew enough to teach. I had to give a few motivational talks to convince them and explain that it was a good way for us to review for the United States Medical Licensing Examination (USMLE). No one is good at teaching when they first start out but they get better with practice. My class is filled with talented individuals and that made me determined to recruit them. Ultimately, my peers were altruistic. Many came into this profession to help others. Before we start helping patients, we could at least start by helping our juniors.

We assessed their needs by sending them surveys before the program started. I worked closely with the MS1 class president, Brian Chan, and we started a peer-tutoring Facebook group. Through this platform we contacted our juniors, made announcements, and answered questions. The Facebook group enabled tutors and juniors to interact. Although they were allowed to ask any question, we had guidelines on the kind of questions that were appropriate to prevent them from asking questions that can be googled easily. We also encouraged them to answer their own questions and express their opinions, which enhanced their understanding of the concepts.

Besides the Facebook group, we also conducted physical teaching sessions. Most sessions were based on requests we received as we did not want to be pushy or provide too much information. The Objective Structured Clinical Examination (OSCE) during the *Normal Body* module is usually a big stressor and we felt we could relieve some anxiety by having a mock session, pointing out some knowledge gaps they had and giving advice for review. We sought to give them bite-sized information to cope with the scope they had to cover and tried to limit each session to two hours to get the maximum amount of retention.

For the MS1 tutoring program, there were six of us. Since I oversee the program, I would get requests from the students while Andrew created the lesson outlines. We distributed the work equally and got everyone to contribute resources. They gave meticulous feedback, provided teaching materials and gave me ideas to improve the program. Everyone contributed in different ways.

MS3 tutors (L-R): Aponso, Choo Min, Olivia Tan, Anu Pandey, Petty Chen and Andrew Chou

Our own hectic schedules made it hard for us tutors to meet, so we communicated mainly by text messages and emails to discuss who could attend the teaching sessions. There were hiccups along the way, but they were resolved immediately. Additional teaching materials were also distributed online via the Facebook group. For instance, whenever I came across good YouTube videos on certain topics, I would post them. Junjie shared his old notes for the MS1s to review while Andrew read through a long discussion among the students on respiratory physiology and summarized the correct answer. We wanted to guide them without feeding them information.

Our latest session was an upper and lower limb crash course. To make the session interactive, we devoted more time to topics they found challenging. Clinical correlation was the best way

Pillars of support, MS3 tutors Olivia Tan and Aponso explaining concepts to their MS1 junior

to engage students when it came to memorizing the anatomy. We shared what we thought was important, based on our own experiences. I think students tend to respond better when they know they can apply material towards a bigger goal rather than just on a test. We also focused on study strategies and resources that were helpful for them.

The students were grateful and appreciative that the program helped them and some even bowed to me! Some of my fellow tutors also shared that they wished they could have done more to help. More often than not, we also provided emotional support and encouragement for our juniors.

Faculty support

The faculty was supportive and encouraging of this initiative. Prof. Pierce Chow gave us the green light on topics we could cover for the mock OSCE while Dean Mara McAdams showed up at the mock OSCE session to praise my peers. This program was meant to supplement our existing curriculum and they gave us the approval we needed to initiate it. Dean Mara and I discussed many ideas that I incorporated into the program. She is a student advocate and tries very hard to make learning easier and interesting for students.

Prof. Pierce Chow and Dr. Mara McAdams, Assistant Dean (Student Life)

Mary Ng from Student Affairs and the MERE team also supported us by providing us the facilities for our tutoring sessions. I think the biggest strengths we have at Duke-NUS are the flexibility and amenability that meet the needs of our students.

Goal and vision for the peer tutoring program

Sustainability and accountability are important. The program should not stop when I leave and the spirit of teaching should be inculcated in the student body. My goal is to see a third- year student take over my current role next year while I focus on developing the second-year peer-tutoring program. Many of my peers are very interested in teaching second-year students as well and I would like to recruit more senior students who are part of Prof. Chow's gross anatomy lab teaching assistants to join this initiative.

> **"To me, teaching is rewarding and an inherent responsibility. It is my duty to teach what I know. This mindset cannot be inculcated overnight, but we have to start somewhere.**

Looking back, I was surprised by what I learned from the program. Teaching is a lot of work. Coordinating a mock OSCE was tough and I cannot imagine what Prof. Chow has to do to conduct three! I have grown to appreciate how much time each professor puts in to help us learn. Through this process, I also identified my own inadequacies and insecurities, and learned to embrace them. I am never going to know

everything but I can utilize my strengths. Unfortunately, I am not so curious anymore. I used to ask questions but I realized I have gotten so busy and used to doing things a certain way that I stopped asking questions!

