Issue 40 Mar - Apr 2020

A Newsletter For The Research Community In Singapore

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Launch of Singapore's First Brain Bank

Prof Richard Reynolds (Director of Brain Bank Singapore) (leftmost) addressing distinguished guests at the launch of the brain bank

On 27 November 2019, **the tripartite partners of Brain Bank Singapore – NTU Lee Kong Chian School of Medicine (LKCMedicine), National Neuroscience Institute (NNI), and National Healthcare Group (NHG) – launched Singapore's first donor-based research brain bank at Flexispace, Medical Library, Clinical Sciences Building at HealthCity Novena.** Officiated by Guest-of-Honour Associate Professor Benjamin Ong, former Director of Medical Services, Ministry of Health, the launch ceremony was attended by an audience of over 100 guests, including the leadership of NTU, LKCMedicine, NHG, SingHealth and NNI.

Click *here* to find out more.

Results for the NHG CMTi-NHIC Joint MedTech Grant Call 2019

In May 2019, NHG Centre for Medical Technologies & Innovations (CMTi) launched the NHG CMTi-NHIC Joint MedTech Grant Call, co-funded by National Health Innovation Centre (NHIC) Singapore.

The grant call was open to staff holding primary appointments with NHG institutions. The grant aims to fund the development of technological solutions that is commercially viable to resolve unmet needs in healthcare, and to leverage on the outcomes of this seed funding to seek further competitive funding at the national level to bring the solutions to implementation.

After a rigorous evaluation by the panel, a total of 5 applications were selected for funding.

Congratulations to the following successful grant awardees!

Principal Investigator	Project Title	Institution
Dr How Kwang Yeong	SERA, Surgical Enhanced Recovery Assistant (Mobile App Development for ERAS patients)	TTSH
Prof Steven Thng	Developing the Handheld Confocal Raman for In-Vivo Study of Skin Biochemistry: A Prospective Clinical Study on Effects of Moisturisers on Skin Biochemistry	NSC
A/Prof Tey Hong Liang	Alleviation of Procedure-Related Pain Using a Non-Invasive Vibratory Device	NSC
Dr Tan Siyun, Lucinda	Artificial Intelligence-Incorporated Automated Attachable Dermatoscopy for Bedside Algorithmic Diagnosis of Melanoma	NSC
Dr Aung Myint Oo	Pilot Project of a Modular Assembled, Multiple Surgical Procedures Training Simulator	TTSH

To find out more about the NHG CMTi-NHIC Joint MedTech Grant Call, please click *here*.

Contributed by:
CMTi Office, Group Research, NHG

DID YOU KNOW?

Self-Management Interventions in Young Adults with Diabetes

Did you know that existing self-management interventions in young adults with diabetes have no improvements on their clinical outcomes, lifestyle behaviours, mental health and quality of life?

Click *here* to read now!

Life of a Research Assistant in IMH

When my seven-year-old niece asked what I do at work a few months ago, I told her that I read and write for a living. Indeed, March 2019 saw the publication of my commentary on peer support in Singapore, and 28 August 2019 marked the publication of my first original article about binge drinking among Singapore residents. **I spent a substantial amount of time this year reading about peer support and binge drinking; and writing manuscripts and replies to reviewers. Outside the office, I can be found in IMH's outpatient clinics trying to recruit participants for various studies.**

At the moment, I am part of the recruitment team for a study on smoking habits among IMH patients. In another study, I am recruiting participants for a study on post-traumatic growth in persons with psychosis. During the design of this study, I combined both my life experiences and knowledge from existing literature on post-traumatic growth to build the research premises. **The primary aim of the post-traumatic growth study is to explore the possibility of growth from first episode psychosis in the local first episode psychosis patient population, and to understand the facilitators and barriers to growth of psychosis.** Together with the team from the research department, we also embarked on a systematic review to build a conceptual framework for mental healthcare peer support.

I am grateful for the opportunities that I have received from my department. Their openness to ideas and different perspectives allowed me to bring a patient's perspective to various projects, value-adding to the multi-disciplinary team here. I am also glad to be able to put my research training to good use. In many ways, working in this department is like coming full circle after my personal struggles with a mental illness while completing my doctoral degree in neurobiology.

