

e-catalist ACCELERATING RESEARCH

The "Sweet Story" Behind Arterial Stiffness in People with Type 2 Diabetes



The Equine Connection



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Strengthening Our Community's Resilience Against Threats from Emerging infectionS (SOCRATES)



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Dissolving
TriamcinoloneEmbedded
Microneedles for the
Treatment of Keloids



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RESEARCHER'S FEATURE

Research and Clinical Work Are Not Mutually Exclusive: They Can Co-Exist and Complement Each Other - The Story of Dr Geoffrey Tan



RESEARCH EDUCATION

- Research Training Events
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NHG-LKCMedicine Research Career Development Programmes Results For Call For Applications

Congratulations to the following Awardees!

NHG-LKCMEDICINE CLINICIAN-SCIENTIST FELLOWSHIP (CSF)



Dr Benjamin Lam*
Consultant
Department of Family & Community Medicine
Khoo Teck Puat Hospital

Investigation of Environmental, Genetic and Gut Microbial Factors Underlying Obesity Amongst Chinese, Malays And Indians In Singapore

NHG-LKCMEDICINE CLINICIAN-SCIENTIST CAREER SCHEME (CSCS) – FY 2019



Dr Etienne Wang Consultant Department of Dermatology National Skin Centre

Role of Macrophages in Human Hair Cycling And Alopecia

For more information, please visit www.research.nhg.com.sg (Grants & Programmes → Research Career Development)

*NMRC Research Training Fellowship (RTF) Awardee - Click here to find out more about the NMRC RTF

Outcomes of NMRC May 2018 Call for Applications

Congratulations to our NHG researchers who have received the National Medical Research Council (NMRC) Talent Development Awards during the May 2018 NMRC grant call. The results were announced between October - November 2018.

Name	Institution	Project Title	NMRC Grant/Award
A/Prof Angela Chow	TTSH	Patient, Physician, and Organizational Factors Influencing Decision-Making for Antibiotic Use, and N-of-1 Trials of Interventions to Improve the Decision-Making	Clinician Scientist Award – Investigator Category
Dr Benjamin Lam	КТРН	Investigation Of Environmental, Genetic And Gut Microbial Factors Underlying Obesity Amongst Chinese, Malay And Indians In Singapore	Research Training Fellowship
Dr Bryan Tan	TTSH	Collaborative Model of Care between Orthopaedics and Allied Healthcare Professionals Trial (CONNACT)	Research Training Fellowship
Dr Michael Yam	TTSH	Sarcopenia Prevention And Reversal with physical Training And Nutrition in distal radius fracture patients (S.P.A.R.T.A.N trial)	Research Training Fellowship

To find out more about NMRC Talent Development, please click here.

<u>Strengthening Our Community's Resilience Against</u> <u>Threats from Emerging infectionS</u> (SOCRATEs)

Emerging infectious diseases know no borders; Singapore has experienced and continues to face threats from a host of such agents. These emerging infections and their spread to Singapore is dependent on multiple factors but a key element to reduce the risk of such infections spreading within Singapore and to mitigate any impact from their spread, is the "resilience" of the community against such threats.

Intended as a long-term (5-10 years) programme at National Centre for Infectious Diseases (NCID), it aims to address key gaps in pandemic preparedness, planning and response by assessing risk perception and knowledge, communication of risk and the

necessity of outbreak interventions among the general population in Singapore.

Led by investigators based at NCID, in collaboration with experts within key partner institutions in Singapore, the research programme will establish and maintain a cohort of individuals, who are representative of the Singapore population, in order to conduct studies to assess our community's resilience and test health interventions against different emerging infections throughout the continuum of pandemic phases.

Recruitment of the cohort will take place in various waves with the first wave commencing

in the first quarter of 2019 and being conducted by a group of fourth-year medical students from the Yong Loo Lin School of Medicine, National University of Singapore. Subsequent waves will be performed to enlarge the cohort in either the later half of 2019 or first half of 2020.