> **Never stop asking questions. We only learn because we want to know more.**

Petty Chen is a third-year MD student at Duke-NUS.

Watch the students share their thoughts on the peer tutoring program:

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Duke-NUS Challenge Returns



The Duke-NUS Challenge is an annual event to raise funds for worthy causes in medical research and education. It is an occasion where staff, faculty, students and friends come together to have fun while contributing to medicine and improving lives.

This year, participants and contributors can look forward to a range of causes to support, from pediatric, geriatric or autism research to supporting overseas medical missions by Duke-NUS students.

For more information, go to: www.duke-nus.sg/2014challenge or contact the Development Team at development@duke-nus.edu.sg or 65162585.

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Fulfilling Dreams, Building the Future of Medicine

Since 2007, the generosity of our donors has enabled our medical students to pursue their dream of becoming clinicians and clinician scientists to serve the medical needs of the community. Driven by their passion, our students – all armed with at least an undergraduate degree – have deferred their careers in various fields to take up medicine. However, medical school, like other fields of study, comes with a heavy financial responsibility. Our students share how scholarships and study awards have motivated and encouraged them to dedicate their time fully to focus on their training without being burdened by their financial obligations.

Being able to take up an MD/PhD means a lot more to me than just the prestige of attending a top-notch university. It means having the privilege to touch lives through clinical care, innovate, and push forth the frontiers of medicine as a future investigator. The Ngee Ann Kongsi Scholarship has opened the door and gave me the courage to pursue this path which few have traveled. Thank you so much for your generosity and this life-changing opportunity.

An Jingzhi
Class of 2015

I am delighted to be a Duke-NUS Shaw Foundation Scholar. Their generosity has helped not only me but many other students in pursuing our dreams. As an international student here, I find Singaporeans, especially the ones in my class, very welcoming. I am happy to make Singapore my new home, and I hope to contribute my skills to society. Thank you very much for your support.

Chen-Yi Liu
Class of 2017

I would like to extend my sincerest gratitude to the Shaw Foundation for providing the Duke-NUS Shaw Foundation Scholarship. I was both honored and humbled when I was informed of becoming a Duke-NUS Shaw Foundation Scholar.

The continual generosity of the Shaw Foundation has served as a reminder that with success, we should readily give back to society. I have always aspired to be a clinician who not only treats patients, but strives to improve the standard of healthcare in Singapore. As an MD/PhD student, this scholarship has served as an encouragement and a reminder in fulfilling that desire.

Mohamad Fadhli bin Masri
Class of 2016

To me, being a doctor is a very tangible experience, where there will be difficult moments but also times where we will forever cherish and remember. I hope to be an encouragement to those around me and help to meet their needs. Although the road ahead is filled with long hours and hard work, I am grateful to the Goh Foundation for the opportunity to improve patients' lives. The frailty of life will keep me motivated to serve my patients each day!

Carmen Lim
Class of 2016

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DNMA Elects Committee at Inaugural Annual General Meeting

On November 15, 2013, Duke-NUS Medical Alumni (DNMA) saw more members assuming leadership roles and new blood being injected into the new Committee at the inaugural Annual General Meeting (AGM) and Elections, which were convened at Duke-NUS' premises.

Since DNMA's inception in April last year, the society has been committed to and engaged in activities such as the first alumni reunion and community service project. To enable DNMA to achieve its objectives, nominations were called to fill various key leadership positions, encouraging more alumni to step forward to represent and serve the needs of the alumni community.

The event witnessed incumbent Dr. Chia Ghim Song garnering unanimous member votes to be re-elected as President of DNMA's new Committee. Nominations for the remaining 12 positions were successfully voted through, with good representation from the 2011, 2012 and 2013 graduates.

Congratulations to the following new DNMA Committee:

1. President - Dr. Chia Ghim Song
2. Vice President - Dr. Padmastuti Akella
3. Treasurer - Dr. Lim Jing Wei
4. Assistant Treasurer - Dr. Syeda Kashfi Qadri
5. Secretary - Dr. Kaavya Narasimhalu
6. Assistant Secretary - Dr. Karen Nadua
7. Committee Member - Dr. Bianca Chan
8. Committee Member - Dr. Dixon Grant
9. Committee Member - Dr. Cecilia Kwok
10. Committee Member - Dr. Charmain Heah
11. Committee Member - Dr. Andrew Green
12. Honorary Auditor - Dr. Lim Kheng Choon
13. Honorary Auditor - Dr. Wong Sook Yee

In accordance with the Constitution, the reins of the DNMA will now be handed over to the newly elected office-bearers. Besides casting their votes for the candidates, members also adopted the DNMA Annual and Financial Report (for the period April 15, 2013 to September 30, 2013) at the AGM.

