

Research and  
Innovation for the

# Future of Healthcare





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# MESSAGE FROM CHAIRMAN

## COLLABORATIONS AND INNOVATION FOR CHANGE

Since its establishment in 1994, NMRC has been a major driver of medical research through the provision of research funds and scholarships to build and strengthen medical research in Singapore. In 2006, the Ministry of Health established a new mandate to support translational and clinical research and NMRC is leading, promoting and coordinating the funding, including creating inter-disciplinary partnerships and international collaborations.

Besides providing grant and infrastructure support, NMRC has emphasized and nurtured talent to drive translational research in Singapore. As research and innovation moves to clinical translation and application, it is now also important to foster clinician innovators. The Clinician Innovator Development Award (CIDA) was hence launched in 2018, to support clinician innovators with both grant and salary support towards the development of innovative medical technology. With the expectation that the awardees would be able to bring their ideas to the next level and apply for grants for proof-of-concept, such as the National Health Innovation Centre (NHIC) Innovation to Develop (I2D) grant and the Innovation to Startup (I2Start) programme.

Over the years, the Government's efforts to build up and develop basic research infrastructure has formed a firm foundation for translational research. In this next phase the focus is to move the research to the bedside.

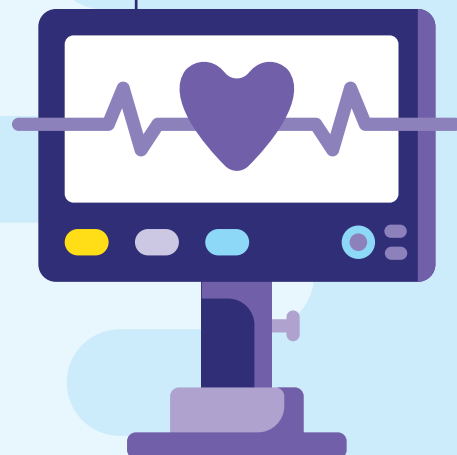
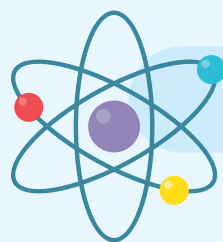
As we commence preparations for RIE2025 planning, I am hopeful to the integration of the respective areas of expertise in closely-knitted fashion, and look forward to greater achievements harnessed including impactful research, for the benefit of Singapore and Singaporeans.

**Prof Ranga Krishnan**

Chairman NMRC

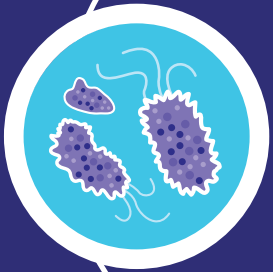
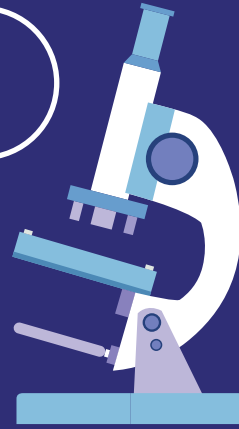
“

*In order to make breakthroughs and push excellence peaks further, a marriage between research and innovation is required to translate into a thirst for new knowledge and insights”*





ABOUT



NMRC

Established in 1994, the National Medical Research Council (NMRC) oversees the development and advancement of Translational and Clinical Research (TCR) in Singapore. Awarding competitive research funds to public healthcare institutions, programmes and projects, NMRC supports the development of core clinical research infrastructure. Additionally, NMRC also supports the development of clinician scientists through awards and scholarships and fosters interactions and knowledge exchange within the clinical and research community.

In 2006, the Ministry of Health (MOH) established a new mandate to support TCR in areas where Singapore has great potential. With this in mind, NMRC's role is even more important in leading, promoting, coordinating, and funding TCR in Singapore. Aligned with this aim, NMRC-funded research has led to interdisciplinary partnerships and international collaborations, helping to boost the role played by Singapore's biomedical sector on the global stage.

The Research, Innovation and Enterprise 2015 (RIE2015) plan aimed for greater integration of activities across the Biomedical Sciences (BMS) community, including public-private partnerships, hospitals and government agencies. NMRC spearheads these investments to realise long-term health and wealth outcomes.

Under the RIE2020 Plan<sup>1</sup>, Singapore saw continued support for research, with an increase in investment from \$16 billion in the previous tranche to the current \$19 billion. Funding was prioritised in four strategic technology domains where Singapore had competitive advantages and/or important national needs, including Health and Biomedical Sciences (HBMS). NMRC is one of the beneficiaries of this boost in funding, reinforcing the Council's mandate as the champion for translational and clinical research in Singapore.

NMRC spearheads MOH's vision for healthcare research to deliver better health and wealth outcomes for Singaporeans. To better realise the goals of HBMS in RIE2020, five therapeutic areas of focus have been identified by MOH as national priorities. These are (i) cancers, (ii) cardiovascular diseases, (iii) diabetes mellitus and other metabolic / endocrine conditions, (iv) infectious diseases, and (v) neurological and sense disorders. Besides supporting top-down directed strategic research, NMRC also funds bottom-up investigator-led research through various competitive funding schemes. In 2013, the National Health Innovation Centre (NHIC) Singapore was established to coordinate across the industry cluster to support a vibrant ecosystem comprising local enterprises, start-ups and multinational corporations.

Human capital continues to play a key role in the success and growth of Singapore's TCR industry. A critical mass of clinician scientists in tandem with thought leadership, is crucial to drive the translation of bench discoveries to bedside and clinical applications.

With this in mind, NMRC has also stepped up efforts to support clinician scientists and grow talent through research grants, human capital awards and talent development programmes.



<sup>1</sup> RIE2020 Info from NRF Website: <http://www.nrf.gov.sg/research/rie2020>

# NMRC BOARD

The NMRC Board advises the Council on the formulation of strategies and priorities to promote excellence in translational and clinical research in Singapore, with the objective of improving human health. In overseeing the implementation of the research programmes approved by MOH and the HBMS Executive Committee, the Board ensures that the Council meets its mission and key performance targets.

The Board also ensures that governance frameworks are in place, such that NMRC's budget is effectively managed and utilised optimally. As of FY2019, the NMRC Board comprises 18 members.



**Prof Ranga Krishnan**  
Chairman,  
National Medical Research Council



**A/Prof Tan Say Beng**  
Executive Director,  
National Medical Research Council



**Prof Edward Holmes**  
Advisor, National Research Foundation  
and Senior Fellow, Agency for Science,  
Technology and Research (A\*STAR)



**Prof Ivy Ng**  
Group Chief Executive Officer,  
SingHealth



**A/Prof Benjamin Ong**  
Director of Medical Services,  
Ministry of Health



**Prof John Wong**  
Chief Executive,  
National University Health System





**Prof James Best**  
Dean, Lee Kong Chian  
School of Medicine,  
Nanyang Technological University



**Mr Jean-Luc Butel**  
Global Health Care Advisor  
and President, K8 Global



**Dr Cheong Wei Yang**  
Deputy Chief Executive Officer,  
National Research Foundation



**A/Prof Chong Siow Ann**  
Vice-Chairman of Medical Board  
(Research), Institute of Mental Health



**Prof Chong Yap Seng**  
Dean, Yong Loo Lin School of Medicine,  
National University of Singapore



**Prof Thomas Coffman**  
Dean, Duke-NUS Medical School



**Prof Ian D Graham**  
Professor, School of Epidemiology, Public  
Health and Preventive Medicine, School  
of Nursing, University of Ottawa



**Prof Lim Tock Han**  
Deputy Group CEO  
(Education & Research),  
National Healthcare Group Singapore



**Prof Michael Merson**  
Vice President & Vice Provost for Global  
Affairs, Wolfgang Joklik Professor of  
Global Health



