A NEWSLETTER FOR THE RESEARCH COMMUNITY IN SINGAPORE

catalyst

ACCELERATING **RESEARCH**

JUL/AUG 2012
MICA (P) 243/03/2012

National Healthcare Group
Adding years of healthy life

EXCLUSIVE INTERVIEW **ASSOCIATE PROFESSOR LEO YEE SIN**

FROM THE EDITOR IN CHIEF

Dear Readers

I thank you for your continued support to our NHG research newsletter – Catalyst.

From this issue on, you will enjoy a richer scope and depth of contents with the recent formation of our first ever NHG Research Editorial Workgroup comprising of members from NHG institutions as well as our academic partner – Nanyang Technological University.

In this 2nd issue of Catalyst for 2012, we are honoured to have Associate Professor Leo Yee Sin, Head, Department of Infectious Diseases, Tan Tock Seng Hospital, and the recipient of the prestigious S$25 million Translational Clinical Research (TCR) award for "STOP Dengue" share her insights on collaborative research in the cluster and beyond.

This issue also features updates on the development of a vaccine by Inviragen for the Hand, Foot and Mouth Disease (HFMD) which remains prevalent amongst children in Singapore. We are also privileged to have Dr John Ovretveit from the Karolinska Institutet, Stockholm to share his thoughts on the importance of "Implementation Research" on healthcare. In addition, recipients of the National Medical Research Council (NMRC) Transition Award (TA) – Dr Jimmy Lee (Consultant, Institute of Mental Health (IMH)) shares on his journey as a Clinician Scientist in Psychiatry, and Dr Ng Oon Tek (Consultant, Tan Tock Seng Hospital (TTSH)) brings us through his journey in Infectious Disease.

I would also like to take this opportunity to update that NHG has successfully launched 2 major grants this year. Launched in February 2012, the Clinician Scientist Career Scheme (CSCS) was aimed to develop a sizeable pool of Clinician Scientists in the cluster. To further develop the clusters' research capabilities, NHG has also launched the NHG Thematic Grant on the 4th of July 2012. Each program is valued at S$1 million for over 3 years. We will continue to keep you updated on our awardees in future issues of Catalyst. Stay tuned!

I hope you will enjoy reading this issue of Catalyst. Nonetheless, we are always happy to hear from you should you have any suggestions for improvements.

'Till next time.

Yours Sincerely,
Farah

National Healthcare Group
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contents

YOUR NEWSLETTER, YOUR COMMENTS

Do you have... Research articles to share? Research topics that you want covered? Comments /Feedbacks on published contents of this newsletter? Comic strips / Cartoon Illustrations that is science / research-related that can bring smiles to your colleagues?

If you have answered "YES"to any of the above, we invite you to write in and share with us your throughts, feedback on published articles or cartoon clips (original materials, jpeg format please). And if your contribution is accepted for print, we will send you a token of appreciation with compliments from the Editorial Workgroup!

Do remember to add in your contact details, where applicable for our future communications with you.

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INVIRAGEN AIMS TO CONTINUE DEVELOPMENT OF INV21

An Inactivated Vaccine Candidate for the Prevention of Hand, Foot and Mouth Disease caused by Enterovirus 71

Dr Joseph Santangelo
Chief Operating Officer
Invragen, Inc.

Hand, Foot and Mouth Disease (HFMD) is caused by enteroviral pathogens such as enterovirus 71 (EV71). Although this is generally a self-limiting disease characterised by fever, mouth ulcers, and a rash, HFMD caused by EV71 can lead to viral meningo-encephalitis, myocarditis or poliomyelitis-like paralysis, and may be fatal.

EV71 and HFMD are endemic in Asia, causing significant morbidity, mortality and economic impact in recent years. INV21 is a purified, inactivated EV71, alum-formulated vaccine, developed for the prevention of HFMD caused by EV71. Invragen recently completed a Phase 1 clinical trial of INV21 in Singapore with Dr Paul Tambyah of the National University Hospital as the Principal Investigator.

Thirty-six healthy males and females aged 21 to 45 years were enrolled into a randomised, double-blind, placebo-controlled study at the Investigational Medicine Unit, National University Hospital, Singapore. Subjects were enrolled to either Low Dose [12 on INV21 (0.6 μg EV71/dose); 6 on placebo] or High Dose [12 on INV21 (3 μg EV71/dose); 6 on placebo] group. Subjects received two injections (Day 0, Day 28) intramuscularly, and were followed for safety and immunogenicity assessments through Day 56.

35/36 subjects completed the study through Day 56. Most common adverse events in INV21 and placebo subjects (cough: 5/36 subjects; rhinorrhea: 5/36 subjects; pyrexia: 4/36 subjects; influenza: 3/36 subjects) were mild and time-resolved. Minimal reactions were observed at the injection site, with similar profiles seen at both dose levels.

Mild (Grade 1) pain, tenderness and pruritis were reported in 1 subject in each treatment group. Grade 1 erythema and induration were reported in 1 subject in High Dose group. No clinically significant changes in chemistry, haematology and urinalysis parameters were observed in either group.

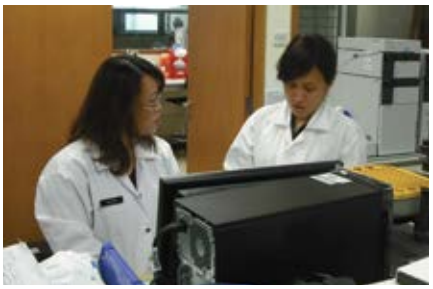
Highest EV71-neutralising antibody titres were detected 2 weeks post second dose (Day 42), with all subjects seroconverting (≥ 4-fold rise in titre compared to baseline) at this time point (Low Dose GMT = 323; High Dose GMT = 452). Long term assessments through Day 196 are now complete and the immune responses continue to be positive.

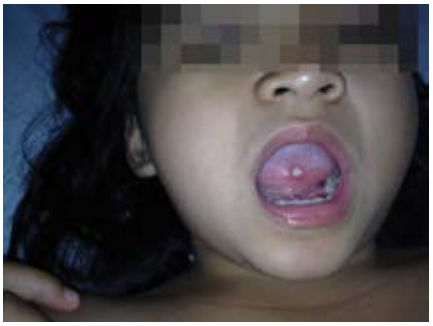
This "first-in-man" trial demonstrated that INV21 is a safe and immunogenic vaccine candidate for the prevention of HFMD caused by EV71. An appropriate team of clinical investigators is now being organised to conduct a Phase 2 clinical trial in Singapore. The planned Phase 2 clinical trials are needed to address the ongoing regional HFMD epidemic, and ultimately reduce mortality and morbidity due to EV71 infection. INV21 was developed in Singapore by local researchers and Invragen desires to continue this clinical program in Singapore.

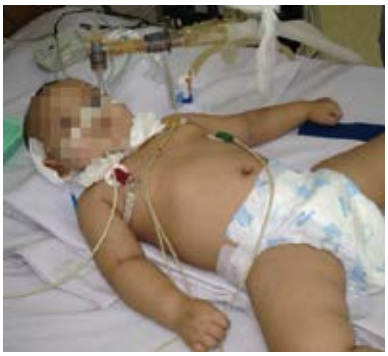
It is hoped that INV21 will be a successful product to meet an unmet clinical need not only in Singapore, but also more widely in Asia. Development of vaccine candidates like INV21 is part of the industry's efforts to address this growing problem of HFMD infections in Asia. Invragen is focused on developing vaccines to protect against infectious diseases worldwide.

Founded in 2005 with offices in Singapore, Colorado and Wisconsin, Invragen's investors include EDBI subsidiary Bio*One Capital Pte. Ltd. (Singapore), Phillip Private Equity (Singapore), Charter Life Sciences (Palo Alto, CA) and Venture Investors (Madison, WI).

See www.invragen.com for more details.







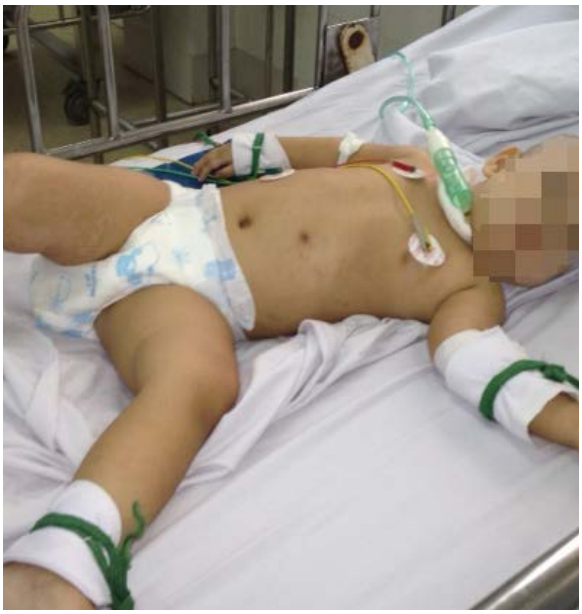


Photo courtesy of Oxford University Clinical Research Unit, Vietnam and used with permission.

IMPLEMENTATION RESEARCH

Why it is useful, and why it is an exciting new frontier for researchers

Dr John Ovretveit
Director of Research, Professor of Health Innovation Implementation and Evaluation
Medical Management Centre, The Karolinska Institutet, Stockholm
Email: jovret@aol.com

It took me an embarrassing length of time as a researcher to realise that obtaining evidence that a change is effective, is only a minor ingredient in achieving improvements in healthcare. Much more important are the actions taken to enable clinicians and managers to make the changes. Some of these actions are local, like those taken by an implementation project team. Some actions are by people at higher management levels of the health system and which create conditions and incentives to encourage the change, as well as reducing factors which hinder the change.

Implementation is how people put knowledge into practice to improve health or healthcare. Research into implementation seeks to understand what people do that is effective for changing clinicians' behaviour or health service organisations so as to adopt changes which has been proven elsewhere. Implementation research is a new and rapidly developing field, and is an exciting new research area with the significant potential to help make improvements more effective. Already the value of some of such research can be seen in the journal "Implementation Science", for example.

Many clinicians and researchers know about the changes which will reduce central-line blood stream infections – the CLABSI bundle.

In Michigan State, 102 Intensive Care Units (ICUs) took part in a breakthrough collaboration to reduce CLABSIs to zero.

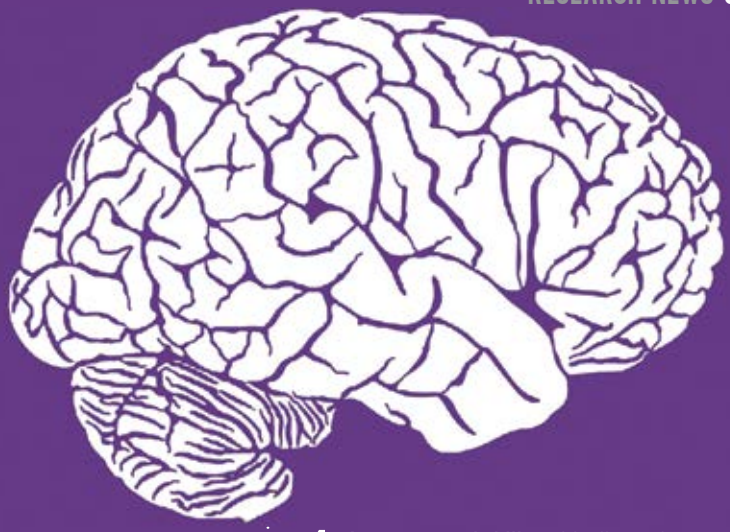
Implementation research was able to find out why some of the ICUs which implemented these changes, were much more successful than others.