The newly-elected DNMA Committee (L-R): Drs. Bianca Chan, Chia Ghim Song, Wong Sook Yee, Padmastuti Akella, Karen Nadua, Lim Kheng Choon, Syeda Kashfi Qadri, Lim Jing Wei, Andrew Green and Cecilia Kwok

Committee members not pictured: Drs. Kaavya Narasimhalu, Dixon Grant and Charmain Heah

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Discovering Dengue's Stealth Mechanism

Scientists at Duke-NUS have made a major breakthrough in the search for a dengue vaccine. Associate Professor Ooi Eng Eong and his team have uncovered the mechanism that dengue uses to exploit antibodies to its advantage.

The dengue virus infects almost 400 million people annually and is a major health concern in Singapore. The development of dengue vaccines are complicated by the presence of four different dengue strains since these vaccines can only target a single strain at a time. While antibodies produced following an infection or vaccination usually prevents a person from being re-infected, this doesn't happen with dengue. Antibodies produced after infection with any of the four types of dengue virus can instead enhance infection with the remaining three viruses. How the dengue virus exploits our antibodies to enhance infection, without triggering the innate immune responses that are normally activated by the receptor that antibodies engage, is not known.

Assoc. Prof. Ooi Eng Eong

Dr. Ooi's research however, has discovered that dengue evades the immune response activated by receptors for antibody by binding to the inhibitory receptor LILRB1 (leukocyte immunoglobulin-like receptor-B1) on our white blood cells. Binding to LILRB1 dampens the immune response. Hence, by activating this inhibitory receptor that is naturally present in humans, the dengue virus enters white blood cells using the antibodies that were developed from a previous infection, but without triggering the immune response that would otherwise suppress its replication.

These findings suggest that strategies that block the dengue virus from activating this inhibitory receptor would render a more efficient immune clearance of the virus. If vaccines could be engineered to produce antibodies that block the dengue virus from binding to, and hence, activating LILRB1, the risk of antibody-enhanced infection following vaccination would be reduced. This would alleviate a major safety concern in dengue vaccination.

Dr. Ooi, who is also Deputy Director of the Emerging Infectious Disease Program at Duke-NUS, and his team are currently studying exactly which part of the dengue virus binds to which part of LILRB1. The knowledge can be used to develop a more targeted vaccine therapy. The study was published on January 2014 in the journal *Proceedings of the National Academy of Sciences USA*. This research is supported by the Singapore National Research Foundation under its Clinician Scientist Award (CSA) and is administered by the Singapore Ministry of Health's National Medical Research Council.

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Boosting Singapore's Translational Medicine Network

Last December, Duke-NUS Graduate Medical School and SingHealth signed a memorandum of understanding with the Eureka Institute for Translational Medicine. The Eureka Institute is a global research network that aims to bridge the gap between patients and treatment, specifically by providing solutions and inculcating the creativity needed to inspire research that will generate solutions to disease.

Already united in the Academic Medicine partnership, Duke-NUS and SingHealth's affiliation with the Eureka Institute will enable both to tap on the knowledge, resources and technologies from across the network which includes medical institutes from Europe and North America.

Professor Salvatore Albani, President of the Eureka Institute for Translational Medicine explained that the move strengthens the cluster's commitment to translational research. "SingHealth and Duke-NUS will add to the network with their strengths in biomedical research, and as the network's Asia-Pacific hub, with their insights into diseases common in Asia."

Profs. Salvatore Albani and Patrick Casey sign the MOU

Clinician-scientists and researchers within the network will be offered places on the Eureka Institute's translational medicine certification program which trains professionals with skills necessary to achieve meaningful clinical breakthroughs.

The Eureka Institute for Translational Medicine also has plans to develop a Master's program in translational medicine. "Eureka's emphasis on developing skills to encourage critical thinking and problem solving as key elements in health research resonates with the approaches of Duke-NUS," said Professor Patrick Casey, Duke-NUS' Senior Vice Dean of Research.