We would like to acknowledge the Estate of Ong Tiong Tat and Irene Ong-Tan Liang Kheng for its kind donation towards this research programme

Contributed by:

The Safety of Continuing Sodium-glucose Co-transporter-2 (SGLT2) Inhibitor during Ramadan Fasting in Muslim Patients with Type 2 Diabetes

Sodium-glucose co-transporter 2 (SGLT2) inhibitors, a new class of oral anti-diabetic drug with rapidly increasing use, could potentiate the risk of ketoacidosis and dehydration during Ramadan fasting due to its mechanism of action. However, the available evidence on its use during Ramadan fasting is limited. Hence, we undertook a prospective observational controlled cohort study in 2017 to evaluate the safety of continuing SGLT2 inhibitors during Ramadan fasting in Muslim patients with Type 2 Diabetes.

Findings from our study showed that continued use of SGLT2 Inhibitor treatment during Ramadan in patients with Type 2 Diabetes did not increase risk of ketonemia, hypoglycemia and dehydration as compared to those patients not on SGLT2 inhibitor. However, careful pre-Ramadan assessment and education, including hydration advice, is still required for all patients as Ramadan fasting itself is associated with significant changes in weight, blood pressure and Estimated Glomerular Filtration Rate, regardless of whether the patient was on SGLT2 inhibitor treatment. Further details can be found from our research paper published in Diabetes Research and Clinical Practice.

"This is the first time I am a principal investigator, and it provided me an opportunity to have deeper understanding of the whole research process from planning, conducting, data analysis and manuscript preparation. I am grateful for the opportunity and very appreciative of the guidance from senior clinicians from diabetes centre".

-APN Shao Yanli (Advanced Practice Nurse, Admiralty-Diabetes Centre, Khoo Teck Puat Hospital)

"Participation in this project provided me with insights into the processes involved in clinical research. I am also very grateful to Dr Angela Moh who supervised me in performing the beta-hydroxybutyrate assays. I am also glad that these findings will be useful in patient-care, and that we have played a small part in adding on to the knowledge of medicine."

-Gwyneth Joy Lim (Medical Student, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore)









KTPH / Admiralty Diabetes Centre Study Team From left to right (Top): Ms Gwyneth Joy Lim, APN Shao Yanli(Pl), APN Chua Chin Lian, A/Prof Sum Chee Fang, (Bottom) Dr Serena Low, Dr Ester Yeoh, Dr Wong Yip Fong.

Contributed by:

Ms Shao Yanli

Advanced Practice Nurse

Admiralty Diabetes Centre

KTPH

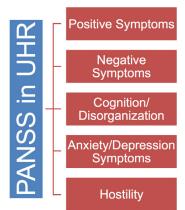
Ms Gwyneth Joy Lim Medical Student LKCMedicine, NTU Singapore

Factor Structure Of The Positive And Negative Syndrome Scale (PANSS) In People At Ultra High Risk (UHR) For Psychosis

The Positive and Negative Syndrome Scale (PANSS) is a comprehensive psychopathology assessment scale. Its factor structure has been robustly demonstrated in populations with schizophrenia. In recent years, it has also been used in the Ultra-High-Risk (UHR) population. The UHR population defines a group of individuals with attenuated psychotic symptoms and some degree of functional impairment. However, no study has examined the dimensional structure of PANSS in UHR, which hinders the understanding and measurement of clinical symptom dimensions manifested in people with UHR. This paper aimed to examine the dimensional structure of the PANSS in a UHR sample.

The study sample consisted of a group of participants with UHR (n = 168) from the Longitudinal Youth at Risk Study (LYRIKS). LYRIKS is a prospective, observational study assessing the risk factors of psychosis. The participants were evaluated on PANSS, the Comprehensive Assessment of At-Risk Mental States (CAARMS), Calgary Depression Scale for Schizophrenia (CDSS), Beck Anxiety Inventory (BAI), Brief Assessment of Cognition in Schizophrenia (BACS), and Global Assessment of Functioning (GAF).

We performed Exploratory Factor Analysis (EFA) to identify the PANSS factorial structure and the following five symptom factors were derived:



This 5-factor solution showed good concurrent validity as shown by the strong associations between the PANSS positive factor and the CAARMS composite score, PANSS mood factor with depression and anxiety score, as well as the PANSS cognitive/disorganization factor with cognitive performance measured by

BACS. Among the five factors, positive symptoms, negative symptoms and anxiety/depression factors, were the factors that were associated with functioning. UHR individuals who had more severe positive, negative and mood symptoms had lower level of functioning.