In the successful ICUs, the changes were sustainable due to professional and effective project team management, on top of a culture and higher level leadership that was absent in the lower performance ICUs.

> Implementation research is not just about studying how one health service takes a proven treatment and spreads it to different units within the service.

It is also about finding out which changes need to be adapted to fit the service, and which part of the change can and cannot be adapted for the change to be effective. This involves using new types of research methods such as action evaluation methods. If I had to make my career choice again, I would have stated this field of research as the combination of practical relevance and scientific challenge is one which attracts me. At this time of constraints on finance and personnel and the imperative for change in healthcare, implementation research promises to be of great value and a fertile ground for scientific research.

IMH DEVELOPS POSITIVE MENTAL HEALTH INSTRUMENT



Ms Deborah Koh
Institute of Mental Health

Institute of Mental Health (IMH) has developed and validated an instrument to measure the positive mental health of Singapore residents. The Positive Mental Health (PMH) instrument is one of the first validated scales on mental health developed in Asia that is culturally and locally relevant to our population.

Traditionally, instruments to measure mental health and well-being are largely developed and often used within Western populations; this compromises their validity in other cultures. The multi-dimensional instrument covers all key and culturally appropriate domains of mental health, and can be used to compare levels of mental health across different age, gender and ethnic groups.

The PMH instrument was developed by IMH's Research Division in partnership with the Ministry of Health, Nanyang Technological University , National University of Singapore and RAND Health, a research division within RAND Corporation, an American non-profit research organisation. The PMH instrument was developed as part of the Singapore Mental Health Study.

"The PMH instrument can be used to collect data on individuals and various subgroups in the population which would be crucial when reviewing existing mental health policy and services. Such information may also contribute to adequate mental health training, education and public awareness, and lead to improved health outcomes in the population," said Dr Mythily Subramaniam, Deputy Director of Research, and one of the two IMH researchers who led the study.

The other lead researcher was Ms Janhavi Vaingankar. An additional implication of using this instrument in a research setting will be to measure and observe changes to positive mental health among the Singapore population over time.

* Some 2,500 Singapore residents participated in the development and validation of the PMH instrument which was conducted from April 2008 till February 2011. Focus groups and surveys were conducted among Chinese, Malay and Indian adult residents, aged 21 to 65 years old.

KEY ASPECTS OF THE POSITIVE MENTAL HEALTH INSTRUMENT

The PMH instrument includes six dimensions (47 items or statements) and encompasses the notion that mental health can be achieved by the balance, influence and strengths of multiple domains. The six dimensions identified for positive mental health are:

1 **General coping** – how a person reacts and copes during stressful situations and his ability to think positively and engage in choice activities.

2 **Emotional support** – the assurance of feeling loved and wanted by a person's family and friends is important to help him cope with difficult life situations. It provides compassionate, realistic counseling and care which helps the person to share his burdens and fears with others.

3 **Spirituality** – this domain covers both spiritual and religious practices and beliefs that influence one's faith and behaviour in life. It contributes to positive mental health as a coping mechanism and helps in building strong social support and networks.

4 **Interpersonal skills** – this dimension strongly contributes to all other aspects of mental health and the skills are crucial in helping one develop and maintain good relationships, which in turn will provide the support and network needed during times of distress.

5 **Personal growth & autonomy** – knowing one's goals in life and ways to achieve them is a sign of good mental health. It reflects on a person's level of confidence, freedom, sense of purpose, and the ability to self-evaluate and take control of situations.

6 **Global affect** – the experience of positive mood is a sign of mental health. Being calm, happy and enthusiastic are indicative of emotional stability and vitality. This is a more transient dimension, yet the most predictive of one's recent experiences.

Although the key domains of positive mental health are similar to the other reports from Western countries, the study highlighted that spirituality was deemed important in the context of Singapore.

This article was first published in IMH LINK (MICA (P) 162/07/2011), a quarterly publication by Institute of Mental Health, January ~ March 2012 Issue.

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H5N1 TEST TRIAL FOR HEALTHCARE AND WELLNESS KIOSK AT WOODLANDS POLYCLINIC

National Healthcare Group Polyclinics (NHGP) has partnered A*STAR (Agency for Science, Technology and Research) to develop Healthcare and Wellness Kiosks that allow patients to measure and record their health conditions prior to consultation. The project's test trial was launched in Woodlands Polyclinic on 10 May.

Fully funded by A*STAR, the Healthcare and Wellness Kiosks allow patients to enter their medical conditions and symptoms relating to Upper Respiratory Tract Infection (URTI) while getting their weight measured. This information will then be transmitted to their personal medical records which will be viewed by the doctor during consultation. The Kiosks cut down process waste as they eliminate repeated information gathering at different service stations as all presenting symptoms are captured by the Kiosk during registration.

After the completion of the test trial, the clinic team will launch phase two of development which allows the Kiosks to measure patients' temperatures as well as assign those who display symptoms of flu and fever to the URTI cluster.

Article courtesy of NHGP Corporate Communications

LAUNCH OF CONVIDOSE™: SAFER, EASIER MEDICINE

On 8th May, the National Healthcare Group Pharmacy (NHGPh) launched ConviDose™ - Singapore's First Multi-dose Medication Management Services at the Institute of Mental Health. The guest-of-honour Professor Chee Yam Cheng, CEO, NHG delivered the opening address and together with Ms Chan Soo Chung, Executive Director of NHGPh officiated the Convidose™ launch.

Representatives from nursing homes, partners of NHGPh, media, senior management staff from NHG and IMH attended the event. They were given a tour of the Pharmacy Services Centre-NHG Pharmacy's centralized facility for ConviDose™ – at IMH. With Convidose™, patient's medicine dosage can be conveniently pre packed into individual sachets, according to the stipulated quantity and time the pills need to be consumed.

Article courtesy of National Healthcare Group Corporate Communications

(Top)1. Professor Chee Yam Cheng, CEO, National Healthcare Group and Ms Chan Soo Chung, Executive Director NHG Pharmacy with the nursing homes representatives. (Left to Right) 2. Professor Chee Yam Cheng, CEO, NHG together with Ms Chan Soo Chung, Executive Director, NHGPh officiate the Convidose™ launch. 3. Pharmacy technician collecting the Convidose™ sachet from the Automated Tablet Dispensing and Packaging System (ATDPS) 4. Pharmacy Services Centre, NHGPh's centralized facility for Convidose™.

DEVELOPMENT OF SUSTAINED RELEASE GANCICLOVIR IMPLANT FOR TREATMENT OF CMV RETINITIS IN HIV-AIDS PATIENTS.

CLINICAL LEAD-PRINCIPAL INVESTIGATOR
Dr Rupesh Agrawal, Associate Consultant
Dept. of Ophthamology
Tan Tock Seng Hospital

TECHNICAL LEAD-PRINCIPAL INVESTIGATOR
Dr Terry W J Steele, Assistant Professor
Materials Science & Engineering
Nanyang Technological University

Project was awarded the NTU-NHG Innovation Seed Grant (ISG) of SGD 48,000

Cytomegalovirus in AIDS patients: The Human Immunodeficiency Virus (HIV)/ Acquired Immune Deficiency Syndrome (AIDS) pandemic, now affects between 30.6 and 36.1 million people world-wide.

The human immunodeficiency virus (HIV) has pervasive effects on culture, economics, policy and human development. All organs can be affected by complications of HIV/AIDS, including the eye. Many HIV+ patients develop eye complications, both infective and non-infective, CMV (cytomegalovirus) retinitis being the most common. Specific ocular therapy is critical to avoid blindness in the early months before immune recovery can occur, or if antiretroviral therapy is unavailable.

Ganciclovir has traditionally been considered the recommended treatment for CMV retinitis; however due to side effects and the possibility of developing viral resistance, local therapy is preferred.

Current treatment for CMV retinitis: Ganciclovir has traditionally been considered the recommended treatment for CMV retinitis. Systemic therapy with intravenous ganciclovir was initially the only option available but subsequently, other antiviral drugs were also used in treatment of CMV retinitis including the use of cidofovir, prodrug of ganciclovir i.e., vala-ganciclovir, and intravenous foscarnet. Unfortunately, these drugs are limited by its cost constraints and systemic side effects. Local therapy, in the form of intra-vitreal injections with ganciclovir and cidofovir was pursued since ocular infection was the most common manifestation of CMV.

Current local treatment involves injecting antiviral drugs directly into the vitreous, a therapy that requires multiple injections, week after week. Repeated ocular injections can be traumatic, with risk of ocular complications like endophthalmitis, retinal detachment and drug resistance.

Importantly a patient with CMV retinits needs to come over to eye clinic for repeated injections and there is always a chance of patient getting defaulted for repeated injections. Hence, development of cost effective long lasting sustained release ganciclovir implants are currently needed for safe and effective treatment of cytomegalovirus retinitis.

Peri-ocular implants designed for patient comfort and long-term drug release: To circumvent the practical hurdles in delivering anti-CMV drugs to the retina, collaboration between TTSH and NTU was embarked on designing a unidirectional nano-drug delivery pellet that provides drug delivery into the vitreous over several months while maintaining an adequate concentration of drug in the vitreous cavity.

The biodegradable implant is designed to suppress viral replication, halt the progression of disease, minimize retinal damage, prevent drug resistance, prevent local complications and preserve visual function. Secondary operations for removal will not be necessary, as the polymer components are designed to slowly dissolve and be metabolized into the tissue.

Collaborations between clinicians and implant engineers: This project allows a synergy of long term collaboration between technology and medicine. In the long run, the technologists and clinicians will work towards facilitating the similar platform for many other therapeutics required to be used for posterior segment disorders such as corticosteroids for chronic uveitis and anti-vascular endothelial growth factors for age related macular degeneration.

NTU-NHG Innovation Seed Grant 2011t Award presentation to Dr Rupesh Agrawal (right) by Prof Stephen Smith, Vice-President Research, NTU and Founding Dean of Lee Kong Chian School of Medicine (left)

THE IMPACT OF GENETIC VARIATION IN THE HIV-1 PROTEIN COAT ON IMMUNE CELL DEATH

Dr Ng Oon Tek
Consultant, Department of Infectious Diseases
Tan Tock Seng Hospital

Dr Ng completed Internal Medicine training in Singhealth cluster and obtained the MRCP(UK) and MMed (Int Med) in 2004. Subsequent Infectious Disease subspecialty training was completed in Tan Tock Seng Hospital (TTSH) in 2008. He received a Master of Public Health degree from Johns Hopkins School of Public Health in 2010 sponsored by a National Medical Research Council Overseas Research Fellowship. As a recipient of the NMRC Overseas Research Fellowship, Dr Ng completed the MPH degree followed by a year-long research attachment with a US NIH funded group. Dr Ng has an interest in research integrating public health, laboratory medicine and clinical medicine to improve patient outcomes. Accordingly, he works closely with clinical colleagues, and the Ministry of Health Communicable Disease Division, as well as running funded studies in the TTSH Infectious Disease Research Laboratory. He is the TTSH site investigator for the Treat Asia HIV Observational Database, a US NIH funded project examining HIV in Asia.