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Using Technology to Stave Off Dementia

A pilot study was conducted to test the efficacy of a brain-computer interface (BCI)-based program as an alternative treatment for patients with dementia. Participants of the technology-based trial, led by Clinical Co- Principal Investigator, Associate Professor Lee Tih-Shih of Duke-NUS, demonstrated promising cognitive improvement.

In 2003, the prevalence of dementia in a Singapore Chinese elderly cohort was 5.2 per cent for those above 60 years, six per cent for those above 65 years and 13.9% for those above 75 years. Unfortunately, medication approved to help with age-related cognitive decline (anticholinesterases and memantine) have limited efficacy and cannot halt disease progression. Costs for such medications are minimally S$300 a month and may have side effects.

As a result, BCI was considered to help train memory and attention. In the intervention, healthy elderly between the ages of 60 to 70 years used their concentration to engage in a memory-

A participant in the Brain Computer Interface (BCI) memory and attention training game

pairing game. The training sessions were held thrice weekly for eight weeks after which many participants showed improvements in immediate memory, visuospatial skills, attention, delayed memory, global cognitive functioning pre- and post-training.

Dr. Lee, who is also a Senior Consultant Neuropsychiatrist at Singapore General Hospital, commented on how the preliminary outcomes could be implemented for future therapies, “The next step will be to target those with mild cognitive impairment. If they show a positive response, BCI might potentially be a cost effective and sustainable way to treat cognitive impairment in the elderly.” The EEG based-BCI for cognitive enhancement was first used in an intervention as a treatment for Attention-Deficit Hyperactivity Disorder (ADHD) last year. Following the successful implementation, Dr. Lee sought to test the technology on a different patient set. A larger trial set to be conducted this year will include elderly with mild cognitive impairment and aims to target the enhancement of delayed memory.

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Duke-NUS Professor Honored as AAAS Fellow

Prof. David Virshup

The American Association for the Advancement of Science (AAAS) has elected 388 new members for its new class of fellows, which include 13 members of the Duke faculty. The appointment is bestowed on AAAS members by their peers to honor their scientifically or socially distinguished efforts to advance science or its applications.

Among the Duke faculty appointed is Duke-NUS Professor David Virshup, Director of the Cancer and Stem Cell Biology Program at Duke-NUS Graduate Medical School. Dr. Virshup, who also has a joint appointment as a pediatric oncologist at the Duke University Medical Center, was recognized for his distinguished contributions in the field of signal transduction, particularly in the areas of protein phosphorylation and Wnt signaling.

He joins three Duke-NUS colleagues (Professors Mariano Garcia-Blanco, Patrick Casey and Soman Abraham) who were elected in 2011 and 2012.

“I am humbled to follow in the footsteps of colleagues,” said Dr. Virshup. “It is an honor, and it's particularly exciting to share it with my mentor Vann Bennett, as well as with my long-time colleague Mike Kastan.” Professors Bennett and Kastan are both Duke University School of Medicine faculty who were also elected Fellows.

The AAAS Fellows of 2013 were formally announced in the November 29 edition of journal *Science* in the AAAS News & Notes section.

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New Study Pays Participants to Be Active

Physical activity is beneficial in many ways, whether it be the prevention of obesity, delaying the onset of Alzheimer's or a host of other chronic illnesses such as hypertension and diabetes. However, a recent National Health Survey showed that 40 per cent of Singaporeans do not participate enough in physical activities. Full time employees were found to be the most inactive group of all, performing "well-below" the Health Promotion Board's (HPB) Physical Activity Guidelines for Professionals.

In order to come up with solutions, a new study conducted by Duke-NUS and HPB aims to determine if cash or charity incentives could motivate full time employees to engage in increased physical activity. TRIPPA (Trial of Incentives to Promote Physical Activity) uses technology, economic incentives, and recommended activity goals to help people improve their health.

Full time employees were recruited and divided into four research groups; Control, Fitbit Only, Cash Incentive and Charity Incentive. All participants (except those in the Control group) used a wireless pedometer called Fitbit which measures the number of steps they take daily.

Group	Physical Activity Goals	Incentives (SGD$)
Control	None	$4 weekly for 6 months
Fitbit Only	None	$4 weekly for 6 months
Cash Incentive	Less than 50,000 steps weekly 50,000 – 69,999 steps weekly At least 70,000 steps weekly	$0 $15 $30
Charity Incentive	Same as Cash Incentive	Same as Cash Incentive except the amount is donated to a charity of the participant's choice

Prof. Eric Finkelstein

The study is conducted over six months with those in the Cash and Charity Incentive groups receiving monetary incentives that increase once they reach a certain activity goal (number of steps) performed and while those in the Control and Fitbit Only groups receive a flat SGD4 a week and have no activity goals. The amount is low so as not to incentivize them to change their behaviors but to still keep them engaged.