To the best of our knowledge, this is the first paper reporting on the PANSS factor structure in UHR individuals. The 5-factor PANSS model demonstrated good construct validity and is associated with functioning. The present PANSS factorial structure can be adopted in research studies or in a clinical setting to comprehensively evaluate psychopathology along dimensions in the UHR population.

For more information about the study, please click <u>here</u>.



Contributed by:
Ms Yang Zixu
Senior Research Psychologist
Research Division
IMH



Dissolving Triamcinolone-Embedded Microneedles for the Treatment of Keloids

Patients with keloids typically seek treatment to reduce the size of the scars, or when the lesions are painful and itchy. Currently, patients visit National Skin Centre (NSC) on a monthly basis to receive injections of triamcinolone, a corticosteroid, into the elevated scars. Repeated doses over a prolonged period of time are required to progressively reduce the size of the keloids. As keloids are sensitive in nature, high levels of pain during injection are a deterrent to many patients receiving treatment. Children, for whom pain-inducing treatments are not feasible, typically are not able to receive an effective treatment, as there are no good alternatives.

Recognising a deficiency in good treatment options for this common affliction, we developed an innovative method that uses the technology of dissolving microneedles. The dissolving microneedles are composed of hyaluronic acid, a natural ground substance of the skin, and serve as a carrier to deliver the medication under the surface of the affected skin.

Subsequent to preclinical and clinical studies, a clinical trial was conducted. Volunteers suffering from keloids were taught to self-administer

triamcinolone-embedded dissolving microneedles onto one of their keloids daily for a month and the elevated volume of the keloid was monitored using a high-resolution 3D scanner. The trial was conducted over two phases, using two doses of the medication. Results revealed that there was a significant reduction in keloid volume after the treatment and this reduction was greater with the higher dose of medication used. There were no side effects, in particular infection and contact dermatitis, amongst the subjects. All the subjects who completed both phases of the trial, felt that the treatment was not painful and 88% of the subjects felt that it was more convenient compared to their previous monthly injections at a dermatologist's clinic.

Our primary aim is to provide keloid sufferers who are unable to undergo current conventional therapies an avenue of treatment. The new treatment modality also serves as an additional treatment option for keloid patients in general.

The single-use circular dissolving microneedle patch is to be applied onto the keloid scar for two to three minutes each day. Inducing minimal or no pain, the treatment can be used in patients with sensitive keloids and in children

(although the labelled age of the medicine is 6 years and above). The patients can administer the treatment themselves; this saves them the time and cost of making regular trips to NSC for injections, and makes treatment accessible to patients residing far away or overseas.

As this use of dissolving microneedles to treat a disease in humans is the first of its kind in the world, a patent application has been filed. The dissolving microneedle patch is expected to be made available on a prescriptive basis at the NSC at the end of 2018. This project is funded by the National Medical Research Council Transition Award.

Asst Prof Tey is a recipient of the <u>NMRC</u> <u>Transition Award (TA)</u> and FY2013 awardee of the <u>NHG-LKCMedicine Clinician-Scientist Preparatory Programme (CSPP)</u>. Click on the respective links to find out more.



Contributed by:

Asst Prof Tey Hong Liang
Head of Research & Senior
Consultant, NSC
Assistant Professor,
LKCMedicine, NTU Singapore

Integrating Research into Practice – Finding the Right Synergy

As a family physician, I feel that my industry scope goes beyond clinical practice to include finding potential gaps in the health care -so as to improve healthcare practice and delivery. This will benefit both the providers and the patients, and in turn, make the system more efficient. One way to achieve this is to integrate research with our practice and harness the complementarity of both aspects.

After completing my residency in Family Medicine, I got to know of the NHG-LKCMedicine Clinician-Scientist Preparatory Programme (CSPP), while embarking on further training in the Fellowship in the College of Family Physician Singapore (FCFPS). I grabbed this opportunity to develop my research skills and explore potential gaps in one of my areas of interest, which is post-stroke secondary prevention.