Human Immunodeficiency Virus (HIV) is extremely variable genetically. Just as no two human beings are similar, potentially no two HIV viral particles are exactly the same. A major reason for this variability is the inconsistent error checking of the enzymes which copy the HIV genetic material.

This is multiplied by the production of an average of 1,000 million viral particles a day in an infected person. Researchers using laboratory techniques have been able to define subtypes, or strains, of HIV, in different geographical regions in the worldwide pandemic, now infecting more than 30 million people.

A unique feature of the HIV epidemic in Singapore is the presence of two different strains, scientifically labeled “subtype B” and “CRF01_AE”, documented in the mid-1990s. This two strains are likely (although unable to be proven beyond doubt) to have arisen from different geographical areas.

The “subtype B” strain accounts for approximately 90% of HIV infection in Western countries, and is believed to have entered Singapore from there. The “CRF01_AE” strain is the overwhelming strain in Southeast Asia, the likely source of entry to Singapore.

Recently, funded by a National Medical Research Council training grant, a collaborative effort between investigators at the Communicable Disease Centre and Johns Hopkins Medical Institution, documented the emergence of a new strain (or hybrid) of HIV in Singapore, formed as a result of intermixing of genetic materials from the previously documented dominant strains. This phenomenon had been documented globally 50 times prior to our report, and is a marker of active disease transmission.

The current Transition Award grant funded project examines whether different strains of HIV affect the immune system of infected individuals differently. A prior published study conducted by the same group above had documented that CRF01_AE infected individuals lost immune cells at a much faster rate than subtype B infected individuals.

In this current grant, we plan to conduct laboratory experiments in collaboration with the University of Texas to determine if difference in the HIV-1 protein coat, a major region of the virus which interacts with immune cells, affects the rate of immune cell death. We are also planning to monitor patients infected with all the 3 major strains (subtype B, CRF01_AE and hybrid) to observe for differences in clinical features. Hence, this study adopts a bench and bedside approach to answering the question. The research is potentially important at both international and local levels. At an international level, most of the immense body of HIV research is conducted on the Western subtype B strain, and differences in biology and clinical behavior of non-B strains could render those results not immediately transferable to other regions.

For example, a recent publication from our group highlighted the finding that Singaporeans infected with the CRF01_AE strain present with more severe immune-compromise and do not respond as well to treatment, as subtype B infected counterparts. At a local level, the impact of HIV strain on patient outcome is important as public health and treatment strategies may need to be adapted for the differences.

I thank God for very supportive mentors, both within TTSH, at other institutions in Singapore and at Johns Hopkins, who have provided a lot of insights into medical research. The availability of funding from NHG-level and National Medical Research level grants have also been highly enabling in these endeavors. Thanks also to all the collaborators at National University Hospital, A*STAR (ETC and IBN), Johns Hopkins, and University of Texas, whom I have worked closely with over these few years.

THE ROAD OF DISCOVERY

Reflections of a Young Clinician Investigator from IMH taking the path that is less travelled

Dr Jimmy Lee
Consultant Psychiatrist
Institute of Mental Health

Dr Jimmy Lee is a National University of Singapore (NUS) trained medical doctor. He is currently Consultant Psychiatrist in the General Psychiatry Department and Director of the Clinical Trial Unit at Institute of Mental Health (IMH). He spends more than half his time on research work and continues to see outpatients and heads the Annual Review Clinic team. He has also started to mentor new investigators through an intramural grant. Being awarded the Transition Award from National Medical Council (NMRC) is a strong testament to his work and dedication to research and clinical work for the betterment of patients with mental illnesses. In this issue, the editorial team finds out from Dr Jimmy Lee himself, about choosing the path that is less travelled by others.

Psychiatry

The practice of psychiatry today has come a long way with a deeper understanding of the science behind the art and with more treatment options available. However, there are numerous enigmas that continue to confound psychiatrists daily. Using schizophrenia as an example, questions such as what causes it, which medications are most suitable and who is at greatest risk of developing treatment resistance or side effects to the treatments remain unanswered.

Schizophrenia is a serious mental disorder with potentially disabling outcomes. One of the main drawbacks in psychiatric practice today is the lack of an objective measurement such as a biomarker that clinicians can rely on. A central dogma in psychiatry has been that psychiatric disorders are primarily brain disorders, and most research has focused on the brain. There is now increasing evidence that psychiatric disorders do not just affect the brain, but also on peripheral tissues – at least the medications certainly do.

Journey of Discovery

Our initial studies have shown that it was possible to identify a lipid-based signature in red blood cell membranes, and a gene expression signature in peripheral blood of patients with psychosis. A follow on pilot study demonstrated the stability of the lipid-based signature over a short period of time after anti-psychotic medication exposures. This lead us thinking that a peripheral blood-based biomarker might be feasible, easily accessible and provide additional clues to aid the psychiatrist.

This naturalistic study seeks to expand on the pilot, to recruit and follow up a larger group of participants over a longer duration of time. At regular intervals, clinical status will be monitored and blood samples will be collected, processed and stored.

Our group will attempt to validate the lipid-based peripheral blood signature in this group, and monitor its changes in relation to clinical response and treatment. What is also unique in this study is the parallel recruitment and follow up of a group of healthy controls, to examine how these lipid markers vary over time and the influence of dietary and lifestyle factors. This information is important in understanding normal variations so that our team is better able to filter the noise from the true signal.

While the study focuses on identifying biomarkers as the longer term aim, I also believe in research that benefits the participants. A feature of this study is that participants will have their Body Mass Index (BMI) calculated, blood pressure taken, fasting lipid and glucose profile measured, and the results mailed to them. This pertinent information will hopefully provide the participants a snapshot of their own metabolic health, and encourage them to either maintain their healthy lifestyle, or seek help if needed.

School of "Hard Knocks"

Obtaining this Transition Award is a culmination of years of preparations and hard work. It all started from a simple research project that my mentor got me on 8 years ago, which led me down the "slippery" path towards more research hardship. The pilot studies and follow on study mentioned above were instrumental in helping me obtain the Transition Award, and they would not have been possible without the small grants and the NHG Small-Innovative Grant (SIG).

A point I often make is the need for continued education to understand research methodologies. I have been trained for 5 years to understand the language of medicine and took on further education over the years in the forms of the NHG Clinician Leadership in Research Programme, and the Master of Clinical Investigation (MCI) to understand the language of research.

Telling others that I am embarking on research (including my family) never fails to elicit some form of peculiar response – frequently I would get frowns, worried looks, and queries about my own sanity, to the very occasional interested "tell me more" look. Whenever I face challenges, an adage that a wise psychiatrist once said comes to mind – "The mind is the last frontier" – a statement applicable to my own pursuits, as well my patients'.

CONTINUOUS EDUCATION AND FURTHER CERTIFICATION OF OHRPP STAFF

NHG-OHRPP CIP and CCRP accredited staff From Left: Ms Felicia Wong, Ms Doreen Lim, Mr Charles Wong, Ms Hu Liqin (Absent: Ms Jobyna Ho)

The NHG Office of Human Research Protection Program (OHRPP) is committed to the continuing professional development (CPD) of staff to ensure that staff is confidently equipped with ethics knowledge to facilitate efficient and high quality ethics review and maintain high standards of human research protection.

An important CPD opportunity for Institutional Review Board (IRB) staff to advance and demonstrate their competency would be the Certified IRB Professional (CIP) program. The CIP program was developed in 1999 by Public Responsibility in Medicine and Research (PRIM&R) and tests candidates' knowledge in these four major areas:

1. **Foundations and concepts of IRB practice**
2. **Organizational and personnel knowledge**
3. **IRB functions and operations**
4. **Records and reports**

The CIP credential is a validation of an individual's professional experience and competency in IRB and HRPP administrative practices and strengthens the administration of IRB processes.

Another platform to accredit clinical research professionals would be the Society of Clinical Research Associates (SoCRA) certification program.

This certification program validates and accredits Clinical Research Coordinators or Professionals with at least 2 years of relevant experience, and who are able to demonstrate professional competency in the area of clinical research.

The NHG OHRPP is proud to announce 100% passes among staff who undertook the above programs in March 2012. Congratulations to all Certified Clinical Research Professionals (CCRP) and Certified IRB Professionals (CIP)!

NHG RESEARCH QUALITY MANAGEMENT PROGRAM

QUALITÉ

THE PROGRAM WITH A MISSION TO ENSURE AND ENFORCE THE RESPONSIBLE CONDUCT OF RESEARCH MEETING HIGH ETHICAL STANDARDS.

Informed Consent Documentation

The Use of Short Form Consent Forms

What is the Short Form Consent?

Informed consent must be obtained from all human subjects, prior to their participation in any research studies approved by the NHG Domain Specific Review Board (DSRB), unless the process has been waived by DSRB.

In addition, DSRB recognizes the requirements of Good Clinical Practice and United States Food & Drug Administration Code of Federal Regulations, that the informed consent document should be in a language understandable to the subject. However, in view of the budget constraints of investigator-initiated research studies, DSRB recognizes the fact that sometimes it is not possible for investigators to develop translated versions of the consent document.

Considering the above, DSRB created a Short Form Consent Template for these researchers to obtain consent from non-English speaking subjects, where a translated version of the complete set of consent documents is not available. The Short Form Consent Template is intended to be used as a tool, in addition to the original English consent document, and the consent process and procedure has to be performed or obtained in the presence of an investigator, translator, impartial witness and subject. The subject would then sign on the Short Form Consent Template which was in the language understandable to him/her.

Health Sciences Authority's Recommendation on the use of Short Form Consent

In HSA's recommendations of the informed consent process, for subjects who were unable to read the informed consent form, there is no legal provision for the subjects to sign on the Short Form Consent alone (without signing on the original English consent document).

Hence, in order to harmonize with HSA's requirements, DSRB will be recommending some changes to the practices of informed consent for non-English speaking subjects.

New Recommendations on the Use of Short Form Consent

Consent from non-English speaking subject
The preferred method of obtaining informed consent from non-English speaking subjects, is to provide the subjects with consent forms written in the language understandable to the subject (i.e. translated version of the complete Patient Information Sheet & Consent Form).

For Investigator Initiated Studies
For all types of research studies (for the recruitment of non-English speaking subjects, where a fully translated ICF is not available), investigators are allowed to conduct the informed consent process for the non-English speaking subjects using the DSRB-approved Short Form Consent Template. However, the short consent form must be used together as a complete set with the DSRB-approved English version Patient Information Sheet & Consent Form.

- The Subject, Investigator and Impartial witness need to sign on BOTH the Short Form Consent Form and the English version Patient Information Sheet & Consent Form.
- These 2 documents are considered a set of documents, and a copy of the full set of documents is to be provided to the subject.
- A document footer and a page number will be required as essential elements on these documents. This is an added measure to ensure the study team and the subject understand that they are indeed a set of documents.

(continued from previous page)

Translation of consent documents
For investigator-initiated research studies, investigators should include the costs of consent documents translations into grants and contracts. It is the responsibility of the Principal Investigator to ensure that there is provision of adequate resources to obtain proper informed consent from the subjects.

DSRB has developed the following recommendations for translated consent documents, applicable for all types of research studies:

- A certified translation is preferred. This should be accompanied by a letter of certification from the translator or translation service provider.