Professor Eric Finkelstein, from the Health Services and Systems Research Program at Duke-NUS, is optimistic about the outcomes of the study. "We hope that the study will be extended beyond research and be deployed eventually in the workplace of employers once they see that it is worth it. The amounts are also set to be high enough to encourage certain behaviors but not so high that employers would be unwilling to invest in it."

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A Story of Collaboration

Collaboration between Duke-NUS and the Singapore Eye Research Institute (SERI) has resulted in a comprehensive and intuitive database system able to manage a research project from pre- to post-

award. The integrated system can track research and intellectual property output such as publications, patents and licenses. The idea for a new system was proposed several years ago by Lydia Tan, Director of Sponsored Research at Duke-NUS, who recognized the need for a system to better manage the long and complicated research project journey. At the time, there was an absence of automation for grant management and existing “off-the-shelf” systems lacked the capability to properly manage research projects according to local needs.

What was needed was a system customized to the needs of the Singapore context, such as allowing key performance indicators (KPIs) to be exported, principal investigators to monitor the movements of funds, and the review of the number of publications. In 2012, the Duke-NUS Grant Management System was licensed to PatSnap Pte Ltd, an IT company which owned a Global Patent Search and Analysis Platform.

Discovering that the clinical capabilities SERI’s database management system fit with Duke-NUS’ strengths in fundamental research, Lydia and SERI’s Sharmila Kannan, Director of Administration, Research Affairs & Support Services, then worked together to develop an integrated system for both institutions. Last year, PatSnap licensed over the SERI’s Grant Management System, ReDOz, in collaboration with Duke-NUS. Today, the new integrated grant management system of Duke-NUS and SERI allows for comprehensive project management of both basic and clinical sciences research projects across the pipeline.

The advantage of this new integrated system is its ability to share data while its curriculum vitae module connects researchers with one another. This enables basic science researchers to link with clinicians when they are conceptualizing a study that requires clinical studies.

The collaboration reflects the shared ideals of innovation and looks to benefit and bolster the Duke-NUS and SingHealth research ecosystem.

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GRANTS AWARDED

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No.	PI	Dept	Project Title (Please click titles for details)	Grant Call	Duration (Months)
1.	Koh Woon Puay	OCS	Metabolite Signatures And Risk Of Type 2 Diabetes In Singapore Adults	NMRC CS-IRG Nov 2012 Call	36
2.	Koji Itahana	CSCB	Novel p53-Glut9 pathway in antioxidant and immune response	MOE Feb 2013 Call	36
3.	Bindu Sukumaran	EID	Negative regulation of NOD2 mediated innate immune response	MOE Feb 2013 Call	36
4.	Marc Fivaz	NBD	Mitochondrial dynamics in neural circuits implicated in schizophrenia	MOE Feb 2013 Call	36
5.	Marcel Bilger	HSSR	A Randomized Controlled Trial To Improve Diabetes Outcomes through Financial Incentives	NIHA 2013 Call	24
6.	Eric Finkelstein	HSSR	A Randomized Controlled Trial to Motivate and Sustain Physical Activity using Financial Incentives	NIHA 2013 Call	24
7.	Wang Linfa	EID	Establishment of serological diagnostic capability for highly virulent zoonotic viral infections in Singapore	CDPHRG Nov 2013	36
8.	October Sessions	EID	Viral determinants of EV71 neuroinvasive potential	SIDI Catalyst Grant 2013	12

9.	Eric Andrew Finkelstein	LCPC	Knowledge and preferences for treatment of end stage renal disease among elderly patients and their family caregivers	SMF 3rd Grant Call	24
10.	Wang Linfa	EID	Multiplex Oligonucleotide-linked Signal Amplification Technology (MOST) and Its Application to the Investigation of Encephalitis of Unknown Etiology	NRF POC 9th Grant Call	12
11.	Wang Linfa	EID	Learning From Bats: From Genomics To Controlling Viral Infection And Combating Cancer	NRF CRP 10th Call 2012	60
Total Amount of Funding Received: S$ 15,656,390.70					