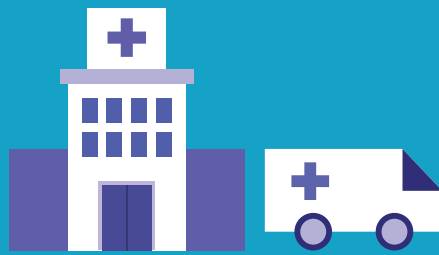
**Dr Benjamin Seet**  
Executive Director,  
Biomedical Research Council,  
Agency for Science, Technology and  
Research (A\*STAR)



**Prof Wong Tien Yin**  
Medical Director,  
Singapore National Eye Centre



**Prof Yeoh Khay Guan**  
Deputy Chief Executive,  
National University Health System



NMRC RIE2020



FUNDING



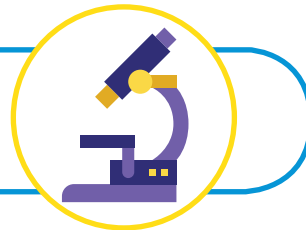
PORTFOLIO

Under the RIE2020's HBMS Domain, NMRC will continue to drive translational and clinical research through sustained and strategic investment in **three key areas**:

### Human Capital & Talent Development Programmes



- Singapore Translational Research (STaR) Investigator Award
- Clinician Scientist Award (CSA)
- Transition Award (TA)
- Clinician Innovator Development Award (CIDA)
- Clinician Scientist & Clinician Investigator Salary Support Programme (CS/CISSP)
- NMRC Research Training Fellowship
- MOH Healthcare Research Scholarship – Master of Clinical Investigation (MCI)



### Research Grants

#### NMRC-FUNDED

- Centre Grant (CG)
- Clinical Trial Grant (CTG)
- CS-Individual Research Grant (CS-IRG)
- CS-Individual Research Grant-New Investigator Grant (CS-IRG-NIG)
- Health Services Research Grant (HSRG)
- Health Services Research New Investigator Grant (HSRG-NIG)

#### OPEN FUND

- Large Collaborative Grant (LCG)
- Individual Research Grant (IRG)
- Young Individual Research Grant (YIRG)

### Knowledge Enablers & Infrastructure Grants



- Bioethics Advisory Council (BAC)
- Centre of Biomedical Ethics (CBmE)
- Clinical Research Coordinators (CRC)
- Health Sciences Authority Cell Therapy Facility (HSA CTF)
- Institutional Review Boards (IRBs)
- Investigational Medicine Units (IMUs)
- National Health Innovation Centre Singapore (NHIC)
- National Large Animal Research Facility (NLARF)
- Research Space Funding (RSF)
- Singapore Clinical Research Institute (SCRI)



**HUMAN CAPITAL**

  
**& TALENT**



**DEVELOPMENT**

**PROGRAMMES**





# NURTURING A VIBRANT COMMUNITY OF CLINICIAN SCIENTISTS

Manpower is one of three cross-cutting programmes under the RIE2020 framework. Singapore aims to nurture a sustainable pipeline of skilled clinician scientists to advance strategic goals across the health and biomedical sciences sector.

Clinician scientists play a critical role in translational and clinical research: Their first-hand interaction with patients enables them to identify gaps in detection, diagnosis and treatment of diseases; while their scientific expertise allows them to frame these clinical insights into pertinent research hypotheses. NMRC recognises the need to train and develop clinician scientists who are able to plug these knowledge gaps and, over time, develop breakthrough research that translates into impactful health outcomes.

To help Singapore nurture a vibrant community of clinician scientists, NMRC has in place various human capital awards and talent development programmes to support clinician scientists through their clinical and research progression.



# HUMAN CAPITAL

## SINGAPORE TRANSLATIONAL RESEARCH (STaR) INVESTIGATOR AWARD

The prestigious STaR Investigator Award is the most prestigious award amongst the human capital awards. Designed to attract and nurture world-class clinician scientists to undertake cutting-edge translational and clinical research in Singapore, the STaR Investigator Award provides up to five years of funding for salary and grant support.

## TRANSITION AWARD (TA)

The TA is designed to help budding clinician scientists who have just completed formal research training. This award provides research funding and salary support to help recipients build up their research capabilities, facilitating their transition to stable, independent research roles, which in turn, enhances their ability to successfully obtain independent research support in the future. The TA is non-renewable and awardees are encouraged to apply for national-level independent, research grants going forward.

## CLINICIAN SCIENTIST AWARD (CSA)

The CSA is structured to develop local research talent and provide clinician scientists valuable protected time to focus on their research. The Senior Investigator (SI) tier of the CSA, offers up to five years of funding, to support senior doctors actively involved in highly productive research. The Investigator (INV) tier offers three years of funding and targets younger doctors with the potential to become independent investigators.

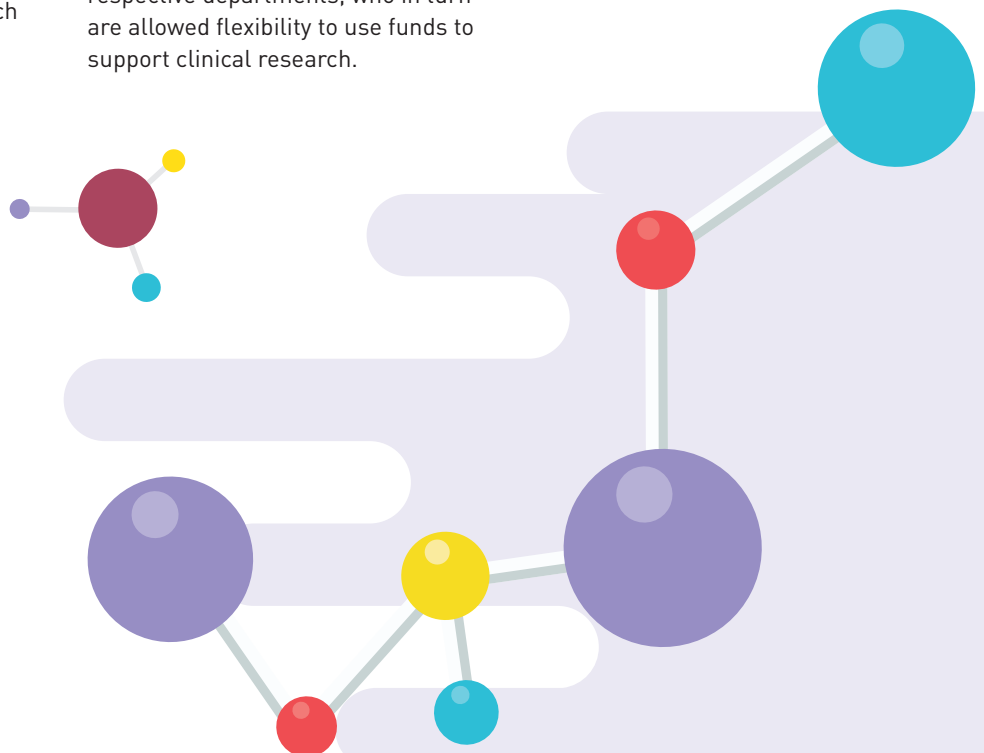


## CLINICIAN SCIENTIST/ CLINICIAN INVESTIGATOR SALARY SUPPORT PROGRAMME (CS/CISSP)

The CS/CISSP supports clinical research by providing salary support or full-time equivalent (FTE) for clinicians to do research. In recognition of support received from clinical departments for their clinicians' time and participation in research, the funding award is channelled to respective departments, who in turn are allowed flexibility to use funds to support clinical research.

## CLINICIAN INNOVATOR DEVELOPMENT AWARD (CIDA)

The CIDA is a pilot programme introduced to support clinicians with medical innovation ideas. Through the provision of seed fund and salary support, the clinician innovators could generate pilot data and scale their ideas to the next level. The award is non-renewable and recipients are required to apply for follow-on funding.