- For Investigator-Initiated studies, whereby cost of translation is a factor of concern, DSRB accepts documents translated by an individual fluent in the given language in place of a certified translation. A letter from the translator describing their qualifications should be provided with the translated documents.
  More information on the guidance will be released to the research community in the coming months as DSRB seek to help Investigators ensure compliance to the recommended revisions in the informed consent processes.

Other References:
Health Sciences Authority Website (Frequently Asked Questions) - [H] INFORMED CONSENT FORM (ICF)
http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/clinical_trials/faqs.html#(H)

Protocol Non-Compliance:
Compromising the Privacy and Confidentiality of Subject's Information

Background
A multicenter study involving several sites in Singapore recently have been sending hardcopies of the Case Report Forms (CRFs) from the various participating sites to the overall Principal Investigator for consolidation and filing. However, attached to the CRFs were also copies of the source documents and records from the various participating sites. This included subjects' admission records, medical history, etc.

Findings & Implications
The study team had attached a copy of source document/records with the CRFs to facilitate in the verification and clarification of potential discrepancies.

However whilst doing so, the study team had inadvertently compromised on the research subjects' privacy and confidentiality as records containing their identifiers and medical information had been sent out to the various institutions.

Tips and Recommendations

a. Data entry should be completed at site and data should be verified with source data/ documents before it is entered into case report forms.

b. Case report forms should not contain any subject identifiers (eg. Name and NRIC number). Instead, unique codes could be assigned to subjects when data is being collected. These codes would be linked to subject identities in a separate and secured document to minimize the risk of exposing subjects' identities.

c. Research data sent outside the institution should not contain any subject identifiers, unless specific approval has been obtained from DSRB. Principal Investigators should also check their institution policies with regards to data management or transfer of data outside of the institution and obtain necessary approval before releasing patients' records to members located outside the institution.

d. If there is a need to send copies of source records outside your institutions; subjects' identifiers should be obliterated or obscured.. This can be done by using a black marker and photocopying the document to ensure that the subject identifiable information cannot be seen.

References from NHG – Proper Conduct of Research SOPs (PCR-SOPs):

[PCR 501-B08 Item 4.] The CRFs should not contain patient identifiers such as name, date of birth, address, etc. Each subject should be assigned a unique subject identification code which should be used in the CRFs, serious adverse event reports, UPIRTSOs and any other research related data. In addition to the subject identification code, subject initials may also be entered. The link between the subject identification code and the subject identifiers should be stored in a separate document.

[PCR 501-B05 Item 9.] To protect the confidentiality of subjects, the CRF should not have a provision to enter the subjects' name. The CRF should be linked to the subject only by subject identification code and if needed the subject initials. Sticky labels with the subject name and other personal information that is generally used in institutions for medical records and other forms should never be stuck on CRF pages. When laboratory test results are filed as part of the CRF, the subjects' name should be obscured.

PCR 501-B05 (Definition) b. Source Data – All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial that is necessary for reconstruction and evaluation of the research. Source data are contained in source documents.

The NHG Proper Conduct of Research Standard Operating Procedures are found at the following portal:

http://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops

Protocol Non-Compliance:

Compromising the Privacy and Confidentiality of Subject's Information

Q1: What is the Purpose of having Source Documents?

The fundamental purpose of source documents is to confirm the existence of the subject; confirm the validity of the trial conducted and the integrity of data collected. Therefore, in a clinical trial, records on which clinical observation are initially recorded are considered source documents. These records are also legitimate raw data that supports a trial's findings. At an investigational site, usually a hospital, the medical record is often the source documentation. It can also be a computer print out of laboratory value results or patients' diaries.

Q2: What are source documentations and how is it used in clinical trials?

Source documentation serves to substantiate the integrity of the trial data collected, which include original documents related to the trial, to medical treatment, and history of the subject. To substantiate the integrity of the trial data collected, the information on a subject's medical record should correspond to the data on the case report form, and in turn should support the data listings and statistical results which are provided to regulatory agencies.

According to Singapore Guideline for Good Clinical Practice (SGGCP) 4.9.3, data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

Definition/Glossary:

Source data are information in original records and certified copies of original records inclusive of original records of clinical findings, observations, or other activities in a clinical trial that is necessary for reconstruction and evaluation of the research. Source data are contained in source documents.

Source documents refers to all documents that have source data, including original documents, data, and records (i.e. hospital medical records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subjects files, and records kept at a pharmacy) at the laboratories, and at medico-technical departments involved in the research.

Case report forms are printed, optical or electronic document designed to record all of the protocol required information for each study subject.

References:

- Singapore Guideline for Good Clinical Practice (SGGCP
- NHG PCR SOP 501-B05: Documentation
- Good Clinical Practice: A Question & Answer Reference Guide, May 2011 (Published by Barnett Education Services)

Reference Guide: Protecting Privacy and Maintaining Confidentiality

The Office of the Human Research Protection Programme of UCLA published a quick reference guide or tool intended to aid researchers and IRB members to ensure that adequate provisions exist for the protection of research participant privacy, the maintenance of confidentiality of identifiable research data and data security.

Some of the issues to consider in protection of subject's privacy are explained in this guide.

Protecting Privacy:

Privacy is about people and their control over the factors of extent, timing, and circumstances of sharing oneself whether physically, behaviorally, or intellectually with others.

For privacy in research, the following factors are considered:

a) Subject Population (cultural norms and age may affect privacy preferences)
b) Recruitment Methods (acceptable methods of identifying and contacting subjects)
c) Sensitivity of the Information being collected (the greater the sensitivity, the greater the need for privacy)
d) Method of Data Collection (e.g focus group, individual interview, covert observations)

Maintaining Confidentiality:

Confidentiality pertains to data and is explained as treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

For the maintenance of confidentiality, the following factors are to be considered:

a) Research Design (minimizing the need to collect and maintain identifiable subject information)

b) Collecting and maintaining Identifiable Data (protocol includes safeguard to maintain confidentiality of data and data security appropriate to the degree of risk from disclosure)

c) Provisions to maintain confidentiality of data (should be included in the protocol)

d) Limit access to Data (the informed consent states who should have access to the data, usually authorized personal e.g auditors, regulatory inspectors)

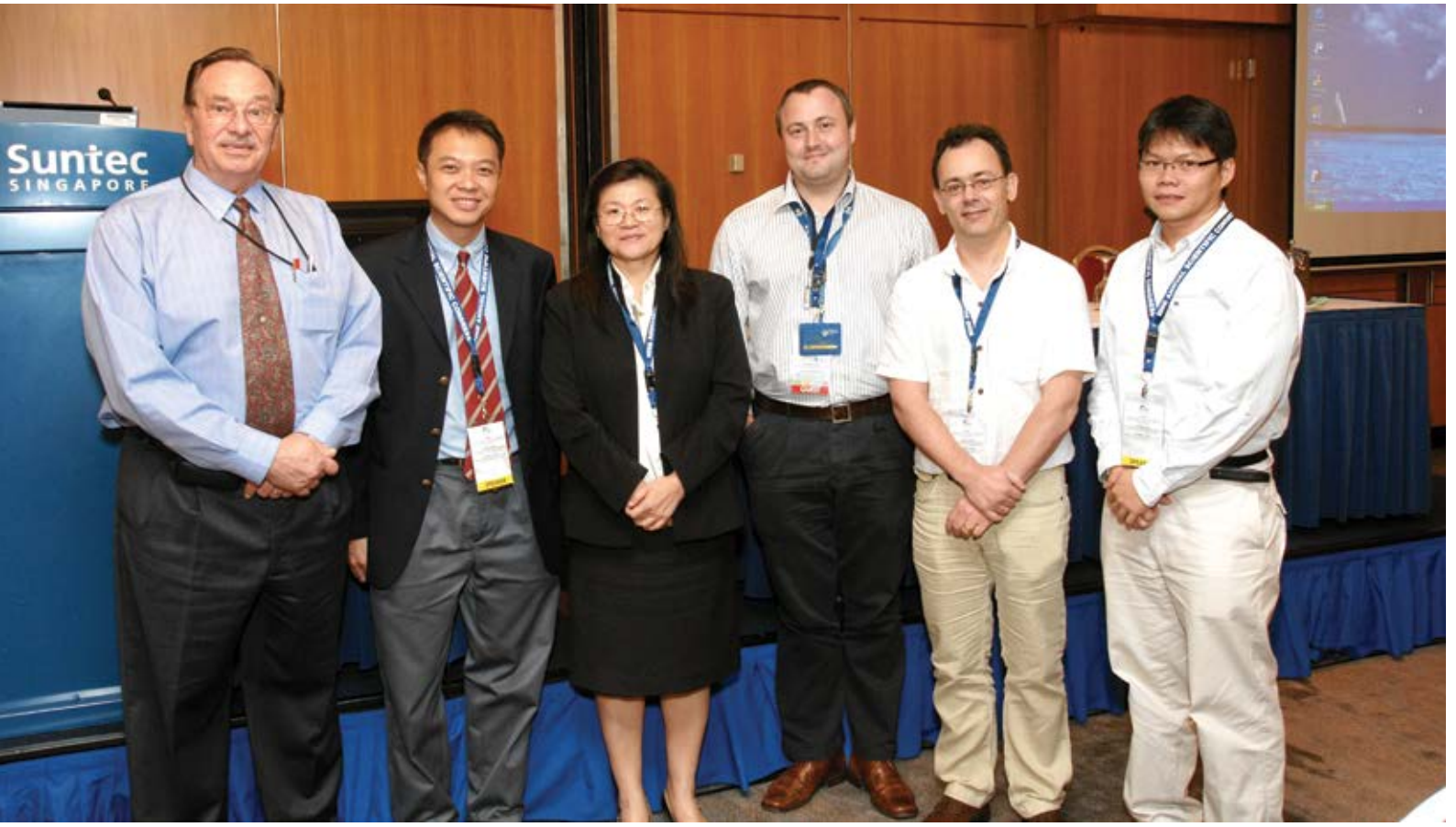
For more detailed information, reference to the guidance document is recommended (link below).

Reference:

UCLA Office Of Human Subject Protection Program (OHRPP)'s Quick Reference: Protecting Privacy and Maintaining Confidentiality in Research, AAHRPP Elements – II.2.B., II.3.D-F, II.5.A.

KNOWING OUR HEALTHCARE LEADERS

Associate Professor Leo Yee Sin, Head, Department of Infectious Disease, Tan Tock Seng Hospital



Associate Professor Leo Yee Sin (third from left) with collaborators of STOP Dengue

1. What are your thoughts on the current state of collaborative research in your institution?

Tan Tock Seng Hospital (TTSH) prides itself as a service-oriented hospital. It was founded as a pauper's hospital and is the second largest acute care general hospital. TTSH houses many renowned clinical groups and through the years has invested in clinical research aiming to improve patient care.

TTSH has a particular strength in infectious disease housing the Communicable Disease Centre (CDC) which is also the National Outbreak Response Centre that handled the SARS and 2009 H1N1 influenza outbreaks. Infectious disease is a unique non-organ specific sub-specialty that by nature works well and collaborates well with many other specialties.

Examples of intra-hospital collaborations currently in progress include antibiotic utilization with intensive care physicians and pharmacists, bone and joint infectious with orthopedics and viral encephalitides with neurologists at the National Neuroscience Institute.