Synopsis

1. Metabolite Signatures And Risk Of Type 2 Diabetes In Singapore Adults

Koh Woon Puay, Office of Clinical Sciences

The etiology of type 2 diabetes (T2D) is multifactorial and involves a complex interplay among genetic, metabolism and environmental factors. The recent advances in metabolite profiling techniques (metabolomics) have offered a unique approach for measuring a full profile of small-molecular metabolites, providing a comprehensive picture of an individual's metabolic status. Although some studies suggest that blood amino acid and lipid profiling predicts T2D, these existing studies are limited in scope and did not adequately consider the role of diet, lifestyle and genetic factors. Moreover, studies have been mainly conducted in western populations, and no prospective data on circulating metabolite signatures and risk of T2D are available in Asian population. We will therefore evaluate the associations of circulating metabolite signatures with risk of incident T2D in a large nested case-control study of 800 incident cases and 800 matched controls within the Singapore Chinese Health Study. The aims of this project are: 1) To examine individual metabolites and metabolomic patterns associated with T2D in Singapore Chinese through a combination of non-targeted and candidate approaches; 2) To explore whether the clinical standard and novel biomarkers for T2D mediate the relationships between metabolomic signatures and T2D risk; 3) To identify genetic loci associated with individual metabolites and metabolomic patterns implicated in T2D, and estimate the causal effects of the metabolites on T2D using SNPs that are robustly associated with the metabolites as instrumental variables; 4) To examine whether the T2D-metabotypes mediate the relationships between specific dietary and lifestyle factors and T2D risk. This project utilizes data from a well-established cohort with high-throughput assessment of novel metabolite signatures to study an important public health problem. The results can directly advance our understanding of the pathophysiology of T2D, and the development of measures to reduce the burden of T2D in Asia.

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2. The Role Of Sphingolipids In the Pancreatic Beta-Cell

Koji Itahana, Cancer & Stem Cell Biology

Only humans and higher primates have high uric acid in blood, and this has been postulated to be a cause of enhanced human longevity. How uric acid keeps us young is not well understood. Despite the public's negative image of uric acid as a cause of gout and kidney stones, Dr. Itahana's laboratory found that cells can use uric acid as an antioxidant source via a recently identified uric acid transporter that is regulating by a tumor suppressor. Their findings provide a potential explanation about why we maintain high uric acid blood levels. Uric acid has been also reported to act as a danger signal for immune system, and Dr. Itahana awarded MOE Tier 2 grant for studying the role of this transporter in tumor suppression and immune system. Understanding the regulation of this uric acid transporter may provide a stepping stone for developing novel therapeutic approaches against cancer as well as several

immune disorders.

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3. Negative regulation of NOD2 mediated innate immune response

Bindu Sukumaran, Emerging Infectious Diseases

Inflammation is critical to control infection; however, excessive inflammation is detrimental to the host. Uncontrolled innate immune response leads to exacerbated inflammation and leads to several pathophysiological conditions such as sepsis. Therefore, the innate immune system must be tightly regulated by negative feedback mechanisms to keep the inflammation under control. The innate immune pattern recognition receptor NOD2 is a well-defined model for studying negative regulation of innate immunity and immune tolerance to bacteria. Uncontrolled NOD2 signalling leads to many inflammatory disorders, including Crohn's disease. Chronic NOD2 activation induces tolerance to additional NOD2 stimulation by MDP (termed MDP tolerance), indicating the existence of specific feedback regulatory mechanisms. Our proposal will characterize a novel mechanism by which a newly discovered E3 ubiquitin ligase negatively regulates NOD2-mediated innate immune response and maintain immune homeostasis. This knowledge will lead to the identification of novel targets and therapeutic strategies for treating infection and inflammation.

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4. Mitochondrial dynamics in neural circuits implicated in schizophrenia

Marc Fivaz, Neuroscience & Behavioral Disorders

DISC1 (Disrupted-in-Schizophrenia-1) has been firmly established as one of the most probable susceptibility gene for psychiatric illness, but the impact of this gene on synaptic circuits underlying cognitive (dys)function remains poorly understood. Work from our laboratory has recently shown that DISC1 regulates mitochondrial dynamics and synaptic transmission in excitatory neurons of the central nervous system. Based on these results, we hypothesize that DISC1 impacts neurotransmission in the brain by regulating mitochondrial homeostasis in presynaptic terminals. The objective of this proposal is to determine the impact of DISC1 and mitochondrial (dys)function on neural circuits implicated in memory formation, pattern separation and neuropsychiatric disorders. A multidisciplinary approach, combining quantitative live-cell imaging, electrophysiology and a DISC1 knockout mouse model, will be employed to attain our central objectives.