## SINGAPORE TRANSLATIONAL RESEARCH INVESTIGATOR AWARD RECIPIENTS



**Prof  
Toshio Suda**

**Senior Principal  
Investigator,**  
*Cancer Science  
Institute of  
Singapore*

**Professor,**  
*National University  
of Singapore*

### Expansion of Hematopoietic Stem Cells by the Modulation of Mitochondrial Metabolism

Our ongoing studies conducted under the STaR project (2013-2018) have discovered that the micro environment directly alters hematopoietic stem cell (HSC) metabolism and their fate – either to self-renew or to differentiate into mature cells. Our data suggests that appropriate regulations of the metabolic state of hematopoietic stem cells (HSCs) may allow HSCs to self-renew and expand.

For the STaR project renewal (2019-2024), we propose to build on existing findings, and expand the following areas that will impact clinical implications in terms of HSC expansion for application in disease settings.

The difficulty in recapitulating HSC self-renewal in vitro is mainly due to the difficulty of inhibiting their differentiation under normoxic culture conditions containing growth factors.

This suggests that, unlike embryonic stem (ES) cells and induced pluripotent stem (iPS) cells, HSCs cannot be expanded in vitro by self-renewal divisions.

Our novel and innovative approach differ from the cytokine-based culture and can complement the previous approach. This project will focus on the metabolic regulation of HSCs and optimising the environment surrounding the stem cells for efficient self-renewal. We hope to cultivate the most advantageous system for the ex vivo expansion of HSCs.

### Early Detection and Novel Treatment Through Epigenomic Studies in Endemic Asian Cancers

It is well-known that Asian-prevalent cancers are often associated with a pathogen or carcinogen. For example, hepatocellular carcinoma (HCC) is associated with Hepatitis B and C viruses, gastric cancer with *Helicobacter pylori*, and nasopharyngeal cancer with Epstein-Barr virus.

Increasingly, more and more studies are pointing towards epigenomic changes that are associated with chronic carcinogenic exposures – these causative changes may be manipulated not only for diagnostic detection but also for therapeutic intervention using emerging epigenetic drugs.

For scientific studies, we propose to examine the underlying epigenomic changes related to chronic exposure to their respective carcinogen – liver fluke (*Opisthorchis viverrini*) for biliary tract cancer (cholangiocarcinoma) and aristolochic acid for hepatobiliary cancer.

Specifically, we will profile and study DNA and histone modifications as well as RNA-Seq (expression) in these cancers and carcinogen exposure in model systems, on both the bulk and single-cell level. For translation studies in biomarker development, we will focus on DNA hydroxy-methylation and methylation, and non-coding RNA (e.g. miRNA, lncRNA) all of which can be further validated in a very large number of liquid samples like plasma and urine.

These biomarkers will have potential for both early -detection screening and disease monitoring. For translation studies into novel drug development, we will focus on epigenetic targets and epigenetic drugs.

These findings, coupled with further molecular, biochemical, proteomic, in vitro and in vivo studies will hopefully, shed light on how chronic exposures of these agents contribute to epigenomic changes, and subsequent tumorigenesis.

Our studies will also allow us to explore the accumulative strength of combining epigenetic drugs and other forms of treatment modalities.

Through these studies, we will take our research to greater heights, from new breakthroughs to translating research findings, clinical applications, and preventing or reducing cancer risks in different populations.

**Prof  
Teh Bin Tean**



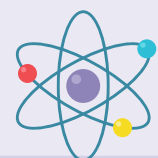
**Deputy Director (Research),**  
*National Cancer Centre Singapore*

**Deputy Director (Scientific),**  
*SingHealth Duke-NUS Institute  
of Precision Medicine*

**Professor,**  
*Duke-NUS Medical School*

**Senior Principal Investigator,**  
*Cancer Science Institute of Singapore*

**Senior Principal Investigator,**  
*Institute of Molecular and Cell Biology*





**Prof Daniel G Tenen**

*Professor,  
Department of  
Medicine, Yong  
Loo Lin School of  
Medicine, National  
University of  
Singapore*

*Director,  
Cancer Science  
Institute of Singapore*

**Targeting Transcription Factor Pathways in Liver Cancer**

Our long-term goal is to translate knowledge on cancer and transcription factors into clinical applications and therapies.

Our overall hypothesis, it will take a combination of targeted therapies, including those aimed at transcription factors, to effectively treat cancer. For this STaR application, we propose

to focus on two transcription factors -- the oncofetal protein SALL4, and the tumour suppressor CEBPA -- for selectively targeted therapies in hepatocellular carcinoma (HCC), a critical disease in Singapore with dismal prognosis and no effective drug therapies.

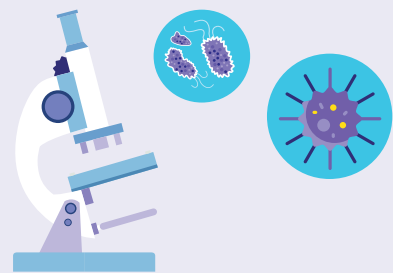
SALL4 is not expressed in most normal adult tissues. It is expressed in approximately 30% of cancers, including HCC. Specifically, we propose the following aims:

- (i) In order to develop small molecules targeting SALL4 in liver cancer, we will optimise and further develop SALL4 inhibitor compound leads using structure-based drug discovery, develop SALL4 degraders, and define the mechanism(s) of the inhibitor and degraders in SALL4-mediated HCC.
- (ii) We will also develop novel RNA-based therapies targeting the transcriptional network of SALL4 and CEBPA in HCC by:
  - Investigating the mechanism of CEBPA short-activating RNA (saRNA) therapeutics in HCC

- Defining the therapeutic effects of SALL4 siRNA in HCC and comparing them against small molecule inhibitors and degraders
- Defining the therapeutic effects of combination therapy of CEBPA-activating RNA and SALL4 siRNA (sasi)
- Clustered regularly interspaced short palindromic repeats (CRISPR)-based novel RNA therapeutics in HCC.

This proposal will involve cross-interactions with scientists, clinicians at the National University Hospital, and industry partners.

Successful outcomes, will lead to novel therapeutics that target pathways not engaged by other therapeutic approaches.



**Prof Karl Tryggvason**

*Professor,  
Programme in  
Cardiovascular &  
Metabolic Disorders,  
Duke-NUS Medical  
School*

**Laminin-based Human Embryonic Stem Cell Differentiation and Cell Therapy Approaches for Diabetic Complications**

The goals are to develop new cell therapy-based treatments for prevention and treatment of diabetes complications, which cause loss of insulin production, severe skin ulcers, retinopathy and non-alcoholic liver disease and fibrosis.

We elucidate the mechanisms of islet cell proliferation using transcriptome and single-cell RNA-seq of islets and cells cultured on bio-relevant laminins.

Using laminin-based methods, we aim to generate human embryonic stem cell (hESC) derived islet cells, keratinocytes, endothelial cells and hepatocytes for treatment of diabetes and its complications.

These methods, many of which were developed in our lab, have been successfully used to generate other types of cells. We will continue a phase 1 clinical trial for burn wound treatments with our novel method to culture skin keratinocytes.

Using whole transcriptome and single-cell RNA-seq analyses, we will decipher the expression signatures and pathways of proliferating islet cells to identify which genes are needed to turn on cell proliferation, which can help identify drug targets that increase islet cell mass.

We have already shown the power of several cell type-specific laminins to induce and maintain stable differentiation of hESC to e.g. endothelial cells, cardiomyocytes, retina RPE and photoreceptors, as well as to culture human skin keratinocytes without feeder cells -- this has not been possible before.