The award of the flagship infectious disease translational clinical research grant to STOP Dengue led by CDC in 2008 promoted inter-institution collaboration, with active partners in National University of Singapore, Genome Institute of Singapore, Duke-NUS, Environment Health Institute and other local research institutes.

We also collaborate with other healthcare institutes in Singapore, with the first inter-hospital infectious disease network set up for a clinical trial in dengue, and with a polyclinic network for recruitment of early dengue infection.

Industrial collaboration has been initiated, for example in dengue diagnostics, and we have started exploring international collaborations with other centers experienced in dengue research. Continued collaborative research will depend on further grant support, and we have joint proposals for diagnostics with NTU and A*STAR under review.

2. Is there a simple analogy that you would use to describe the "As Is" and "To Be" state of your research in your institution?

Clinical research strengths at TTSH are currently in health services outcome research given the high patient load and emphasis on service provision. While maintaining this emphasis which has proven fruitful especially in infectious disease and rehabilitation medicine, we would like to move forward by leveraging on local expertise for example in implementation research. With the opening of the Lee Kong Chian School of Medicine based at TTSH with NTU and Imperial College, London, in 2013, we hope to build our relationship with these universities and synergise with the strengths of NTU particularly in bioengineering.

3. What do you think are the qualities of your institution that allows it to catalyse collaborative research?

As the second largest acute general hospital in Singapore, with the pioneer geriatric medicine department and continue strength in the care of older persons, we are well placed to support large clinical cohorts necessary for health services operations research and clinical translational research. The Communicable Disease Centre is also a key resource as its position as the national outbreak response centre puts it in the best position to study a range of outbreaks. During the 2009 H1N1 pandemic, clinicians moved fast to gather data while managing the emergent clinical situation. The plethora of high-quality outbreak research that has been published is testament to the willingness to collaborate not only between clinicians in different disciplines, but also with laboratory researchers.

4. Could you share an example of a piece of collaborative research that you are involved in and how it has benefited the various stakeholders?

As the Lead Principal Investigator on STOP Dengue, the national flagship infectious disease translational clinical research program, it has been my privilege to coordinate a spectrum of research on this pressing disease with half the world's population at risk. We see the backbone of the program as the two large prospective cohorts, the primary-care based EDEN (Early Dengue Infection and Outcome Study) and the hospital-based PADS (Prospective Adult Dengue Study) with a combined enrolment of over 3500 to date. These are critical sources of clinical data as well as samples that feed into all areas of our research
We contribute to ongoing national surveillance through our collaborators at the Environment Health Institute (EHI). Our samples allow for molecular epidemiology studies to be done, which can detect strain shifts. The introduction of new strains of dengue viruses is associated with fresh outbreaks as occurred nationally in 2007, and on a smaller scale with clusters of dengue serotype 3 reported in the news last year. Quick response is vital to detect and stamp out these clusters and it was successfully managed.

Collection of clinical virus isolates was critical to the development of a new and improved mouse model of dengue virus by A/Prof Sylvie Alonso at the National University of Singapore. This mouse model is now being used by other researchers in our team to develop new ways to prevent and treat dengue.

Development of the first serotype--specific, non-crossreactive human monoclonal antibody against dengue serotype 1 by A/Prof Paul MacAry at NUS is another example of how clinicians were able to collaborate with immunologists in time-sensitive research. Our collaborators responded to the availability of clinical samples by also studying the T-cell response to dengue with major advances in our understanding of lymphocyte response to dengue. Plans are in progress for clinical trials for the monoclonal antibody and other dengue treatments.

We have initiated a biomarker discovery project with a range of collaborators with expertise in genomics and transcriptomics (GIS), metabolomics (SMART), and lipidomics and proteomics (NUS) to discover prognostic markers for severe dengue. Together with collaborators from the Department of Statistics, NUS, we plan to pool data together to demonstrate, often for the first time, the utility of these new technologies for infectious disease, to improve the management of dengue, and to spur new implementation technologies with bioengineers and biotech companies to bring solutions to the clinic.

Finally, in terms of healthcare outcomes, our clinicians at Tan Tock Seng developed, validated and modeled the cost-benefit of a prognostic algorithm that prioritized hospitalizations for dengue together with statisticians and economists at NHG and NUS. By improving healthcare resource utilization, we hope to contribute to a more effective national healthcare system, the importance of which can be seen from the recent healthcare budget. We are currently engaged in international collaborations to investigate the applicability of our findings.

5. On a lighter note, what do you like most about your job?

Infectious disease, and in particular outbreak research is forever challenging: facing rapidly developing outbreaks from the Nipah virus to SARS to the 2009 H1N1 pandemic, managing clinical operations while simultaneously ensuring high-quality research is being done keeps me on my toes. The potential to have a revolutionary impact is a great source of satisfaction, for example with the global pandemics of HIV, influenza and dengue. Finally, bringing research findings back into the clinic to improve patient care, safety, and cost management is what I find most rewarding.

6. How do you handle the tight demands of your schedule and yet find time for your family?

Strong family support has been absolutely critical to help me balance work and home life. Help from parents in childcare and an understanding husband have brought our family through the difficult school-age years. Now my older girl has graduated from university and my second child is awaiting national service. I can't stress enough how rewarding it is to be able to balance work and family, especially as you see your children grow up.

7. What do you like to do in your spare time? Do you have any hobbies?

Reading good books and tending to my garden are two activities I would like to be able to spend more time on. Unfortunately, the truth is there is very little spare time!

8. Does your personality and love for your hobbies help in making decisions in your research work?

What motivates me is finding answers to the real-life problems I face as a clinician. Being able to implement well-researched and effective solutions is very rewarding. This is what drives me through the process of deciding what issues will benefit from research, what research is currently feasible and then using the findings in innovative ways to help patients.

COLLABORATIONS IN RESEARCH

INFECTIOUS DISEASES

Infectious diseases remain the leading cause of death worldwide. The threat of infectious disease is imminent even in Singapore, despite its excellent healthcare infrastructure and high standards of living. Singapore being a major global trading hub will continue to be plaqued by emerging infectious diseases like SARS, HIV, H1N1, re-emerging infectious diseases like dengue and tuberculosis as well as drug resistant infections because of various factors like changes in the population demographics and behavior and increased international travel.

Tan Tock Seng Hospital (TTSH), as the National Referral Centre for communicable diseases and HIV infection and for infectious post exposure management, is also the MOH/NEA designated outbreak management centre. Research and knowledge is one of the pillars in TTSH's pursuit of excellence in medical advancement in infectious diseases.

The TTSH Communicable Disease Centre (CDC) aims to become a regionally and internationally recognised centre for clinical care, training and research into infectious diseases. Amongst the key research programmes in TTSH CDC, the STOP Dengue programme led by TTSH CDC's Clinical Director, Associate Professor Leo Yee Sin, who also heads the Infectious Disease department at TTSH focuses on optimising early diagnosis, prognosis and case management for adult dengue infection.

STOP Dengue Translational and Clinical Research (TCR) funded by NMRC since December 2008 serves as the focal point for Dengue Research collaboration in Singapore. It integrates established groups from Infectious Diseases departments of TTSH, NUS and Duke-NUS to form internationally competitive programs.

This multi-disciplinary 5-year programme seeks to integrate knowledge gathered on topics such as developing optimal dengue management strategies; understanding disease pathogenesis; discovery of prognostic makers; prevention of the spread of Dengue and effective targeted therapy.

An effort to make Singapore the preferred location for innovative drug studies, research on biomarkers and disease mechanisms for dengue, STOP Dengue aims to improve collaborations between scientists and clinicians, with the purpose of translating discoveries in the laboratory into interventions that can improve dengue care.

The first three years of STOP-dengue's collaborative research has accomplished key research outcomes. The team of basic science and clinician researchers have published 58 peer-reviewed journal papers, contributed to 12 book chapters, had 11 oral presentations and 42 poster presentations. They have trained 12 PhD, five Masters students and won additional competitive research grant funding.

STOP dengue also marked the inaugural ASEAN dengue day on 15 June 2011 together with the Minister for the Environment and Water Resources, Dr Vivian Balakrishnan, and the World Health Organisation's Regional Director for the Western Pacific, Dr Shin Yong-Soo.

This preceded an educational dengue symposium attended by the local and international scientific community and Singapore general practitioners. In conjunction with the symposium, a public exhibition on dengue was also held at TTSH's Atrium to commemorate the inaugural ASEAN Dengue day, graced by Minister for Health, Mr Gan Kim Yong.

HIV research is another area in TTSH that has led promising programs and achieved extensive collaborations internationally. Being the national reference centre for HIV clinical care in Singapore, TTSH is the largest HIV treatment centre caring for 2,500 patients (70% of national patients). The CDC HIV treatment programmes has been at the forefront of research, collaborating extensively to bring progress to HIV patient care, publish results to contribute generalisable knowledge and patent ideas to commercialise benefits.

Locally, CDC investigators are heading a multi-centred collaboration involving NUH, SGH and CGH documenting the molecular epidemiology of HIV-1 in Singapore. Regionally, CDC is the Singapore representative on the sole pan-Asian HIV database - the Treat Asia HIV Observational Database (TAHOD). The associated Treat Asia Quality Assurance Scheme (TAQAS) has also facilitated quality control for a locally developed genotypic resistance test at the CDC.

Collaborations with international partners like the Johns Hopkins Medical Institution, University of Texas and University of New South Wales have also been forged. Projects examining molecular epidemiology, inter-subtype differences in bystander T-cell apoptosis and the different treatments for HIV patients have since been conducted.

Additionally, an NMRC-funded collaboration with A*STAR had resulted in a locally developed HIV-1 quantitation assay which has been successfully patented. The cost of the HIV viral load test used to be a major barrier for inclusion as a routine part of clinical care. Research done on in-house viral load assay (2008-2009) by TTSH CDC has enabled TTSH to have a cheaper in-house assay for TTSH patients.

These various research have helped to improve the care for HIV patients. The locally developed viral load and genotypic resistance test has facilitated access to these tests for our patients. The patenting of the viral load kit helps to ensure continued and affordable access for our patients.

Research into the molecular epidemiology of HIV-1 in Singapore has also helped the identification of a novel recombinant strain, CRF51_01B, which was generated in Singapore as a result of recombination of the two existing strains, CRF01_AE and subtype B. These enable us to effectively manage and treat our patients with HIV effectively.

RESPONSIBLE CONDUCT OF RESEARCH (RCR)

CONFLICT OF INTEREST

In the previous issues of Catalyst, we have introduced 2 out of the 8 components of Responsible Conduct of Research (RCR) – Research Misconduct and Protection of Human Subjects. In this issue, we will look at the 3rd component of RCR - Conflict of Interest.

Researchers are motivated to work hard for many reasons - to contribute to advancing knowledge, to make discoveries that will benefit individuals and society, to further their individual professions and to achieve personal gain and satisfaction, among other reasons.

While the advancement of knowledge is best served by the sharing of ideas with colleagues, legitimate research interests can create competing responsibilities and lead to what is commonly called conflict of interest (COI).