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5. A Randomized Controlled Trial To Improve Diabetes Outcomes through Financial Incentives

Marcel Bilger, Health Services & Systems Research

We propose to test three theory-based intervention strategies aimed at improving diabetes outcomes amongst a population of uncontrolled patients. The first strategy does not involve incentives but includes a Diabetes Educational Program (DEP) to help the patient manage their condition. Included in the program are daily text messages to encourage participants to take their medications as prescribed and prompt good dietary and exercise practices. Subsequent strategies incorporate incentives as core components. The incentives are tied either to processes aimed at improving blood sugar levels (glucose testing, physical activity and medication adherence) or directly to the intermediary outcome (blood glucose in the acceptable range). While process incentives are likely to provide more motivation for treatment adherence, as these goals may be comparably easier to meet, these incentives only reward intermediary outcomes and it might be more effective to reward successfully achieving a health outcome directly.

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6. A Randomized Controlled Trial to Motivate and Sustain Physical Activity using Financial Incentives

Eric Finkelstein, Health Services & Systems Research

There is overwhelming evidence that many age-related diseases can be prevented through sustained physical activity (PA). However current data reveal that fewer than half (42%) of older Singaporeans engage in regular leisure-time PA. In efforts to identify an effective long-term strategy to increase activity among older adults, this study aims to test the effectiveness of two types of financial incentives – cash and taxi rental credits – in increasing and sustaining physical activity among older taxi drivers aged 50 to 75 through a 7-month Randomized Controlled Trial (RCT). We hypothesize that participants receiving incentives in the form of rental credits will show greater activity (as well as greater improvements in secondary health outcomes) compared to those receiving cash of equal value. Additionally, we will also ascertain the effect of incentive type on work by assessing if drivers receiving rental credits are more likely to take time off work i.e. days or hours off in the week following incentive receipt relative to those receiving cash.

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7. Establishment of serological diagnostic capability for highly virulent zoonotic viral infections in Singapore

Wang Linfa, Emerging Infectious Diseases

Zoonoses caused by previously unknown aetiological agents represent a significant proportion of the global challenge posed by emerging infectious diseases (EIDs). Due to the large number of international travelers passing through, Singapore is at risk from these emerging infections. Ongoing surveillance programs include a Ministry of Health sponsored program, SIDPIC and a multi-centred research network, PROTECT. Although nucleic acid based detection systems are an important tool in EID investigation, they are limited by the short viremic period for many of these infections. Hence we propose to develop serological methods, which would help in the diagnosis and surveillance for viral emerging infections.

In this project, we will use two complementary approaches to establish the serological diagnostic capabilities in Singapore. The first employs the multiplex and high sensitivity nature of the Luminex technology. Recombinant antigens from key pathogens will be coupled to different fluorescent beads for detection of antibodies against multiple viruses in a single assay. The second platform is the surrogate virus neutralization test (VNT) based on recombinant pseudoviruses. The target pathogens for this project are all at biosafety levels 4 or 4. Hence traditional VNT requiring live viruses will be difficult, and impossible for most of them, to be carried out in Singapore. So the pseudovirus VNT approach will be an extremely important capability to have in Singapore. The viruses selected for the current project include some of the most deadly viruses present in our region.

The outcome of this project will have a significant impact on our national capability in the surveillance of known severe emerging viral infectious diseases. In addition, the technological platforms established in this study will also ensure a more rapid response to severe infections caused by novel viral pathogens in the future since the same principle of the technologies can be easily adapted to different and newly emergent viruses

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8. Viral determinants of EV71 neuroinvasive potential

October Sessions, Emerging Infectious Diseases

Enterovirus 71 (EV71) is responsible for a spectrum of clinical syndromes that range from hand foot and mouth disease (HFMD) to encephalitis, similar to other enteroviruses. CNS infections occur most frequently in children, which can lead to long-term sequelae or death. Currently, there is no vaccine or

antiviral treatment to ameliorate the course of EV-71 associated disease. Since 1997, the documented cases of EV71 in Asian countries have dramatically increased in both their regularity and severity. Moreover, a specific association between EV71 and brainstem encephalitis also emerged in these recent outbreaks. The viral determinants that may potentiate invasion of the CNS or even confer specificity on the site of infection is unknown. Additionally, the replication of the RNA genome of EV71 is, like many RNA viruses, error prone, leading to mutations that may be acquired over the course of a single infection and allowing the emergence of a virus subpopulation with increased neurotropism. In this proposal we will use a we will utilize deep sequencing, a recently developed mouse model of infection and two non-mouse adapted strains of EV71, one of which displays a neuroinvasive phenotype and the other one that does not to assess the neuroinvasive potential of specific genomic loci. The changes in the intra-host genetic diversity of these viruses will be measured by deep sequencing prior to oral challenge, at early (3 days) and late (12 days) post-challenge time points. For all time points post oral challenge, we will measure viral quasispecies (when present) in the intestine, limb muscles, blood and CNS. In the second part of this proposal, we will also conduct these experiments with two clinical isolates from Vietnam that are representative of the pre-epidemic strains and a strain from the ongoing epidemic that started in 2011.