Stroke is one of the top contributors of burden of disability-adjusted life-years (DALYs) worldwide and within Singapore. Moreover, after an acute stroke event, post-stroke patients have an

increased risk of recurrence with poorer health outcomes. More patients are surviving the acute event, highlighting the need for optimal secondary prevention measures. Patients have an important role in adhering to the recommendations provided by the clinical guidelines. More importantly, family physicians have an imperative role to engage the post-stroke patients and their caregivers, to help them adhere to these recommendations, so as to ultimately pursue and achieve their own personal goals in life.

Our study aims to explore quantitatively the achievement of treatment goals for secondary prevention of major cardio, or neurovascular ailments in patients with a previous stroke. We also know that patients and caregivers face multiple challenges which might hinder the optimal practice of secondary prevention. Therefore, acknowledging the importance of patients' and their caregivers' perspectives, we will explore the experiences of post-stroke patients and their caregivers in

adopting practices related to secondary prevention. This will enable us to have a more complete understanding of the issues surrounding post-stroke care.

Like any project, it requires perseverance and passion, and I hope that our findings can benefit the wellbeing of our patients and their caregivers, by providing useful insights for health professionals towards management of post-stroke patients in primary care.

Dr Vivek Bansal is an FY2018 awardee of CSPP. Click <u>here</u> to find out more about the programme.



Contributed by: **Dr Vivek Bansal** Family Physician NHGP



Choroidal Vascularity Index (CVI) as a Measure of Vascular Status of the Choroid: Measurements in Healthy Eyes from a Population-Based Study

Find out more about the study establishing a normative database for CVI and how to identify factors associated with CVI in healthy eyes.

Click here to read now!



Increased arterial stiffness is an early marker of atherosclerosis in Type 2 Diabetes (T2D). Hyperglycemia may cause vascular damage through formation of advanced glycation endproducts (AGEs), such as pentosidine. Pentosidine may lead to vascular injury through the regulation of matrix metalloproteinases (MMPs). However, the relationship between AGEs & MMP and arterial stiffness is unclear. Therefore, we studied the relationship between these biomarkers and arterial stiffness (estimated by central aortic Augmentation Index (AI)) in our cohort - the Singapore Study of Macro-Angiopathy and Micro-vascular Reactivity in Type 2 Diabetes (SMART2D), among 440 participants recruited between 2011 and 2014.

Advanced Glycation Endproduct (AGE): a heterogenous group of glucose-modified amino acids formed by non-enzymatic glycation and oxidation (glycoxidation) reactions between carbohydrate-derived carbonyl compounds and protein amino acids.

Metalloproteinase (MMP): a family of zinc binding proteolytic enzymes that normally remodel the extracellular matrix.

Augmentation Index (AI): a surrogate measurement of wave reflection and arterial stiffness derived from central arterial pressure waveform.

In our study, we observed the following:

- Pentosidine was negatively correlated with MMP-2 even after adjusting for demographics and demographics and clinical covariates with β=-1.33 (p=0.022).
- MMP-2 remained significantly associated with higher AI even after adjusting for demographics and clinical covariates.

The association between pentosidine and decreased MMP-2 production could be explained by a couple of key mechanisms.

- Glycation induced cross-linking formation may have altered the mechanical integrity of the fibrillar collagen, which in turn, inhibits MMP-2 processing on the collagen fibrils.
- Pentosidine may have potentiated the short term effect of hyperglycemia, thereby leading to increased tissue inhibitor of MMP and decreased activity of MMP. This was demonstrated by the significant negative correlation between HbA1c and MMP-2 (β =-0.119, P=0.012) in our study.

MMP-2 may lead to increased arterial stiffness by pro-inflammatory events (e.g. disruption of equilibrium between MMP-2 and tissue inhibitors of metalloproteinases) and disruption of the cross-linking of collagen and elastin with resultant accumulation of stiffer, uncoiled collagen.

In conclusion, diabetic vascular injury may involve extracellular matrix modelling, which is a potential therapeutic target. Going forward, we aim to further investigate other important related questions - for instance, how glycemic burden leads to arterial stiffness and how arterial stiffness can mediate other diabetic complications.