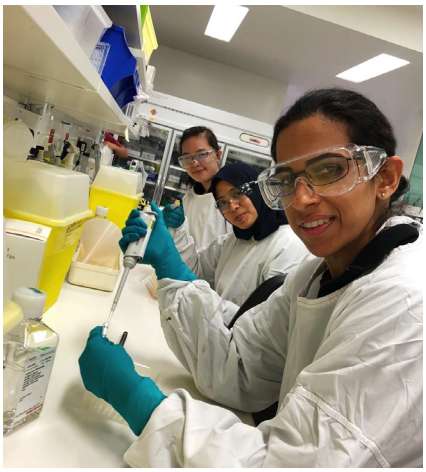
Contributed by:
Ms Lee Ying Ying
(in picture)
Research Assistant
Research Division
Institute of Mental Health

My Research Journey

Clinical medicine as we know it today stands on the shoulders of prior clinicians and scientists who invested their time and creativity to discover the pathophysiology of disease, develop interventions to cure or manage disease and improve health. I am incredibly fortunate to have been able to lead my own small research project during my Infectious Diseases Fellowship at the Mayo Clinic (Rochester, MN) mentored by Prof Gregory Poland (Mary Lowell Leary Emeritus Professor of Medicine and Director, Mayo Vaccine Research Group). I was able to foster my curiosity while working on an important clinical question/problem via an influenza vaccine translational research project. I enjoyed working in the lab, interacting with other scientists and learning more about translational research.

When I returned to Singapore in 2015, I wanted to be able to continue participating in clinical/translational research. **My passion has been in vaccine-preventable diseases which is very relevant in Singapore and our region.** I reached out to various colleagues with my proposed study idea and was fortunate to be able to form a study team. I was supported and mentored through the process of **grant application in the NHG-LKCMedicine Clinician-Scientist Career Scheme (CSCS).** We recruited participants (older adults) from the community for an influenza vaccine immune response project that aims **to evaluate metabolic predictors associated with vaccine response (Evaluation of Metabolic Predictors of Influenza Vaccine Immune Response in the Singapore Elderly Population – the DYNAMIC trial).** It was an incredible journey to conduct this trial at various community sites in Singapore. I presented the preliminary findings from our study at the European Congress of Clinical Microbiology of Infectious Diseases in Amsterdam in 2019, and the Options X conference for the Control of Influenza in Singapore.

We will be delving deeper, seeking to evaluate other immunometabolic factors associated with immune response, made possible by the NMRC-funded CS-IRG New Investigator Grant in 2019. I have realised that collaboration and team-science is integral to discovery and in the process of leveraging discoveries to improve health despite all the hurdles and obstacles one might face. I am grateful to NHG, TTSH Department of Infectious Diseases, my colleagues, my mentors A/Prof Yeo Tsin Wen (Senior Consultant, NCID and Associate Professor of Infectious Diseases) and others, study team, collaborators at Singapore Immunology Network (SIgN), community sites and of course the study participants.



From left: Ms Rachel Lim Liyu (Research Assistant), Ms Nurhidayah Binte Mohamed Yazid (Research Assistant), and Dr Sapna Sadarangani conducting haemagglutination inhibition assays in WHO Collaborating Centre for Reference and Research on Influenza (VIDRL), Melbourne, Australia, as part of the CSCS project

Contributed by:
Dr Sapna Sadarangani
Consultant
NCID / TTSH

Comparative Genetic Architectures of Schizophrenia in East Asian and European Populations

The human DNA represents the code of life. Our height, weight, personality, health and mental well-being is shaped by the biology underlying human life. **The human DNA plays an important contributing role to psychiatric illnesses. Family studies of schizophrenia suggest that schizophrenia is highly heritable.** The illness is profoundly debilitating and challenging to treat. Aside from distressing symptoms, such as hallucinations and delusions that accompany the illness, cognitive impairments, lowered quality of life, side effects from psychiatric medication are some of the many challenges that patients who suffer from schizophrenia and their caregivers have to face.

Identifying genes that might give rise to schizophrenia is one of the starting points to which scientists, and clinicians could identify new and more effective medications that could relieve symptoms related to schizophrenia, or rescue cognitive disabilities that accompany such severe mental illnesses. Most large schizophrenia genetic studies have studied people of primarily European ancestry, potentially missing important biological insights. A few years ago, a global team of scientists and clinicians came together, determined to identify genes that could predispose one to schizophrenia. Further, we sought to compare if the genes that gave rise to schizophrenia were similar for individuals of European and Asian ancestry.