It is important to understand that COIs are not entirely bad. In this day of research, the complexity and demanding nature of research inevitably gives rise to competing obligations and interests. Not only are researchers expected to serve on committees, train aspiring researchers, teach, etc., they are at the same time, expected to pursue their own research. However, in the crucial areas of financial gain, work commitments and personal and intellectual matters, it is necessary to take appropriate measures to ensure that COIs do not contest with the responsible practice of research.

Financial Conflicts of Interest

Personal interests and prospects of financial gain can unfortunately influence a researcher's elemental obligation to truth and honesty. Researchers should not, but may find unreasonable ways to delay a competitor's work so as to secure a patent or other financial advantage for themselves. Financial interests can provide a strong incentive to overemphasise or underemphasise research findings or even encourage research misconduct. Financial COI are situations that create perceived or actual tensions between personal financial gain and adherence to the fundamental values of honesty, accuracy, efficiency and objectivity.

If a researcher and or his/her study team (inclusive of immediate family members) has financial interests (e.g. stocks, stock options or other ownership interests in the assets or liabilities of any company that may benefit from the research activity), the researcher must declare this on the DSRB Application. The declaration should provide a full disclosure of the facts giving rise to the financial interest and should detail the steps proposed to eliminate any potential conflict of interest that may arise from the financial interests.

Conflicts of Commitment

At any one time, a researcher is likely to be wearing more than one hat, i.e. working on one or more grant-funded projects, working as a paid employee of an institution or sitting on an advisory board etc. Therefore, these activities place competing demands on the researcher's time and loyalties, leading to conflicts of commitment. Special care is thus required to ensure that these commitments do not interfere with one another.

For example, if a researcher has two concurrent grant-funded studies, he/she should minimally honor the time commitments made, by devoting a specific percentage of his/her time to either study.

Personal and intellectual conflicts

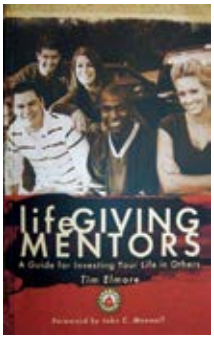
Personal conflicts are usually easier to identify and resolve. Generally, researchers should not review grant applications, publications or ethics applications submitted by close colleagues or students that they are mentoring. This is because their presumed interest in wanting to see their colleagues or students succeed could possibly conflict with their obligation to make objective, evidence-based judgements. Thus, most grant funding agencies as well as DSRB requires reviewers to disclose any conflict of interest beforehand.

Intellectual conflicts are more difficult to identify. If a researcher holds strong personal views on the importance of a particular area of research or a set of research findings (i.e. If a researcher holds a strong view that bone marrow aspiration must be carried out first to accurately diagnosis leukaemia in a patient suspected of leukaemia), these views should be disclosed so that others can take them into consideration when judging the researcher's statement(s).

Likewise is true of strong moral convictions that could influence a researcher's scientific opinions. This might be particularly evident when researchers serve as expert advisors (e.g. A researcher/expert advisor who has strong moral convictions against the termination of unwanted pregnancies has been tasked to review a study involving tissue samples obtained from foetuses prior to the termination of the unwanted pregnancy.

In this case, the researcher's personal convictions could influence scientific judgements and may therefore, bias the review outcome). Therefore, researchers should be vigilant and avoid making judgements or presenting conclusions based solely on their opinions or affiliations rather than on scientific evidence.

LIFEGIVING MENTORS: A GUIDE FOR INVESTING YOUR LIFE IN OTHERS BY TIM ELMORE



Associate Professor Sim Kang
Senior Consultant Psychiatrist
Deputy Chief, General Psychiatry Department
Deputy Director, Research Division
Institute of Mental Health

Most of us at various points in our profession will be involved in mentoring either in a formal or informal way. Some of us may be a mentor to juniors in our midst within our vocation and in turn be a mentee to a senior whom we respect and aspire to emulate. This applies to research mentoring as well.

As I reflect and contemplate on this issue of research mentoring and how to do it better, several questions continue to fill my mind such as how can I be a better influence to my mentee (or how I can avoid passing the wrong values to my mentees), what is successful mentoring, how do I confront difficult issues and mentees effectively, what should be reasonable goals and so on.

For those who have been inspired to mentor or be mentored, perhaps abounding questions include how can I find a suitable mentor or mentee and what are common problems faced during mentoring. In this regard, I have found this book entitled "LifeGiving Mentors: A guide for investing your life in others" refreshing and a rich resource of ideas.

The author reminds us to be mindful of the needs of the mentees that are integral to the mentoring journey and how their needs may differ from our preconceived notions of how we were when we started that journey.

As a mentor in the research domain, I am reminded by the author to take note of discovering the strengths of the mentee, determining their focus, discerning their blind spots, and closing the gap between potential and performance or output.

As a mentee, I need to take note that there are no perfect mentors, that I need to ask my mentor to help me ask the right questions in research, develop a discipline to relate to the mentor, and to appreciate that the best mentoring is "intensity in a narrow field" in the areas of learning, practice and assimilation.

The author shares many life examples which should allow some of the principles to stick better in our minds after reading them. Indeed the journey of research mentoring is about helping our mentees through knowing, by showing, to get going and for mentees to see their growth.

I have also realized that three Ps; Process, Preparation and Perseverance, are crucial in this journey, that is, the realization that first, it is a process of learning and relearning, and relating; second, it requires preparation in terms of thoughtful collaborative deliberations about the content of mentoring; and lastly that it takes perseverance and persistence to see it bear fruit. Happy reading and reflecting!

LOCAL TRAINING COURSES

NHG RESEARCH TRAINING CALENDAR

for August - December 2012

Date	Time	Training Programme	Course Category	Module	Venue	No of Seats
Ongoing	00:00 - 23:59	Proper Conduct of Research Online - Basic I & III	Proper Conduct of Research	PC101 & 103	www.elearning.nhg.edu.sg	100
		Proper Conduct of Research – Basic II^		PC102		
17 Aug	09:00 - 18:00	Proper Conduct of Research - Intermediate Workshop		PC201	National University Hospital, Kent Ridge Wing, Level 2, ASTC, STLab	30
22 Aug	14:30 - 17:30	Globalisation of Clinical Trials Forum	-	-	Ren Ci Hospital, Multi-Purpose Hall, Level 4	300
24 Aug	13:00 - 17:45	Manuscript Writing and Presentation Workshop	Research Methodology	-	National University Hospital, Kent Ridge Wing, Level 2, ASTC, STLab	30
14 Sep	12:45 - 17:30	Study Design Workshop		-	National University Hospital, Kent Ridge Wing, Level 2, ASTC, STLab	30
20 & 21 Sep	09:15 – 18:00	Singapore Guideline for Good Clinical Practice	-	SG-GCP	National University Hospital, Kent Ridge Wing, Level 2, ASTC, Seminar Hall	50
28 Sep	08:30 – 17:30	Grant Preparatory Seminar	Research Methodology	RM105E	National University Hospital, Kent Ridge Wing, Level 2, ASTC, STLab	30

For registration and full details, please visit www.research.nhg.com.sg (Training & Education > Search for a Course)

* Dates are subjected to changes without prior notice
^ For more information, refer to (www.research.nhg.com.sg -> Training & Education -> Proper Conduct of Research Courses)

CLINICAL TRIALS ON MEDICAL DEVICES

WHAT YOU NEED TO KNOW ABOUT THE CURRENT CONTROLS AND THE NEW REGULATIONS

The Health Sciences Authority will be introducing new regulatory controls for medical devices investigated in clinical trials. A new piece of subsidiary legislation, the Health Products (Clinical Trials) Regulations, will be promulgated under the Health Products Act. The regulatory scope of this legislation will include medical devices investigated in clinical studies in addition to drug trials, which are currently regulated under the existing Medicines (Clinical Trials) Regulations.

HSA has adopted a risk-based approach in implementing these new requirements and will continue to ensure the requirements are administered in the least burdensome way possible whilst ensuring trial participants are protected.

What are the current regulatory requirements for conducting clinical trials on medical devices?

Under the current Medicines (Clinical Trials) Regulations, a CTC (Clinical Trial Certificate) application is not required for studies assessing the safety, performance or effectiveness of a medical device. It is the sponsor's/ principal investigator's responsibility to seek ethics approval to conduct the trial from the respective IRB(s) (Institutional Review Boards) before commencement of the trial.

Currently, for all medical devices whether they are used in routine practice or in clinical trials, the specific regulatory requirements as per the Health Products (Medical Devices) Regulations 2010 should be followed. The duties and obligations of manufacturers, importers or wholesalers of medical devices that currently applies include:

- Reporting of defects and adverse effects to HSA
- Notification to HSA concerning recall
- Duty to maintain records of supply
- Duty to maintain records of complaints
- Labelling requirements

When will the new regulations for conducting clinical trials on medical devices be implemented?

The new regulatory framework will be implemented upon the introduction of the Health Products (Clinical Trials) Regulations. The target timeline for implementation is in the first half of 2013.

What is the scope of the new regulations?

The scope of the new regulations will include medical devices of a higher risk class (class C & D) regardless of their registration status with HSA. It will exclude medical devices of a lower risk class (class A & B), and "non-invasive " and "non-confirmatory " in-vitro diagnostic products.

How will the new regulations for conducting clinical trials on medical devices be implemented?

The new regulatory controls will be implemented in phases to allow stakeholders adequate time to transit to a full regulatory framework. During the first phase, HSA will administer a CTN (Clinical Trial Notification) system i.e. the sponsor of the clinical trials will be required to notify HSA of their clinical trials assessing the safety/performance of medical device of risk class C & D.

Upon HSA acceptance of the notification, targeted to be within 3 working days, the trial can proceed provided all other applicable requirements such as ethics approvals and contract agreements have been fulfilled.

In the second phase, which will be the full implementation of the regulatory framework, HSA will also introduce the CTA (Clinical Trial Authorisation) system. The CTN system will continue to be applicable for clinical trials investigating registered medical devices, i.e. devices listed on the SMDR (Singapore Medical Device Register).

Sponsors of clinical trials will be required to submit regulatory applications to HSA for clinical trials assessing the safety/performance of unregistered medical device of risk class C & D. This category of applications would be evaluated under the CTA system. An approval is required from HSA before the trial can commence. The target timeline for regulatory evaluation is 30 working days.

How do I apply for the import of an unregistered investigational medical device for clinical trials?

With the full implementation of the regulatory framework for registration of medical devices, import and supply of unregistered medical devices is prohibited. However, import and supply of such devices solely for the purpose of use in clinical trials can be authorised by HSA. Currently, sponsors can submit completed applications of CTM (Medical Devices) for import of unregistered medical devices for use in clinical trials.

The application can be submitted in hard-copy to HSA's Clinical Trials Branch. Upon approval, an import permit number would be indicated on the CTM (Medical Devices) application form. The approval would serve as the regulatory authorisation to facilitate the importation of the unregistered medical device for use in clinical trials. The authorisation of the CTM (Medical Devices) will enable the importer to use it for multiple imports of unregistered medical devices for clinical trial purpose and is valid for 6 months from the date of approval.

Where can further information be obtained?

HSA had conducted a few briefing sessions on the changes to the upcoming regulations specifically on the new controls for medical devices investigated in clinical trials. The presentation slides used in these sessions are available at the following HSA website: http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/clinical_trials/industry_communication.html

There will be more regulatory briefing sessions for stakeholders in Q4 of 2012. So stay tuned!