We are convinced that we will be able to generate new knowledge about islet biology and in vitro generation of islets that can be translated into a new regenerative medicine approach to treat diabetes.

We have already succeeded in attracting a major pharmaceutical company to use our stem-cell differentiation methodologies for development of therapeutic cells for the respective diseases.

This project is both novel and feasible, and it may strengthen Singapore's position in diabetes care and regenerative medicine.





**Prof  
David M Virshup**

**Professor & Director,**  
*Programme in Cancer  
and Stem Cell Biology,  
Duke-NUS Medical  
School*

### Understanding and Targeting Wnt Signaling

Wnt signaling is required for normal development and self-renewal of adult tissues but is dysregulated in many diseases. Over the course of the previous STaR awards, my lab has contributed to our understanding of Wnt biology and pathophysiology.

In collaboration with the A\*STAR Experimental Therapeutics Centre, we developed ETC-159, a highly effective inhibitor of the PORCN gene, which blocks Wnt secretion. ETC-159, now in clinical trials, has great potential to treat Wnt-addicted cancers. It is also a powerful tool to gain a new understanding of Wnt biology.

Here, we propose to build on our prior work on Wnt secretion and Wnt signaling. We will better define which patients might benefit clinically from PORCN inhibitors by studying the role

of RNF43 mutations in human cancers.

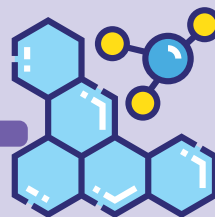
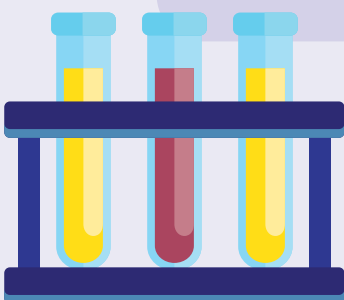
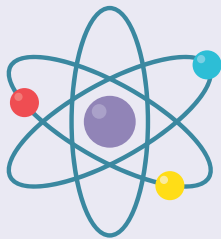
In the last grant period, we characterised how pairs of Wnts could work together via Wnt synergy. Here, we will exploit new findings that provide novel insights into downstream mechanisms and novel Wnt receptors involved in this Wnt synergy.

Our studies of Wnt secretion revealed that essential Wnts in the gut come from intestinal stromal cells rather than epithelial cells; here we extend those studies to characterise these Wnt-producing cells in normal tissues and in cancer.

We have carefully assessed the consequences of PORCN inhibition in normal and cancer cells in vivo. Among our key findings, the unexpected result that Wnt signaling represses differentiation signals in both normal and malignant tissues.

Better understanding of the underlying mechanism of this process has the potential to provide key insights into how Wnt signaling controls the balance between proliferation and differentiation.

This current proposal builds on the collaborations and tools generated over the past grant period to translate new knowledge on Wnt secretion into therapeutic advances.



## CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR) RECIPIENTS



**A/Prof  
Mark Chan  
Yan Yee**

**Senior Consultant,**  
*Department of  
Cardiology, National  
University Heart  
Centre Singapore*

**Associate Professor,**  
*Department of  
Medicine, Yong  
Loo Lin School of  
Medicine, National  
University of  
Singapore*

**Deputy Director  
(Clinical Research  
Matters),**  
*Cardiovascular  
Research Institute,  
National University  
Health System*

### **PASSivation of Vulnerable plaques with Alirocumab in acuTE coronary syndrome (PASSIVATE)**

Acute myocardial infarction (AMI), which is caused by thrombotic occlusion of a destabilised coronary atherosclerotic plaque, is one of the top-four rapidly growing diseases in Singapore. Worryingly, mortality within 30 days after an AMI in Singapore is about 1.5 to 2 times greater than in other high-income countries.

We aim to investigate whether a potent cholesterol-lowering monoclonal antibody, alirocumab, can stabilised vulnerable coronary plaques in patients and how treatment with alirocumab modifies the circulating lipidome and proteome.

The methodology will include a randomised controlled trial in which patients recently hospitalised for AMI at 3 hospitals will be randomly assigned to 14 months of alirocumab (N=100) or a placebo (N=100).

Selected patients will undergo hybrid 18F-NaF position emission tomography-computed and tomographic coronary angiography at a baseline of 14 months and 28 months, paralleled by measurement of circulating lipidome and proteome at the same timepoints.

We hypothesise that initiation of alirocumab early in the post-MI period is safe, and that alirocumab will be superior to the placebo in stabilising coronary plaques (efficacy effect).

We further hypothesise that when alirocumab is withdrawn after 14 months of treatment, its protective effect in coronary plaque stabilisation will persist in the subsequent 14 months (legacy effect).

We anticipate that alirocumab will modify the circulating lipidome differentially from statins alone, including a reduction in newer atherogenic lipid species such as ceramides, while serial plasma proteomic analysis may offer new insights into potential pleiotropic and off-target effects of treatment with alirocumab.

Weaving together state-of-the-art cardiovascular imaging and “omic” capabilities positions Singapore as a hub for innovative clinical trials, incorporating deep biological phenotyping. By studying the “legacy effect” of alirocumab, we will be investigating a new strategy to employ powerful but expensive biologics in a sustainable manner.



**Prof  
Roger Foo  
Sik Yin**

**Senior Consultant,**  
*Department of  
Cardiology, National  
University Heart  
Centre Singapore*

**Deputy Director,**  
*Cardiovascular  
Research Institute,  
National University  
Health System*

**Professor,**  
*Yong Loo Lin  
School of Medicine,  
National University  
of Singapore*

While current therapy only delays disease progression, regenerative therapy proposes to reverse the course of disease. In neonatal mouse CMs that retain their proliferative potential, there is effective regeneration and repair response to injury up to post-natal D7.

Much still remains to be discovered for the regulation of dedifferentiation and proliferation of post-natal adult CMs. In the past, we performed single RNA-seq in failing and non-failing adult CMs and identified lincRNA Sghrt as a nodal gene within co-regulatory gene networks.

SGHRT knockdown increased marker expression of dedifferentiation and cell cycle entry in post-natal CMs in vitro. Similarly, SGHRT knockdown increased dedifferentiation markers in neonatal mouse CMs in vivo; and SGHRT knockdown improved cardiac function in an adult mouse model of disease, together with evidence of CM dedifferentiation.

In human ES-derived CMs, we now find that SGHRT deletion also results in increased CM dedifferentiation. Together, these results point to a

role for SGHRT in regulating CM dedifferentiation. Here, we aim to further characterise the role of mouse SGHRT in CM dedifferentiation and proliferation using (a) a conditional knockout and (b) humanised mouse models that we have now generated.

In assessing their response to myocardial stress by pressure overload and myocardial infarction, we aim to determine the therapeutic value of targeting SGHRT in human cardiac diseases.

Furthermore, we will characterise the role of human SGHRT in hES-derived cardiomyocytes and Engineering Heart Tissue (EHT) in response to oxidative stress.

Finally, we aim to dissect the mechanism of SGHRT as a novel mitochondrial micropeptide in the regulation of cardiomyocyte dedifferentiation.

Understanding the biology of how SGHRT regulates CM dedifferentiation and proliferation will allow us to develop a rational approach to target SGHRT in heart failure patients.

### **Dissecting the Role of Long Noncoding RNA Product SGHRT and Targeting it for Heart Failure**

Cardiac regeneration involving limited proliferation of pre-existing cardiomyocytes (CMs) holds the promise for novel and game-changing therapeutic strategies for heart disease.