Research Team
From left to right: A/Prof Lim Su Chi,
Mr Chan Zit Liang, Mr Darren Yeo, Dr Ang Su Fen,
Dr Serena Low, Dr Zhang Xiao, Dr Keven Ang,
Ms Clara Tan, Dr Sharon Pek (Not in photo)

Contributed by: **Dr Serena Low** Consultant Clinical Research unit KTPH

Research and Clinical Work Are Not Mutually Exclusive: They Can Co-Exist and Complement Each Other

The Story of Dr Geoffrey Tan

Ever wondered what clinician-scientists do and why some doctors choose to embark on this path towards research? Dr Geoffrey Tan (Associate Consultant, Department of Mood & Anxiety, IMH) provides some insights to these questions in a candid interview featured in the Jan/Feb 2019 issue of NHG Education's LearniNHG newsletter.

Click <u>here</u> to find out more!



Opening of Symposium by Prof James Best (Dean, LKCMedicine)

Antimicrobial Resistance in the Asia-Pacific & its Impact on Singapore Symposium

A series of lively discussions and workshops on the fight against "Antimicrobial Resistance (AMR) were featured in the "AMR in the Asia-Pacific and its Impact on Singapore" symposium hosted by LKCMedicine. LKCMedicine Dean Prof James Best kicked off the event by congratulating the organising committee for the collaborative effort in his opening remark. During the symposium, Assoc Prof Benjamin Ong (Director of Medical Services, Ministry of Health, Singapore), delivered his speech on the challenges of AMR. Prof Leo Yee-Sin (Director of National Centre for Infectious Diseases) gave a speech on the national role and responsibility of the National Centre for Infectious Diseases (NCID). Click https://

CSPP: An Excellent Step Forward

Twenty years. That's how long ago my first taste of clinical research was. As a first-year junior college student back then, I assisted in data collection for a research study in helicobacter pylori-related gastritis at the National University Hospital. That was the initial catalyst that really piqued my interest and inspired me to constantly seek opportunities to participate in various research projects during my medical school and post-graduate years.

In 2014, after returning from my Health Manpower Development Programme (HMDP) fellowship at St John's Institute of Dermatology in London, I came across an advertisement on the Clinician-Scientist Preparatory Programme (CSPP) and wasted little time in signing up. To me, it was an invaluable opportunity to strengthen my core research skills and knowledge, particularly in areas of research methodology, biostatistics and ethical framework. With dedicated protected time to

attend a series of instructive workshops spread over two years, research mentorship, as well as generous funding for a research study of my choice, joining CSPP turned out to be an excellent step forward.

My research study pertained to a clinical comparison of narrowband ultraviolet B (NBUVB) versus combined ultraviolet A and B (UVAB) phototherapy in the treatment of atopic dermatitis. I was fortunate to have the support of A/Prof Tan Suat Hoon and the senior management at National Skin Centre (NSC), an esteemed research mentor Asst Prof Tey Hong Liang and a capable multidisciplinary study team. The comprehensive CSPP training instilled me with greater confidence as a principal investigator to lead and carry out the project from start to finish. It was also the springboard for me to obtain larger research grants of up to \$200,000 and become a mentor to one of our current CSPP awardees, Dr Sophie Cai.

There is always so much to learn in healthcare and so much more than we can potentially learn from our patients. Through continued innovative research, we will be able to unlock precious new medical knowledge that will benefit not just our current population, but generations beyond. For anyone who is looking to upgrade his/her research skills, I would highly recommend joining the CSPP.

Dr Tan is an FY2015 awardee of CSPP. Click here to find out more on the programme.



Contributed by: Dr Eugene Tan Consultant



Opening of Conference by conference Co-Chairpersons: Prof Naomi Low-Beer (Vice-Dean (Education), LKCMedicine) and Mr Martin Lupton (Vice-Dean (Education), Imperial College School of Medicine)

Inaugural Transform MedEd Launches to Great Success

A two-day conference on the future of medical education was recently jointly organised by LKCMedicine and Imperial College School of Medicine. For a look at what the education landscape holds for medical educators, medical students and healthcare professionals, click here to find out more.

The Equine Connection

Using horses as a form of therapy for youths may be unheard of by many, but it is actually becoming more popular with schools in Singapore, which are turning to horse-assisted learning programmes to improve their students' social and emotional well-being.