UPDATES FROM NHG DOMAIN SPECIFIC REVIEW BOARD (DSRB)

Conditionally Registered Doctors as Principal Investigators in Research

A Principal Investigator (PI) must be qualified by education, training and experience to assume responsibility for the proper conduct of a research study and should meet all qualifications specified by the applicable regulatory requirements.

For research proposals submitted to the NHG Domain Specific Review Boards (DSRB) for ethics review, NHG DSRB now allows Conditionally Registered doctors of Levels 2 and 3 supervision to be Principal Investigators of research studies according to the level of risk, as follows:

- For less than minimal risk research studies, Level 2 Conditionally Registered doctors are allowed to be Principal Investigators; and
- For more than minimal risk research studies, Level 3 Conditionally Registered doctors allowed to be Principal Investigators.

Additional conditions required to be fulfilled:

No.	Conditions	Less than minimal risk studies	More than minimal risk studies
1	Doctor's Profile	The doctor must be at Level 2 supervision – i.e. After 0.5 years at Level 1 and received at least "above average" performance grading for the past 6 months.	The doctor must be at Level 3 supervision – i.e. After 0.5 years at Level 1 and received at least "above average" performance grading for L1, and after 1.0 year at L2 and has been ascertained to be ready to work independently, but have yet to fulfill the specified period of supervised practice required for computation towards Full Registration.
2	Commitment of Supervisor	PI's supervisor must declare in writing that: a. She/he is aware of, and supports, the involvement of the Conditionally Registered doctor as PI b. She/he will provide guidance and include research activities in regular progress reports to SMC c. Based on the doctor's current progress and technical and ethical competency, the Conditionally Registered doctor is deemed competent to assume the role of PI and affirm that the Conditionally Registered doctor has adequate medical expertise to provide medical care and make medical decisions for safety and welfare of the subjects	
3	Declaration to SMC	PI declares that his involvement in research as PI has been provided to SMC and no objection has been received from SMC.	
4	DR/IR Approval	Department Representative and Institutional Representative approve the Conditionally Registered doctor to be PI.	

All written documentation (Items 1-3 in the table above) should be attached to the DSRB Application, for DSRB's consideration in the review of the study. The endorsement of the online application on ROAM by the Department Representative and Institutional Representative will be considered proof that Item 4 has been fulfilled (i.e. no separate written documentation required).

For more information, please contact DSRB at +65 6471 3266 or rdo-dsrb@nhg.com.sg.

NHG NEW TEMPLATES: INVESTIGATOR FILE DIVIDERS

A common question asked by investigators, particularly those new to research, is how to create and maintain Essential Documents required for a study.

The Singapore Guideline for Good Clinical Practice (SG-GCP) defines Essential Documents as documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced.

These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of SG-GCP and all applicable regulatory requirements. To assist investigators in creating and maintaining these Essential Documents, NHG has created the Investigator File Dividers template to help investigators who are conducting Investigator-Initiated studies maintain proper research documentation and adhere to high standards of practice in the conduct of human subject research.

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The Investigator File Dividers template has been added to the existing templates available for download on the NHG research website. Besides its primary function to indicate and separate the main sections required in an Investigator File, the dividers of each respective section also provide elaboration on the types of documents to file in each section and list important notes and links to the relevant guidelines for the investigators' easy reference. The File Dividers templates are categorized into 'PI-Initiated Clinical Trials (involving Drug/Device)' and 'Clinical Research (not involving Drug/Device)' with the respective sections below.

Investigator File Dividers
(For PI-Initiated Clinical Trial involving Drug/Device)

- Study Team
- Study Documents
- Institutional Review Board Documents
- Regulatory Documents
- Study Logs and Signed Informed Consent Documents
- Safety Reports
- Investigational Product
- Laboratory & Biological Specimen
- Financial Documents
- Other Documents

Investigator File Dividers
(For Clinical Research not involving Drug/Device)

- Study Team
- Study Documents
- Institutional Review Board Documents
- Study Logs and Signed Informed Consent Documents
- Laboratory & Biological Specimen
- Financial Documents
- Other Documents

Do log on to the NHG Research Website (www.research.nhg.com.sg --> resources) to take a look and utilize this new template for your study soon!

NATIONAL MEDICAL RESEARCH COUNCIL (NMRC) RESEARCH TRAINING FELLOWSHIP 2011

The NMRC Research Training Fellowship is awarded to outstanding and talented clinicians, health science professionals (e.g., nurses, pharmacists) and biostatisticians for overseas research training or to pursue a graduate degree in research in local institutions. Two of our staff have been awarded the NMRC Research Training Fellowship.

Lam Zhan Yang, Max

Research Psychologist, Research Division, Institute of Mental Health

About

Max had a head start by working as a student research assistant at National University of Singapore (NUS) during his undergraduate days. Research had always been an important part of his life because he was interested to know why people behaved and experienced feelings in certain ways.

When psychological illness struck close to home, it crystallised to him a desire to know more, to generate more knowledge so that sufferers can be better understood and therefore, treated differently. He began his career in mental health research after graduation in 2008.

Max was trained and mentored by experienced clinicians and researchers such as Professor Opler, Professor Michael First and Professor Richard Keefe. He feels privileged and honoured to learn and to be able to contribute back to the field by being involved in the Singapore Translational Clinical Research Project (STCRP) as a researcher.

Being a neuropsychological tester and clinical rater allowed him to spend more time with patients and provided glimpses of the world the patients live in.

Finding the Unknown

Max's PhD training with the Department of Psychological Medicine, Yong Loo Lin School of Medicine, NUS started in August 2011, under the National Medical Research Council (NMRC) Fellowship Award. The title of his thesis is "Elucidating the Genetic Architecture of Neuropsychological Performance". The project investigates the genetic make up of neuropsychological abilities and tries to understand whether they are genetic in nature.

We commonly find ourselves trying to remember someone's telephone number or address, pay attention in speeches or lectures, and make complex decisions in our day to day work. These are basic neuropsychological domains and previous twins and family studies suggest that cognition appears to be heritable.

Capitalizing on the advances in genetic microarray technologies, the thrust of his research is to refine the cognitive behavioural measures that have been collected as part of the STCRP in healthy participants.

Thereafter, a scan of the human genome will be conducted, to identify strong associations with certain genes. He believes that this work will support the many cognitive and behaviour genetics work investigating pathological cognitive processes in mental illnesses.

Personal Reflections

The NMRC research fellowship award was very competitive and Max was pleased and grateful to be awarded it. It was a key enabler for him to pursue his PhD training and made him more determined to push the envelope of innovation and science harder, in an attempt to make breakthroughs in research that will set Singapore's psychiatry and psychological R & D on the international stage.

He is extremely thankful to many people and mentors who helped him throughout the journey. Max believes that embarking on PhD training is an essential step in becoming a scientific investigator. At the same time, it is also a decision that will impact one's career and family life.

To him, it is time and energy invested into generating new knowledge: Knowledge that has the potential to make someone else's world a slightly better one. He believes research is an ideal, a belief, a passion and an identity – all of which is lifelong. The scientific and inquisitive mind never really retires.

For people wanting to follow this path of research, he says, "persistence and patience have been in the equation for me. Bite the bullet, don't give up."

Goh Tze Jui

Senior Psychologist, Autism Services, Department of Child and Adolescent Psychiatry, Institute of Mental Health

About

Tze Jui joined IMH in 2006 and is currently a Senior Psychologist with the Neurobehavioral Clinic under Child Guidance Clinic, Department of Child and Adolescent Psychiatry, Institute of Mental Health (IMH).

She works primarily with children and adolescents with an Autism Spectrum Disorder (ASD) who may present with co-morbid mental health issues, in terms of individualised and group sessions as well as in a collaborative format with parents/caregivers and schools with regards to education and supportive work.

She is trained in the administration of standardized assessments instruments such as the Autism Diagnostic Interview – Revised and the Autism Diagnostic Observation Schedule and is part of the multidisciplinary assessment team at Autism Clinic.

As part of her job, she often participates in sharing or mentoring sessions with colleagues, fellow professionals and students through sit-ins and observation sessions. She is also active in research projects on ASD and has

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assumed the roles of Principal Investigator and Collaborators by initiating studies and working jointly with other organizations.

Learning and Working at the Same Time

Tze Jui is currently pursuing her doctoral studies in Clinical Psychology at James Cook University, Singapore, supported by a Fellowship Award from the National Medical Research Council Singapore. She chose to pursue an accredited local degree to being, as physically present in Singapore allows her to continue her on-going research work at IMH.

Her thesis focuses on ASD which is an area she is passionate about. The project is currently in the planning and conceptualisation stage but aims to apply a clinical psychological focus in the management of ASD in Singapore.

Being of a New Challenge

Tze Jui feels that the fellowship award is an encouragement for her and is an acknowledgment of the valuable contribution of Allied Professionals in research areas. The support from IMH and her mentors allows her to initiate research in important clinical areas and also bridges collaboration with external agencies who are also important stakeholders in fields of clinical psychology and areas related to ASD.

Although she has just started her journey of Fellowship training and doctoral studies, she feels that the award has provided her with a new outlook on the landscape for professional development in the field of psychology in Singapore.

It is a strong motivator in encouraging fellow colleagues and juniors from Allied Health professions to participate in research and other areas of clinical work. She encourages practicing psychologists to adopt a clinician-scientist model in their work, which will provide them with the tools and skill sets to engage in evidence-based practice.

RESEARCH TRAINING FELLOWSHIP 2012

Dr Rupesh Agrawal

MMed, FRCS (Glasg), FAMS, Associate Consultant, NHG Eye Institute, Tan Tock Seng Hospital

Developing a molecular-targeted fluorescent probe as the basis for a human retinal leukogram to image the progression of Intraocular Inflammation and Diabetic Retinopathy

2 year full-time fellowship/training leading to a Doctor of Medicine (Research) at University College London (UCL), UK

Experimentation in numerous animal models of retinal vasculopathy and several lines of clinical evidence support the concept that chronic, subclinical leukostasis and subsequent downstream inflammatory processes within the retina are central to the onset and progression of diabetic retinopathy (DR).

Similarly, intraocular inflammation requires long term immunosuppressive therapy which requires to be monitored based on extent of cellular reaction in the retina, vitreous and aqueous humor.

In this project, Dr Rupesh under mentorship of Prof David Shima at UCL would aims to transform a well-accepted research tool, the live assessment in the animal retina of leukocytes in diabetic, inflammatory and angiogenic disease, into a potential biomarker and diagnostic tool to monitor the onset and progression of DR & intraocular inflammation in humans, as well as an essential enabling tool for the development of novel treatments.

The technique would consist of a fluorescent probe administered systemically to bind intravascular leukocytes, and within minutes routine fluorescence ophthalmoscopy will reveal the number of inflammatory cells in the retina—similar to the process for fluorescein angiography.

The aims of this proposed research are to characterize and evolve several fluorescent peptide candidates for their ability to specifically bind human leukocytes in vitro and to select a lead candidate fluorescent peptide conjugate for further development based on the ability to detect leukostasis in the living rodent retina following systemic administration using scanning laser ophthalmoscopy (SLO).

Once Dr Rupesh completes his dissertation on Human retinal leukogram and gets his Doctor of Medicine in Research, the team will compete for further funds from BMRC or NMRC to complete preclinical development and initiate Phase 1 studies which should provide a safety evaluation and initial proof-of-concept data in collaboration with A*Star, IMRE and Singapore Eye Research Institute locally in Singapore.