**Prof  
Carolyn Lam  
Su Ping**

**Senior Consultant,**  
*Department of  
Cardiology and  
Director, Clinical  
and Translational  
Research Office  
National Heart  
Centre Singapore*

**Professor,**  
*Cardiovascular  
Academic Clinical  
Programme, Duke-  
NUS Medical School*

**Cardiovascular Clinical Trials in Asia:  
Asian Diabetes Outcomes Prevention  
Trial (ADOPT)**

Cardiovascular events are the leading cause of death among patients with diabetes. Early identification of high-risk diabetes mellitus (DM) patients for intensification of preventive therapy may prevent cardiovascular events.

We aim to test biomarker (N-terminal pro-B-type natriuretic peptide or NT-proBNP)-identified high-risk type 2 DM patients without pre-existing cardiac disease if intensive preventive therapy (high-dose renin-angiotensin-aldosterone system inhibitors [RAASi], beta-blockade sodium-glucose co-transporter 2 inhibitors [SGLT2i]) may be associated with reduced cardiovascular events compared with standard of care.

There will be a prospective multinational randomised open-label, parallel group, active-controlled, two-arm, long-term morbidity and mortality trial involving 5 countries (Singapore, Malaysia, China, Taiwan, India; estimated 6 sites each), with patients followed for 2 years.

We will tap adults with type 2 DM without cardiac disease (defined as history of coronary heart disease [prior myocardial infarction of significant coronary artery disease] or heart failure [reduced ejection fraction or hospitalisation for heart failure]) and with NT-proBNP > 125 pg/mL.

Patients will be randomised 1:1 to either:

- (i) Intensive Treatment group (high dose of RAASi and beta-blockers as well as SGLT2i) on top of standard therapy; or
- (ii) Control group (standard therapy where the use of SGLT2i at randomisation is not allowed but RAASi and beta-blockers, with the exception of maximal dosage, are allowed).

Every attempt will be made to use other blood pressure-lowering drugs besides RAASi or beta-blockers, as well as other anti-DM agents, in the control group.

The primary endpoint is combined based on the first occurrence of cardiovascular death and cardiovascular hospitalisation.

An estimated 3000 patients are to be screened to achieve the target of 2400 patients randomised. The trial is event driven, with a total expected trial duration of four years (two years recruitment, two years follow-up).

Results of this trial may change practice in Asia, improving patients' outcomes and saving healthcare costs.

**A Cardiosleep Research Program  
on Obstructive Sleep Apnea, Blood  
Pressure Control and Maladaptive  
Myocardial Remodeling**

The objective of this proposal is to evaluate whether a mandibular advancement device (MAD) is not inferior to continuous positive airway pressure (CPAP) in the treatment of obstructive sleep apnea (OSA) and blood pressure reduction.

OSA and hypertension are highly prevalent, with profound impacts on health. Apart from improving quality of life, an effective OSA treatment could improve cardiovascular risk partly through blood pressure reduction, particularly in patients with high cardiovascular risk, in whom blood pressure control is often suboptimal. Although CPAP is useful, the high non-adherence precludes its widespread use.

East Asians have a restrictive craniofacial phenotype that predisposes them to OSA and the associated cardiovascular stress. CPAP has failed to improve cardiovascular outcomes in randomised trials to date because it is poorly tolerated. MADs are oral appliances that correct the restrictive

craniofacial phenotype present in East Asians by protruding the lower jaw to reduce upper airway collapsibility.

MADs are better tolerated than CPAP, and this may be an important determinant of the overall effectiveness in treating OSA, and so improving adverse health outcomes downstream. We hypothesise that MADs are not inferior to CPAP in treating OSA and reducing cardiovascular risk by blood pressure reduction in East Asians.

We propose to recruit East Asian subjects with hypertension and high cardiovascular risk for polysomnography. Patients diagnosed with OSA (n=220) will be randomly assigned to MAD or CPAP groups in a 1:1 ratio for a treatment duration of 6 months.

The primary endpoint is the 24-hour mean blood pressure as determined by ambulatory monitoring. The secondary endpoints include sleep-time systolic blood pressure, target blood pressure, cardiovascular biomarkers, and myocardial remodelling.

Association between OSA and silent paroxysmal atrial fibrillation will also be determined. If MADs are shown to

be effective, the next step is to evaluate our novel device-drug-eluting MAD that the team is developing.

**A/Prof  
Ronald Lee  
Chi-Hang**



**Associate Professor,**  
*Department of Medicine,  
National University of Singapore*

**Senior Consultant,**  
*Department of Cardiology,  
National University Hospital*

**Principal Investigator,**  
*Cardiovascular Research Institute,  
National University Health System*



**Prof  
Jodhbir Singh  
Mehta**

**Senior Consultant (Head),**  
Corneal and External Eye Disease Service,  
Singapore National Eye Centre

**Deputy Executive Director,**  
Head Tissue Engineering and Stem Cells  
Group, Singapore Eye Research Institute

**Deputy Vice-Chair (Research) of  
Ophthalmology and Visual Sciences  
Academic Clinical Programme,**  
SingHealth Duke-NUS Academic  
Medical Centre

**Professor, Ophthalmology & Visual  
Sciences Academic Clinical Programme,**  
Duke-NUS Medical School

**Adjunct Associate Professor,**  
School of Materials Science and  
Engineering, School of Mechanical  
and Aerospace Engineering, Nanyang  
Technological University

### Targeted Cell-Based Therapeutic Program for Corneal Blindness

Visual loss is a global burden. Corneal diseases are the leading cause of vision loss. While the only treatment option is the replacement of damaged corneas through transplantation using cadaveric donor corneas, the global shortage of donor tissue and its sustainability amid a growing ageing population is of utmost concern.

Our aim is to develop innovative strategies to treat corneal stromal opacities and corneal endothelial dysfunction. This programme will establish targeted cell-based therapy to restore corneal tissue functions and corneal clarity, ultimately aimed at vision recovery.

Success of this programme will be a paradigm shift in conventional corneal transplantation. There are two broad themes:

- (i) A regenerative therapeutic programme for corneal stromal opacities using cultivated corneal stromal keratocytes (first successfully cultivated by Principal Investigator (PI) team), umbilical cord lining mesenchymal stem cells (UCL- MSC) generated in compliance

to good manufacturing practices by an industrial collaborator and MSC exosomes on animal models of corneal stromal haze/opacities.

- (ii) Corneal endothelial cell (CEC) therapy for corneal endothelial dysfunction using cells on bioactive hydrogel as a scaffold carrier for tissue-engineered endothelial keratoplasty, cells cultivated with Food and Drug Administration (FDA) approved, Rho-kinase inhibitor Rhopressa to improve cell quality, and regenerated CEC from putative endothelial progenitors identified in transition zone of posterior limbus for treating bullous keratopathy in a rabbit model, respectively.

The experimental outcomes will be instrumental for translation into a novel therapeutic approach for corneal diseases. We expect deliverables to have a broad impact on the global shortage of donor tissue in Singapore and worldwide. Our long-term goal is to develop Translational Regenerative Medicine to treat corneal blindness, which can attract multi-disciplinary, entrepreneurial, bio-manufacturing and academic platforms for the benefit of disease treatment and management.

### Studies in Chronic Myeloid Leukaemia

Chronic Myeloid Leukaemia (CML) is caused by the fusion gene BCR-ABL1, which transforms normal haematopoietic stem cells into their leukaemic counterparts. While inhibitors of the ABL1 tyrosine kinase (TKI) have turned CML into a chronic condition, several important clinical issues remain.

These include the inability of TKIs to eradicate leukaemia stem/progenitor cells (SPC) and cure chronic phase (CP) patients, inability to accurately identify CP patients at risk of transforming into a terminal blast crisis (BC) stage, and the lack of effective BC therapy.

To understand the mechanisms mediating SPC TKI resistance, and identify risk factors for BC transformation, we undertook a comprehensive evaluation of the CP to BC progression genome, epigenome, and transcriptome. In CP, we identified an RNA-binding protein, SRSF1, to mediate cytokine-dependent TKI resistance.