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9. Knowledge and preferences for treatment of end stage renal disease among elderly patients and their family caregivers

Eric Andrew Finkelstein, Lien Centre for Palliative Care

Understanding patient's preferences regarding treatment for end-stage renal disease (ESRD) is important to guide treatment recommendations and policies. Currently, treatment choices for ESRD are likely to be distorted by a lack of knowledge among patients and their caregivers regarding outcomes and costs that result from a given choice. Therefore, this study proposes to:

1. Assess patient and caregiver knowledge about outcomes and costs of dialysis and conservative treatment (CT), and
2. Quantify the extent to which select features and outcomes of dialysis influence the decision to choose it over CT, and the change in uptake that would result from a given change in one of the attribute levels (or better information on that attribute).

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10. Multiplex Oligonucleotide-linked Signal Amplification Technology (MOST) and Its Application to the Investigation of Encephalitis of Unknown Etiology

Wang Linfa, Emerging Infectious Diseases

Inflammation of the brain, or encephalitis, is a common but life-threatening condition especially prevalent in children. Several hundred cases of encephalitis are reported in Singapore each year making encephalitis an important cause of childhood mortality. Even if these patients recover from their acute illness, many experience long-term medical problems, including seizures, movement disorders and cognitive deficits, despite conventional treatment. To improve treatment strategies and hence outcome of encephalitis, it is important to determine the underlying causes. Although infection is thought to be an important cause, the pathogen responsible for each of the cases is seldom identified. Currently, a diagnosis is not made in up to 70% of cases. Diagnostic testing for encephalitis is often incomplete or late resulting in lost opportunities for early identification of treatable causes and prevention of disability. For the last decade or so, most of the research activities have been focused on the development of new diagnostic/discovery methods based on molecular techniques such as multiplex PCR, microarray and next-generation sequencing. Unfortunately, the success rate has been unexpectedly low, probably due to the fact that genetic materials from aetiological pathogens are present at very low levels or absent by the time of disease onset. Serological testing is limited since the current tests are all based on one-test-for-one pathogen and it is prohibitively expensive and time-consuming to conduct routine serological tests against all pathogens which are known to have the potential to cause encephalitis.

At Duke-NUS, we have developed the Multiplex Oligonucleotide-linked Signal-Amplification Technology (MOST), a platform highly suited for the detection and quantification of different antibodies with great sensitivity and high multiplexing capability. Here, we propose to develop a MOST universal serological test for the investigation of encephalitis, especially for those cases where the underlying causes could not be diagnosed using existing conventional methods.

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11. Learning From Bats: From Genomics To Controlling Viral Infection And Combating Cancer

Wang Linfa, Emerging Infectious Diseases

Bats are one of the most abundant, diverse and geographically dispersed mammals on earth, representing almost a quarter of all the known living mammals in the world. They display several unique but poorly characterized biological features with great significance to human health, such as long lifespan, lower rate of developing cancer and less diseases during infection of highly lethal viruses such as SARS and Nipah viruses, both of them caused significant economic and human impact in Singapore and the region. If we can uncover the cellular and molecular mechanisms for these unique bat biological features, we will be able to learn from bats in better controlling infectious diseases in humans and livestock animals, and prolong life through better prevention of aging and cancer. However, until now there has been little research conducted into these unique bat biological features due to the lack of research tools and genetic information directly relevant to bat research. This proposed program aims to bridge this knowledge gap, and exploit bat biology to find solutions for human health problems. This will be achieved in four integrated projects using cutting-edge technologies covering genomics, bioinformatics, infection diseases, immunology, cancer biology and structural biology. The bat-specific reagents generated through this study will have commercial potential, to serve the international research community that studies bats. This project will promote and facilitate the development of cutting-edge biomedical research infrastructure in Singapore, provide great training opportunities for students, research associates and junior scientists. The proposed study is internationally highly competitive and will lift the level of research activities in Singapore covering many different scientific disciplines.

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