TTSH Pitch-For-Fund Program

TTSH had launched the inaugural TTSH Pitch-For-Fund Program on 1 September 2011.

The aims of the exercise is to enable TTSH staff to quickly obtain some monies for a small research project so that they can present their preliminary data when they apply for a grant at the national level. The judging consists of two steps. First, the applications are read by a group of judges drawn from the Hospital's Clinical Research Committee. Shortlisted candidates are then asked to present to a panel of judges, without any presentation slides. Two of the judges are non-TTSH.

In the first TTSH Pitch-For-Fund Program in 2011, there were 5 awardees being granted $10,000 for a period of one year. Congratulations to the 5 Awardees - Dr Tan Ern Yu and Dr Pek Chong Han from General Surgery, Dr Rupesh Agarwal and Dr Melissa Tien from Ophthalmology and Dr Stephen Chan from Anaesthesiology.

UPCOMING GRANT CALLS IN SINGAPORE

National Medical Research Council (NMRC) Grants			http://www.nmrc.gov.sg
Grant Name	**Grant Description**	**Funding Quantum**	**Application Date**
Clinician Scientist – Individual Research Grant (CS-IRG)	The CS-IRG is provided to Clinician Scientists to enable them to carry out medical research on a specifically defined topic. All CS-IRG applications will be evaluated through a two stage process with an international peer review stage followed by a Local Review Panel.	Maximum of S$1.5 million per project for 3 years with additional 20% indirect costs.	1st Nov 2012
Clinician Scientist – Individual Research Grant – New Investigator Grant (CS-IRG-NIG)	The CS-IRG-NIG is a subcategory of the CS-IRG to cater for new clinical investigators. The CS-IRG-NIG is a step for the new investigator to a first independent national level grant.	Maximum of S$200,000 per project for 2 years with additional 20% indirect costs.	1st Nov 2012
Cooperative Basic Research Grant (CBRG)	The CBRG is provided to non-clinical researchers to conduct research proposals in basic and translational clinical research. The CBRGs also aims to promote basic biomedical sciences (BMS) research collaborations across institutions in Singapore.	Maximum of S$1.5 million per project for 3 years with additional 20% indirect costs.	1st Nov 2012
Cooperative Basic Research Grant - New Investigators Grant (CBRG-NIG)	The CBRG-NIG Is a subcategory of the CBRG to cater for new non-clinical investigators. The CBRG-NIG is a step for the new investigator to a first independent national level grant.	Maximum of S$200,000 per project for 2 years with additional 20% indirect costs	1st Nov 2012
Transition Award (TA)	The TA is provided to assist budding, young clinicians who have just returned from formal research training, to build up their capability in research. It includes funding support for mentored research project with salary and grant funding for up to three years.	Maximum of S$375,000 per award for 3 years with 20% indirect costs	1st Nov 2012
Clinician Scientist Award (CSA)	The CSA aims to provide salary & funding support for selected outstanding clinician scientists, who possess a consistent record of excellence in research, to enable them to carry out internationally competitive translational and clinical research.	Investigator Category: Maximum of 3 years' salary support and grant support of S$675,000 for 3 years with 20% overhead costs. Senior Investigator Category: Maximum of 5 years' salary support and grant support of S$1.75 million for 3 years with 20% overhead costs.	1st Nov 2012
Health Services Research - Competitive Research Grant – New Investigator Grant (HSR-CRG-NIG)	The HSR-CRG is a MOH research grant established in promote the conduct of HSR and enable the translation of HSR findings into policy and practice. The HSR-CRG-NIG is a subcategory of the HSR-CRG to cater for new investigators. The HSR-CRG-NIG is a step for the new investigator to a first independent national level grant.	As HSR-CRG-NIG is a new grant in 2012, more information on the funding quantum will be provided nearer to the grant call	1st Nov 2012

Agency for Science, Technology and Research (A*STAR) Grant			http://www.a-star.edu.sg
Grant Name	**Grant Description**	**Funding Quantum**	**Application Date**
4th Biomedical Engineering Programme (BEP) Grant Call	The BEP is provided to foster Clinician-Engineer collaborations for development of medical devices and solutions to clinical problems. In particular, it supports collaborative research projects with emphasis on devices, procedures, diagnosis, and clinical systems to improve patient care and cost-efficiency of the healthcare system.	Estimated at between S$250,000 and S$500,000 for up to 3 years.	Dec 2012

Note: More information on the application date will be provided nearer to the grant call

NHG Intramural Grants			http://www.research.nhg.com.sg
Grant Name	**Grant Description**	**Funding Quantum**	**Application Date**
Clinician Leadership in Research (CLR)	The CLR is a 2 year programme that consists of 3 components: Mentorship, Training and Assessment. Successful applicants will explore collaborative opportunities with their nominated mentors and receive seed funding and academic allowances to support these research projects.	Maximum of S$5,000 per year with additional S$500 academic allowance for up to 2 years.	1st Oct 2012
Small Innovative Grant (SIG)	The SIG aims to fund clinically relevant research projects that can contribute directly to improve patient care or to enhance clinical research capabilities in NHG. It is designed to support exploratory and innovative studies with the aim of preparing young investigators to initiate larger investigations and vie for competitive grants on a national level.	Maximum of S$50,000 per year for up to 2 years.	1st Oct 2012

IN FOCUS

NEW NHG GRANTS 2012 - NHG CLINICIAN SCIENTIST CAREER SCHEME (CSCS) & NHG THEMATIC GRANT (NTG)

National Healthcare Group Research & Development Office (RDO) has successfully launched the new NHG Clinician Scientist Career Scheme (CSCS) & NHG Thematic Grant (NTG) for 2012. We are pleased to introduce the 2 new NHG grants in this Catalyst issue, and be sure to catch the next issue for the list of successful applicants!

About NHG Clinician Scientist Career Scheme (CSCS)

The NHG CSCS call for applications started on 9 April 2012 and has received a total of 8 applications. NHG CSCS' short term aim is to develop research capabilities of our clinicians to enable them to compete successfully for NMRC's Transition Award (TA) or Clinician Scientist Award (CSA) in the next 2-3 years. The longer term aim of the scheme is to develop clinician scientists who will contribute to excellence in research innovation and improvement in patient care, delivery and outcomes.

This scheme also provides a customized research career development path for all clinicians in NHG who are interested in embarking a career in research immediately or in the near future. Besides research funding, successful applicants will enjoy the benefit of having mentorship by renowned faculty members and support by the various programs under NHG RDO to facilitate their research. Clinicians may apply under the Junior or Mid-Level Clinician Scientist category. The Junior category is open to AST, Registrars, Senior Residents or equivalent and Mid-Level category is open to Associate Consultant s and above or equivalent. Successful applicants would receive up to 0.4FTE salary support, as well as up to S$180,000 (for Junior category) and S$300,000 (for Mid-Level category) for research support over a maximum of 3 years.

About NHG Thematic Grant (NTG)

The NTG grant call opened on 4 July 2012. Applicants were required to submit the Letter of Intent (LOI) by 25 July 2012 and the full research proposal by 3 October 2012. The aim of this grant is to build up NHG's research capabilities in programmatic areas in order to compete successfully for NMRC's Translational Clinical Research (TCR) or equivalent.

This grant aims to facilitate the discovery and application of basic science ideas relevant to the advancement of health, and to provide productive platforms for collaborations within and outside NHG. Potential applications should also include research projects which span from bench to beside. NTG is open to all clinicians in NHG who possess a strong research track record in translational clinical research. Successful applications will receive up to S$1 million over three years, with a maximum of three sub-projects.

HAVE A QUESTION REGARDING RESEARCH?
Drop us a note at the researchtraining@nhg.com.sg and we'll have it answered by experts in upcoming editions! Here's one from our readers.

HOW DO YOU FORMULATE A RESEARCH QUESTION

Pradeep Paul George, Senior Research Analyst, Health Services & Outcomes Research

Every research starts with a question. The success of any research process relies, in part, on how well investigators are able to translate a clinical problem into a research question—a task that is not so simple.

What is a research question?

A research question is a statement that identifies the phenomenon to be studied. A good research question defines the investigation, sets boundaries and provides direction for data collection and analysis. Developing a researchable question can be challenging if you do not know what you really want. Remember: "A question well-asked is a question well-answered"

Where to start?

Forming and framing the right question should be seen as an iterative process that is well informed by literature and peer inputs. You could provide an angle for your research through insights stemming from your personal experience, contemporary issues and engagement with literature and guidance from mentors / peers. Narrowing, clarifying and even redefining your questions are also part of the iterative process of research question development.

Ask yourself the 5W's (Who, What, When, Where and Why). A strong research idea should pass the "so what" test. Think about the potential impact of the research you are proposing. What is the benefit of answering your research question? Who will it help (and how)? If you cannot make a definitive statement about the purpose of your research, it is unlikely to be funded.

Research directions are not always at the full discretion of the research. Be mindful of the practicalities, appropriateness of the topic, and the ability to get peer/ mentor and funding support.

How to frame the research question?
The PICO approach

PROBLEM	▪ The patient, population, or conditions of your interest.
THE INTERVENTION	▪ This could be, for instance, a treatment or diagnostic test, a prognostic factor, or an exposure.
A COMPARISON	▪ This is usually an alternative intervention with which to compare the intervention of interest. ▪ In studies of treatment effects this will usually be a comparison with accepted standard therapy - or if no such therapy exists then with placebo.
THE OUTCOME OF INTEREST	▪ This could be, for example, pain relief, quality of life or survival. ▪ Defining the outcome precisely is critical as sample size for the research study and statistical methods are determined by this.

A well-structured research question should usually contain four parts and be contained within a single sentence. The process of framing a research question can be summarized by remembering the acronym PICO - Problem, Intervention, Comparison and Outcome.

Example: In adults, is binge drinking compared with no binge drinking associated with an increase in mortality?

PICO	Elements
Patient	Adults
Intervention	Binge drinking
Comparator	No Binge drinking
Outcome	Mortality

What are the characteristics of a good research question? "FINER" the better

The FINER criteria state that a research question must be feasible, interesting, novel, ethical, and relevant. When you think you may have a good idea/ question, apply the "FINER" criteria to it to see if the question is good enough.

Components	Question
F - Feasible	Is the question answerable? Do you have access to all the materials you will need to do the study? Do you have access to enough subjects? Will you have enough time and money? Do you have the expertise to do this study or can you collaborate with someone who does?
I - Interesting	The question has to be interesting to the investigator, but should also be interesting to others.
N - Novel	Has this study been done before? Does it add to the current body of medical knowledge?
E - Ethical	Can the study be done in a way that does not subject subjects to excess risks? Will an IRB approve the study?
R - Relevant	Will it further medical science? Will the results change clinical practice, health policy or point towards further avenues of research?

If your question fails on any one of these 5 criteria, it is probably not worth putting much effort into.

Conclusion

It is hard to formulate a good answer to a bad question, so spending time on formulating and refining an interesting, important, well-structured, ethical, and practical research question is worthwhile. It will influence the choice of study design, the interpretation of results and the writing-up of the research report.

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To find out more information on health services research, please visit www.hsor.nhg.com.sg or email hsor@nhg.com.sg

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