We also observed a CML-specific DNA methylation signature, which when analysed together with transcriptional events, identified a set of methylation-silenced genes predicting aggressive behaviour in CP. In BC, polycomb repressive complex (PRC) pathway and RUNX mutations occurred in a mutually exclusive manner in 70% of BC genomes, suggesting that either class of mutation is sufficient for BC transformation.

Additionally, EZH2, a component of PRC2, marked genes in CP for hypermethylation in BC, while DNA methylation cooperated with activation of the PRC1 complex to silence BC tumour suppressor genes. Together, our studies suggest a model in which a limited set of genetic mutations induce BC transformation through reprogramming of the CP epigenome.

Our specific aims are to determine the role of SRSF1 in CP CM, evaluate epigenetic reprogramming of CP SPCs and identify therapeutic targets, and ascertain if recurrent BC mutations contribute to BC transformation.

The completion of our aims has the potential to uncover mechanisms of SPC persistence, identify biomarkers to predict BC transformation, and provide insights into new therapies for both stages of CML.

**A/Prof  
Ong Sin Tiong**



**Associate Professor,**  
Programme in Cancer and Stem Cell  
Biology, Duke-NUS Medical School



**Prof  
Ooi Eng Eong**

**Professor & Deputy  
Director,**  
*Programme in  
Emerging Infectious  
Diseases, Duke-  
NUS Medical School*

### Enabling a Molecular Approach to Live Attenuated Flaviviral Vaccine Development

The recent emergence of Zika virus (ZIKV) as a threat to fetal development, the re-emergence of yellow fever in Brazil and Central Africa and recurrent cyclical dengue epidemics throughout the tropics demand more effective control measures.

Vaccines are one of the most effective tools for controlling diseases. However, deriving safe and effective vaccines against flaviviruses such as

the dengue virus (DENV) has proven challenging. It is further complicated by the need for vaccines to elicit long-term immunity to prevent waning immunity to levels that paradoxically enhance infection.

Among the various vaccine constructs, the live attenuated vaccine (LAV) has been the most successful in eliciting long-term immunity. However, LAV development is more an art than science due to deficient understanding of the molecular attributes of LAVs.

We have begun to address this knowledge gap and have found that successful flaviviral LAVs balance viral replicative fitness with host antiviral responses; replicative fitness ensures adequate antigen expression, while host antiviral responses limit antigenic burden and interrupt pathogenesis.

This proposal aims to extend our findings to establish a molecular approach to flaviviral LAV development, focusing firstly on

DENV and ZIKV. Our overall goal is to define the virus-host interaction that characterises flaviviral attenuation. A unique feature of this study is the elucidation of virus-host interaction in cells with diploid instead of aneuploidic genomes, which are unstable and confounded by abnormal gene copy numbers.

We will also elucidate the virus-diploid host interactions that distinguish successfully attenuated from over- or under-attenuated DENVs.

Finally, we will explore an interesting attenuating mutation in the ZIKV DN-2 strain, which we recently derived and which suggests the intriguing possibility that viral lipid membrane is a determinant of attenuation. If successful, this study could pave the way for a rational approach to LAV development.



**A/Prof  
Allen Yeoh  
Eng Juh**

**VIVA-GOH Foundation Associate  
Professor and Senior Consultant,**  
*Department of Paediatrics,  
National University Health System*

### Ma-Spore ALL-Seq 2020: RNA-Seq and IgH/TCR-Seq to Improve Risk Assignment in Childhood, Adolescent and Young Adult Acute Lymphoblastic Leukaemia

Minimal residual disease (MRD) and genetic factors allow us to better risk stratify patients for treatment of acute lymphoblastic leukaemia (ALL). However, they are still constrained by the limited resolution of real-time quantitative polymerase chain reaction (RQ-PCR), cytogenetics and reverse transcription polymerase chain (RT-PCR). The majority of patients who relapse, lack high-risk MRD or genetic features.

Next-generation sequencing provides both exceedingly high read depths and sequence resolution at nucleotide level. Using a combination of whole genome transcriptomic sequencing

(RNA-Seq) and targeted sequencing of immunoglobulin heavy chain and T-cell receptor (IgH/TCR-Seq), we hope to test whether improved resolutions of both MRD and genetic stratification will help us improve treatment outcome for children, adolescents and young adults (AYA) treated in the Malaysia-Singapore (Ma-Spore) ALL-Seq 2020 study.

"B-others" lacking identifiable genetic factors (hyperdiploidy>50, ETV6-RUNX1, TCF3-PBX1, BCR-ABL1 or MLL-AF4) forms the largest group, account for 56% of Ma-Spore ALL patients. We will RNA-Seq ~280 B-others patients out of 500 patients in the Ma-Spore ALL to find any genetic risk. We hypothesise that we can better genetically stratify ~40% of total patients to, either the standard or high-risk genetic group, which has a clinically significant hazard ratio of  $\geq 4$ .

We will use IgH/TCR-Seq to determine whether an improved MRD depth of at least tenfold to  $1 \times 10^{-5}$  can better predict the risk of relapse. As IgH/TCR-Seq also provides a snapshot of the immune repertoire, we aim to correlate if a limited diversity of the IgH/TCR repertoire is associated with increased risk of severe infections.

Ma-Spore ALL-Seq 2020 hopes to use the improved NGS depth and single nucleotide-level resolution to improve risk assignment for ALL, allowing safe deceleration of therapy in a larger

group of genetic/MRD standard-risk patients and early intensification of therapy in a smaller group of genetic/MRD high risk patients.

Taken together, this will help us further improve the overall treatment outcome of ALL in Malaysia and Singapore.





## CLINICIAN SCIENTIST AWARD (INVESTIGATOR) RECIPIENTS



**Dr  
Anita Chan  
Sook Yee**

**Senior Consultant (Head), Ocular Inflammation and Immunology Clinical Director, Ophthalmic Pathology Service, Singapore National Eye Centre**

**Head, Translational Ophthalmic Pathology Research Platform, Singapore Eye Research Institute**

**Assistant Professor, Ophthalmology and Visual Sciences Academic Clinical Programme, Duke-NUS Medical School**

### Investigating the Role of the Primary Angle Closure Glaucoma (PACG) Susceptibility Gene, PLEKHA7, in Plekha7<sup>-/-</sup> Mutant Rats

Glaucoma is characterised by retinal ganglion cell and optic nerve axonal loss, resulting in glaucomatous optic neuropathy. Primary angle closure glaucoma (PACG), a major form of glaucoma and visual loss in Singapore and Asia, is defined by the presence of iris-angle contact. Iris-angle contact can cause aqueous outflow obstruction and intraocular pressure (IOP) elevation progressing to PACG. The molecular effects underlying this progression are unknown and represent the current gap in knowledge.

PLEKHA7, a recently identified PACG-susceptibility gene, encodes a pleckstrin homology domain containing a GTPase-activating protein that is functionally related to cellular adhesion and extracellular matrix (ECM) remodelling. In normal eyes, PLEKHA7 expression is present in PACG-related structures: the iris, non-pigmented ciliary epithelium (NPCE), trabecular meshwork (TM), and choroid.

In tissues (iris and lens capsule) obtained from PACG eyes, a significant downregulation of PLEKHA7 mRNA

expression is present when compared with controls, suggesting that reduced levels of PLEKHA7 may contribute to PACG pathophysiology. Furthermore, we found that in vitro silencing of PLEKHA7 expression led to decreased cellular adhesion in NPCE cells and reduced contractility of TM cells.

In our colony of homozygous (Plekha7<sup>-/-</sup>), heterozygous (Plekha7<sup>-/+</sup>) and wild-type (WT) rats that have ablated and normal expression of Plekha7 respectively, young Plekha7<sup>-/-</sup> rats compared with WT litter-mates have a phenotype related to PACG risk — shallower anterior chambers, narrower angles and elevated IOP.