In the first data freeze of the project, we obtained data from 58,140 participants of Asian ancestry (22,778 schizophrenia cases and 35,362 controls), identifying 19 regions **in human DNA that are associated with schizophrenia. We also found that genetic variants that confer risk for schizophrenia have highly similar effects in those of East Asian and European ancestry,** indicating for the first time that the genetic basis of schizophrenia and its biology are broadly shared across these world populations. We further extended these efforts, working with colleagues who are part of the Psychiatric Genomics Consortium. We combined our results with the team that studied schizophrenia genetics in European ancestries and **found that 176 regions in the human DNA (53 new) were related to schizophrenia,** implicating hundreds of genes.

Our team also **developed new state of art statistical methods that more precisely isolated schizophrenia causal alleles in 70% of these regions.** We envision that these results would guide and facilitate further experiments within the scientific community studying the biology of schizophrenia. Risk prediction models across populations did not perform as well as models that were ancestry specific, highlighting the importance of including all major ancestral groups with sufficient sample size to ensure the findings have maximum relevance for all populations. Data collection for the next data freeze is currently ongoing.

Lead analysts, Dr Max Lam and Dr Chia-Yen Chen, (Postdoctoral research fellow, Analytic and Translational Genetics Unit and the Psychiatric and Neurodevelopmental Genetics Unit, Massachusetts General Hospital) along with the Principal Investigator, Dr Hailiang Huang, (Instructor, Analytic and Translational Genetics Unit, Massachusetts General Hospital) received **the Elliott Gershon Paper of the Year Award at Anaheim, California** during the World Congress of Psychiatric Genetics on behalf of the global team of scientists and clinicians who contributed to this crucial research effort for psychiatric genetics.

Contributed by:
Dr Max Lam
Research Fellow
Research Division
Institute of Mental Health

Dr Chia-Yen Chen and Dr Max Lam were awarded the 2019 Elliot Gershon Paper of the Year Award

Beginning a Research Odyssey

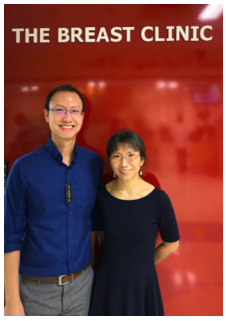
Research is a rather perilous road, full of many unknowns to the young and uninitiated. I was fortunate to be given the opportunity to embark on this journey as an FY16 NHG-LKCMedicine Clinician-Scientist Preparatory Programme (CSPP) awardee. **The CSPP provided a rigorous framework of basic and advanced courses in research, research mentorship, and funding for a research study of choice.** With the support of the General Surgery department and my colleagues, I was able to spend time in the laboratory doing translational research.

My CSPP project was titled **"Characterisation of patient derived xenograft (PDX) models to better understand tumour progression".** Under the guidance of my mentor Dr Tan Ern Yu, we established human xenografts of breast tumours in mouse models. This study confirmed that tumour xenografts changed with growth passage in the mouse models, acquiring characteristics that are distinct from the original tumours, and evolving into a more aggressive and self-renewing phenotype.

While my subsequent research projects are not related to breast cancer, the experience in CSPP and time spent in the lab was invaluable. **No experience is wasted.** I am now working with a team to establish a rodent model of bariatric surgery to better study the pathways through which weight loss and improvement of diabetic control is achieved after bariatric surgery. We have also been awarded the National Medical Research Council (NMRC) Clinician Scientist-Individual Research Grant (New Investigator Grant) to perform a randomised controlled trial to study the effects of intra-gastric Botulinum Toxin A for weight loss.

Some say that research is formalised curiosity, but it is the start that requires the greatest effort. Joining a programme like CSPP and having a great mentor made my beginning to this journey much easier.

Contributed by:
Dr Danson Yeo
Associate Consultant
General Surgery
TTSH



Dr Danson Yeo (in picture with his mentor Dr Tan Ern Yu) is an FY2016 awardee of CSPP. Click here to find out more about the Programme.