By getting youths to work and care for horses, these youths build up social-emotional skills and learn valuable life skills, which they carry over to their daily lives.

Dr Ho New Fei from the Institute of Mental Health (IMH), Research Division, will be conducting a prospective study of equine-assisted learning on social and emotional functioning in youths. She had been successfully awarded the Singapore Millennium Foundation (SMF) Research Grant in October 2018.

The SMF Research Grant Programme

Funded and managed by a local non-profit philanthropic organisation, the

Foundation Innovates, the SMF Research Grant Programme promotes research in the areas of Learning & Pedagogy, Palliative Care, and Food Supply Resiliency & Bio-Mimetics.

While horse-related interventions are communitybased and personal accounts on their impact on socio-emotional wellbeing are effusive, there remains a lack of rigorous evidence on their benefits.

The research team will prospectively study the effects of a horse-assisted learning programme conducted by Equal-Ark Singapore Ltd. The team will adopt a neuroscience approach in determining whether short-term horse-assisted learning improves resilience and socioemotional functioning in at-risk youths, by looking at their socio-emotional outcomes and related brain patterns over time.

Why This Study Matters

The reasons as to why youths fare poorly in the

mainstream curriculum vary, but there are evidence that these youths are at a higher risk for subsequent psychopathology and poor psychosocial functioning that extends into adulthood, including mental health issues and future unemployment. As such, seeking sustainable ways within the community to instill lifelong competencies in these at-risk youths is critical.



Dr Ho New Fei Research Fellow Research Division

Contributed by:

My Research Sojourn

Clinical care always brings up more questions on the why, how and what we can do better, and investigator-led research allows these important questions to be answered. The Tan Tock Seng Hospital's Department of Infectious Diseases provides many opportunities to participate in research and actively encourages research interests. Senior clinicians provided guidance on various research projects and the department supported me in joining the Clinician-Scientist Preparatory Programme (CSPP) in 2017 which provides structured training. The CSPP is a fantastic programme that provides crucial foundation skills and knowledge to be a primary investigator, much needed administrative support for first-timers and a modest fund. This allows us to conduct a research project of our own choice and passion. Generating a hypothesis, conceptualisation and execution of the research project, and analysing the data brings about its own unique rich rewards. The results of my CSPP project were presented at the 28th European Congress of Clinical Microbiology and Infectious Diseases.

CSPP also provides comprehensive career guidance and advice. With the completion of CSPP, I decided to pursue further research training with the support from the department and senior residency programme and I had applied successfully with the National Medical research Council (NMRC) Research Training Fellowship (RTF) and LKCMedicine PhD by Research programme. Research is exhilarating, and to paraphrase Star Trek,

akin to standing at the edge of the frontier and boldly going where no one has gone before. It is trying to chart out the unknown, to build our knowledge base to enhance patient clinical care. I would like to thank the CSPP programme for the opportunities provided, the Infectious Diseases (ID) department and everyone who has guided me this far.

Dr Chia is an FY2017 awardee of CSPP. Click here to find out more about the programme.



Contributed by: **Dr Chia Po Ying** Associate Consultant Infectious Disease Physician NCID/TTSH

Training Calendar				
Date	Training Courses			
Monthly	Good Clinical Practice (Online)			
	(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*			
25 Apr 19	Basic Biostatistics			
16 May 19	How to Start a Research Project? (1)	CRIO		
22 May 19	Research Preparatory & Study Design			

Qualité (Issue 36, Mar 2019)

Education to facilitate high standards of research conduct

- 1. COMMON OBSERVATIONS FROM MONITORING VISITS: ESSENTIAL DOCUMENTS AND INVESTIGATOR FILE
- 2. CASE STUDY: WHO CAN CONDUCT SUBJECT RECRUITMENT IN A STUDY

Coming soon in early March

Stay tuned to this page for updates!

*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 Research & Development Office (RDO), please visit www.research.nhg.com.sg (Training & Education → Register for Courses and Other Events)
- ~ TTSH CRIO, please contact Ms Siti Aisha Binte Jaffar Siti_Aisha_JAFFAR@ttsh.com.sg