Based on these findings, we aim to use Plekha7 mutant rats as an in vivo system to study the ocular effects of PLEKHA7 down regulation.

We will study the Plekha7 ocular phenotype, particularly the degree of iris-angle contact with age and provocation (Aims 1 & 2); as well as altered cellular adhesion and ECM remodelling pathways (Aim 3) in PACG tissues specifically related to choroidal thickness and loss of barrier integrity, in order to determine the role of PLEKHA7 in PACG.

### Patient, Physician, and Organisational Factors Influencing Decision-Making for Antibiotic Use, and N-of-1 Trials of Interventions to Improve the Decision-Making

Upper respiratory tract infection (URTI) is a commonly cited reason for antibiotic use, although antibiotics are not clinically prescribed for the majority. Antibiotic misuse drives antimicrobial resistance. Antibiotic prescribing for URTIs at emergency departments (EDs) is complex and influenced by many patient-, physician-, and organisational-level factors.

The proposed research will be conducted over 2 phases in 4 adult EDs that provide Singapore-wide coverage. Phase 1 will involve mixed methods studies on physicians and patients that include questionnaire surveys and in-depth interviews to better understand the multilevel psychosocial, cultural, and systemic determinants of antibiotic prescribing.

Based on findings from Phase 1, a multi-centre stepped-wedge cluster randomised trial will be conducted in

Phase 2 to evaluate the effectiveness of tailored interventions targeting:

- (i) Patient-level (patient education via tailored information leaflets that address local knowledge gaps and misconceptions)
- (ii) Physician-level (senior physician education through active outreach efforts)
- (iii) Organisational-level (clinical decision support tool via mobile or desktop app, based on local epidemiology) levels, in reducing unnecessary antibiotic use.

The N-of-1 trials study will be used to gain a deeper understanding of prescribing practices at individual physician level in response to interventions.

Unlike conventional methods that evaluate intervention effectiveness with average physicians practicing in adult ED, the N-of-1 trials will enable the assessment of the interventions that work for individual physicians and allow the design of personalised interventions.

With Singapore's rapidly ageing population susceptible to infections and exposure to antibiotics, tailored interventions after elucidation of root causes for unnecessary antibiotic use that target patient-, physician-, and organisational-level factors in EDs are necessary to curb the rising tide of antimicrobial resistance amidst the background of a dwindling antibiotic pipeline.

This research study will contribute to the limited international understanding of the determinants for antibiotic prescribing in EDs.

**A/Prof  
Angela Chow**



**Head and Senior Consultant,  
Department of Clinical Epidemiology,  
Tan Tock Seng Hospital**

**Associate Professor,  
Lee Kong Chian School of Medicine,  
Nanyang Technological University**



**Dr  
Quan Van  
Mahn Hoang**

**Consultant,**  
*Department of Surgical Retina,  
Singapore National Eye Centre*

**Assistant Professor,**  
*Ophthalmology & and Visual Sciences  
Academic Clinical Programme, Duke-NUS  
Medical School*

### **Scleral Biomechanical Properties in Pathologic Myopia and Myopic Glaucoma**

High myopia (HM), or extreme near-sightedness, is a leading cause of blindness worldwide and affects 1 in 12 Singaporeans. By 2050, it is estimated that a billion people will have HM. HM is due to progressive and extreme eye elongation with subsequent eye wall (sclera) thinning, which may allow for focal, ectatic outpouchings called staphyloma.

Staphyloma development often occurs immediately before or together with myopic macular degeneration (MMD) and the irreversible vision loss of “pathologic” myopia (PM). The main threats to vision in HM patients are the development of MMD, staphyloma and/or myopic glaucoma.

Glaucoma is the most common cause of blindness worldwide, affecting greater than 79.6 million people by 2020, with half being of East Asian origin. Glaucoma is an optic neuropathy with unknown pathogenesis that is related to intraocular pressure, and therefore scleral biomechanical properties. A link between myopia and glaucoma has long been reported.

Although scleral changes are believed to underlie both glaucomatous changes and staphyloma development, there are no biomechanical tests available to detect early changes in myopic scleral stiffness and/or reveal whether HM-related biomechanical changes may lead to myopic glaucoma.

A fundamental understanding of the biomechanical alterations in scleral tissue may provide a link between

pathological pathways in glaucoma and myopia, and allow for future therapeutic approaches.

We now have imaging technology to assess the eye wall in vivo, providing unprecedented insight into scleral biomechanical properties and allowing us to map regional stiffness.

We propose to conduct cross-sectional studies on 200 existing low myopia, HM and PM patients. Scleral biomechanical properties will be compared across cohorts, allowing us to:

- (i) Identify and localise scleral regions susceptible to myopia-related remodelling
- (ii) Determine if localised biomechanical weakness in HM is associated with localised functional changes
- (iii) Identify scleral biomechanical changes in myopic glaucoma

### **Study into the role of Cerebrovascular Disease and Amyloid Pathology on Progression of Cognitive Impairment among Patients with Young Onset Mild Cognitive Impairment (SYNC-Longitudinal)**

While cerebral fibrillary beta-amyloid is the pathological hallmark of Alzheimer’s disease (AD), there is evidence that small vessel cerebrovascular disease (svCVD) co-exists and accelerates the amyloid cascade.

Existing studies evaluating the interaction between beta-amyloid and svCVD have been limited to older cohorts with multiple cerebral pathologies, thus not allowing for analyses of the specific contribution of svCVD to beta-amyloid pathology.

Studies focused on younger cohorts will allow for elucidation of the specific pathophysiological contributions of svCVD to cerebral beta-amyloid and AD. Published data from our group has demonstrated that 30% to 40% of Southeast Asian patients with AD have a severe burden of svCVD. Unravelling the contribution of svCVD to beta-amyloid pathology is of high clinical importance to the Southeast Asian population.

In this proposal, we will evaluate the interaction between beta-amyloid and svCVD in 250 young subjects (<65 years) with amnesic mild cognitive impairment (a-MCI). This will be a follow-up study to our cross-sectional Singapore Young Onset Dementia Study (SYNC).

We will evaluate the interaction between svCVD and beta-amyloid pathology on specific cognitive measures (global cognition, episodic memory, executive function), incident svCVD lesions and integrity of specific functional networks (executive control network, default mode network).

As hypertension is a leading mechanism for svCVD, we will carry out a proof of mechanism trial to study the risks and benefits of intensive blood pressure control (<120/80mm Hg) on reducing cognitive decline and reducing svCVD lesions among a-MCI subjects having both svCVD and beta-amyloid pathology.

This study will provide novel data on the magnitude of contribution of svCVD to accumulation of beta-amyloid, cognitive decline and functional network integrity.

The data would be used to plan randomised clinical trials targeting svCVD for the prevention of AD dementia and to develop novel software that

can be commercialised, in order to quantify svCVD and to track cognitive performance.

### **A/Prof Nagaendran Kandiah**



**Senior Consultant Neurologist,**  
*Department of Neurology, National  
Neuroscience Institute*

**Director,**  
*Clinical Research,  
Neuroscience Academic Clinical  
Programme, Duke-NUS Medical School*

**Associate Professor,**  
*Neuroscience and Mental Health, Lee Kong  
Chian School of Medicine*



**Dr  
Nicole Keong  
Chwee Har**

**Consultant,**  
*Department of  
Neurosurgery,  
National  
Neuroscience  
Institute*

**Assistant Professor,**  
*Duke-NUS Medical  
School*

### Mapping the Trajectory and Prognosis of Patients with Mild-Moderate Traumatic Brain Injury – The NEurodegeneration & Understanding of Risk Overlay in Neuroimaging Study (NEURON) 2

Traumatic Brain Injury (TBI) will soon be a leading cause of global death and disability; the greatest rise is in the elderly. TBI consequences may be devastating, including physical, cognitive and psychological behaviours.