Caregiver-centric Screening Tool for Identification of At-risk Family Caregivers

Family caregivers of dependent older adults often experience high levels of stress due to the demands of their caregiving role. However, active support for such 'invisible patients' is currently limited. **To enable the routine identification of distressed caregivers, our team sought to develop a caregiver screening tool suitable for use in the acute care setting.**

From 2015 to 2017, our nurse-led team surveyed 274 pairs of family caregivers-dependent older adults who were hospitalised in Tan Tock Seng Hospital (TTSH). Our study showed that **one-third of these family caregivers were at risk of depression, had high anxiety levels and poor quality of life. We also found that family caregivers' perceived burden and personal mastery can affect their psychological health and quality of life.** Family caregivers with lower levels of mastery reported higher levels of caregiver burden, anxiety and risk of depression. These findings highlighted the need for greater emphasis on psychological factors throughout the caregiver support process, from identification of at-risk caregivers to the provision of appropriate interventions.

Consequently, we developed a brief 11-item caregiver-centric screening tool, incorporating both protective factors and risk factors, for the early identification of at-risk family caregivers of hospitalised care-dependent older adults. **Ours is the first caregiver-centric screening tool that integrates the construct of mastery with caregiver burden and relevant caregiver characteristics.**

Translating our findings to practice, our team has initiated a caregiver support pilot project at TTSH, focusing first on persons with dementia. In this pilot, the caregiver-centric screening tool is incorporated into patients' routine discharge planning evaluation. Family caregivers identified by the tool as being at high-risk of depression are subsequently directed to receive further assistance. In addition, our team is also currently exploring the use of psychoeducational interventions that may increase caregivers' coping ability.

Illustration of the Caregiver Support Process in TTSH's pilot project

Contributed by:
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Mr Melvin Lim
Research Executive,
Department of Nursing Service, TTSH

Novel Association between Genetic Risk Factors and Diabetic Kidney Disease Progression

Type 2 diabetes (T2D) is a leading cause of kidney disease in Singapore. **We previously found that the Asian-specific T2D risk allele, PAX4 R192H, was associated with younger onset of diabetes in our Chinese T2D patients.** Given that a younger onset of diabetes also implies a longer disease duration and therefore an increased risk to complications, **we sought to determine the effect of this genetic variation (present in Chinese and Malay) on diabetic kidney disease (DKD) progression.**

575 Chinese and Malay patients aged 21-85 with an average follow-up of 3.1 years from our Singapore Study of Macro-Angiopathy and Micro-vascular Reactivity in Type 2 Diabetes (SMART2D) cohort were included in the analysis. DKD progression was defined according to KDIGO guidelines i.e. 25% decline from baseline eGFR (<15 ml/min/1.73m^2 excluded) with worsening of eGFR categories. Cox regression was used to investigate the association of the R192H risk allele and DKD progression, with adjustment for demographics, diabetes duration, clinical parameters and medication.

Our findings were as follows:

1. **Patients with one PAX4 R192H risk allele were 1.78 times more prone to DKD progression than patients with wildtype alleles.**
2. **Patients with two PAX4 R192H risk alleles were 3.85 times more prone to DKD progression than patients with wildtype alleles.**
3. **Malay patients were independently associated with 1.84 times higher risk of DKD progression as compared to Chinese patients.**
4. **In addition, higher levels of non-genetic risk factors including HbA1c, systolic blood pressure, baseline eGFR and ACR were also independently associated with DKD progression.**

In conclusion, we found that PAX4 R192H genetic variation is associated with DKD progression in our Chinese and Malay T2D patients. **Determining the genetic and non-genetic risk factors that contribute to DKD progression will be helpful for identification of high-risk patients for appropriate intervention in their disease management.** Our future directions would be to validate these observations and evaluate the inclusion of PAX4 R192H in the development of a risk prediction model for DKD progression in our local population.

This study was awarded the Singapore Young Investigator Award - Bronze at the Singapore Health and Biomedical Congress (SHBC) 2019 Scientific Competition. Please click here to view all award winners.

Contributed by:
Dr Ang Su Fen
Senior Research Officer
Clinical Research Unit
KTPH

My PhD Journey - Development and Clinical Evaluation of Accurate Audiometry Outside of Sound Treated Facilities

The World Health Organization estimates that over **5% of the world's population** (466 million people) suffer from **disabling hearing loss**, defined as HL >40 dB and >30 dB in the better hearing ear in adults and children respectively. The prevalence of disabling HL rises sharply to 30% among older adults aged over 65 and the majority of those affected are from South Asia, Asia Pacific and Sub-Saharan Africa.

According to the 2016 Global Burden of Disease study, **"age-related and other hearing loss" has been identified as the third leading cause of years lived with disability (YLDs) globally**. This translates to 36.3 million YLDs shared amongst 1.27 billion people with varying degrees of HL worldwide and represents 4.5% of all YLDs. The global annual social-economic costs of disability and handicap from untreated hearing loss is estimated to be USD750 billion and has been labelled a **"silent epidemic".**

Addressing the global burden of hearing impairment is severely hampered by the lack of access to expensive `sound treated' audiometry facilities, which are almost exclusively built into healthcare facilities in urban areas. **Having witnessed the poor availability of hearing health during volunteer medical work with poor communities in neighbouring countries, I was inspired to make a difference.**

Through the award of an **NHG-LKCMedicine Clinician-Scientist Fellowship (CSF)** to pursue a **PhD with LKCMedicine,** I had the opportunity to develop and evaluate an audiometry test using innovative applications of noise attenuation technologies with ambient noise monitoring, to help overcome this barrier and to make accurate hearing assessment available for all. I was fortunate to have my supervisors, Prof Gan Woon Seng (Professor, NTU School of Electrical and Electronic Engineering (NTU EEE)) and Prof Teoh Swee Hin (Professor, School of Chemical and Biomedical Engineering, NTU) for the development of a concept prototype to be subsequently validated in real human subjects. Balancing clinical work and research was indeed challenging, but the sacrifices are worthwhile if we get to benefit others ultimately.

Dr Ho Eu Chin is an FY2017 awardee of NHG-LKCMedicine CSF. Click here to find out more about the programme.

Contributed by:
Dr Ho Eu Chin
Senior Consultant
Otorhinolaryngology
TTSH

Inaugural TARIPH Publications Workshop and TARIPH COPD Symposium

Prof Wisia Wedzicha sharing about her research with workshop attendees

Prof Wisia Wedzicha (LKCMedicine Visiting Professor and Clinical Chair of Respiratory Medicine at Imperial College, London), conducted her inaugural visit to LKCMedicine from 2- 6 December 2019. Over her week-long visit, Prof Wedzicha led The Academic Respiratory Initiative for Pulmonary Health (TARIPH)'s inaugural Publications workshop on 3 December at the Clinical Sciences Building together with Asst Prof Sanjay Chotirmall (LKCMedicine Assistant Professor and Provost's Chair in Molecular Medicine, LKCMedicine), who is also an Associate Editor of the American Journal of Respiratory and Critical Care Medicine (AJRCCM). Prof Wedzicha was also the keynote speaker at the TARIPH COPD Symposium on 4 December, which drew a crowd of more than 65 senior healthcare professionals, researchers and industry partners with interest in COPD research and clinical care from across Singapore.

Click here to find out more.

Training Calendar

Date	Training Courses	Course Provider
Monthly	Good Clinical Practice (Online)	NHG Group Research
	(PCR100) Study Start-Up: Budgeting, Case Report Form Design and Database Design*	
	(PCR200) Study Conduct I: Subject Recruitment and Informed Consent*	
	(PCR300) Study Conduct II: Documentation, Safety Reporting and Investigational Products*	
	(PCR400) Monitoring, Audits and Inspections*	

*Blended learning courses involving Online Lectures coupled with a Classroom Workshop on a stipulated date.

Dates are subject to changes without prior notice.

For registration and full details on courses by:
~ NHG Group Research, please visit www.research.nhg.com.sg
(Training & Education → Register for Courses and Other Events)

CHICKEN SOUP FOR THE BUSY COORDINATOR

Education to facilitate high standards of research conduct

1. **Nov 2019: How Should Consent Be Obtained From Subjects Lacking Mental Capacity?**
2. **Dec 2019: How to Manage Voice Recordings of Research Participants (Identifiable Information / Data)**
3. **Jan 2020: How to Set Up a Tissue Bank?**

Click on the respective issues to find out more!