TBI is now known as a major risk factor for lifelong neurological disorders, including Alzheimer's and Parkinson's diseases, and other dementias. Although some patients successfully recover and some adapt with trade-off, others continuously decline.

Currently, it is not possible to differentiate cohorts as they progress towards either good or poor prognoses. We are unable to characterise the spectrum of processes favouring decline, otherwise termed as "Chronic Brain Injury" (CBI). Longitudinal data on CBI is severely lacking worldwide.

In our previous study on normal pressure hydrocephalus (NPH), supported by an NMRC TA award, provides proof-of-concept that different cohorts of disease exist with differing degrees of responsiveness to treatments. NPH is one end-point of TBI. Hence our, hypothesise that post-TBI, different cohorts exist, with differing degrees of adaptation to injury.

It is possible to find markers and milestones to differentiate such

cohorts, and so manage them appropriately and individually. Modelling such trajectories requires knowledge of the spectrum from reversible to irreversible brain injury. There is no comprehensive data in this regard.

To address such gaps, we propose NEURON 2, the first study to confirm CBI, and discover post-TBI markers correlated with good versus poor prognoses.

We aim to explore if it is possible, prior to any clinical manifestations, to distinguish patients within 3 years of mild-moderate TBI, who will recover, from those who will deteriorate from CBI.

We will examine whether advanced brain tissue imaging signatures reflect structural adaptation to injury versus decline, particularly in those with higher risk of CBI. As an experienced team with expertise in NPH, TBI and neurodegenerative diseases, and established exemplar datasets, we are well-positioned to deliver NEURON 2.



**Dr  
Angela Koh  
Su-Mei**

**Senior Consultant,**  
*Department of  
Cardiology, National  
Heart Centre  
Singapore*

**Assistant Professor,**  
*Duke-NUS Medical  
School*

### TO-ChERISh: Trajectory of Cardiovascular Ageing, Its Determinants and Impact on Health

Cardiovascular (CV) ageing is a heterogeneous process that exhibits great variation with advancing age among individuals. Some individuals develop ageing-related deteriorations in CV structure and function, resulting in CV disease (unhealthy CV ageing) while others have relatively preserved CV health with chronological ageing (healthy CV ageing).

Determinants of either CV ageing trajectories remain unknown. We hypothesise that investigations of CV ageing trajectories will unravel determinants of unhealthy and healthy CV ageing.

Our hypothesis is based on data (2014-2017) from a community-based cohort of elderly individuals, with CV imaging and bio-specimens that showed a spectrum of CV functions ranging from preserved to unhealthy measurements, correlated to lifestyle (physical activity), systemic conditions (diabetes mellitus) and circulating metabolites (such as amino acids and acyl-carnitines).

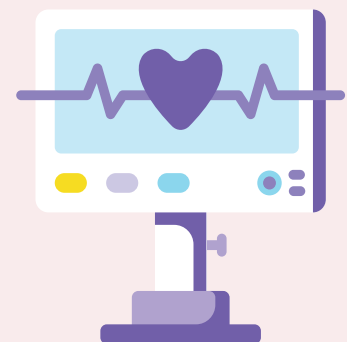
Traditional risk factors such as diabetes mellitus and physical activity could not fully account for the extent of CV ageing observed. The specific aim of this study is to:

- (i) Determine rates of change in CV ageing over time through CV imaging markers
- (ii) Assess circulating metabolites markers present in archived blood samples (2000-2004) are associated with CV ageing 15 years later (2014-2017) and rates of CV ageing progression (2018-2021) and how these differences vary by gender, physical activity and diabetes mellitus
- (iii) Impact of CV ageing on development of clinical CVD and overall physical, cognitive and functional health outcomes.

Participants from 2014-2017 will return in this proposal (2018-2021) for repeat biodata, CV imaging markers, and bio-specimen collection.

Baseline and change in CV imaging and metabolite markers will be analysed from archived (2000-2004, 2014-2017) and fresh bio-specimens, adjusting for longitudinal covariates.

Distinguishing trajectories of healthy versus unhealthy CV ageing will reveal determinants and impact of CV ageing. Targeting CV ageing may therefore improve burden of CV disease and important ageing-related health outcomes among ageing populations.





### A/Prof Ng Oon Tek

**Senior Consultant,**  
National Centre for  
Infectious Diseases

**Senior Consultant,**  
Department of  
Infectious Disease,  
Tan Tock Seng  
Hospital

**Associate Professor,**  
Lee Kong  
Chian School of  
Medicine, Nanyang  
Technological  
University

#### Oral Capsule-administered Faecal Microbiota Transplantation for Intestinal Carbapenemase-producing Enterobacteriaceae Decolonisation

Carbapenemase-producing Enterobacteriaceae (CPE) is a global, antibiotic-resistant "superbug" threat with close to an 80% mortality rate. Despite standard-of-care infection prevention, CPE numbers increase in Singapore and many parts of the world.

CPE-intestinal colonisation, the main human reservoir, is a source for ongoing transmission and progression to invasive disease. Available data supports antibiotic-induced gut microbiota dysbiosis as a leading mechanism predisposing to CPE-intestinal colonisation.

There are no standard-of-care regimens for CPE-intestinal decolonisation. Faecal microbiota transplantation (FMT) by capsule is a safe, proven therapy for recurrent *C. difficile* infection. Limited data from single-arm uncontrolled studies suggests FMT can restore normal gut microbial diversity and decolonise CPE-intestinal carriage.

We hypothesise that oral capsule-administered FMT significantly increases the proportion of CPE-intestinal decolonisation of adult subjects at 2 weeks following FMT administration, compared with a placebo.

We plan to conduct a double-blind, randomised controlled trial at 3 sites (Singapore General Hospital, National University Hospital, Tan Tock Seng, Hospital) where CPE-intestinal colonisation positive adults will be randomly assigned 1:1 to FMT by capsule compared with a placebo.

The primary endpoint, measured 2 weeks post-capsule administration, will be CPE-intestinal decolonisation (defined as two rectal swabs negative by culture-based detection on consecutive days and a rectal swab negative by direct-PCR-based detection).

Subjects will be monitored for 48 weeks post-FMT to determine long-term CPE-intestinal decolonisation rates.

The secondary aims of this study:

- (i) To determine microbiome correlates of CPE-intestinal decolonisation using metagenomic sequencing
- (ii) To use a mouse-model to undertake mechanistic studies of CPE-intestinal colonisation.

*The two secondary studies would use samples collected as part of the primary randomised controlled trial.*

The primary study aims to determine if FMT is an effective and safe intervention for CPE-intestinal decolonisation.

*Data from the secondary study would help determine the mechanistic pathways by which FMT impacts CPE-intestinal colonisation.*



### Dr Monisha Esther Nongpiur

**Clinician Scientist,**  
Glaucoma Research  
Group, Singapore Eye  
Research Institute

**Assistant Professor,**  
Ophthalmology and  
Visual Sciences  
Academic Clinical  
Programme, Duke-  
NUS Medical School

#### Investigating the Genetic and Phenotypic Architecture of Advanced Primary Angle Closure Glaucoma for Stratified Disease Management

Glaucoma is the leading cause of irreversible blindness worldwide, with primary angle closure glaucoma (PACG) a major form of glaucoma in Singapore and across Asia. While we

have made considerable advances in understanding the epidemiology, risk factors, imaging features and clinical phenotypes of PACG, among the key unanswered questions, who is at risk of developing advanced PACG/blindness.

Current strategies for patient stratification are inadequate to identify those who progress to advanced disease stage. Our recent work has demonstrated that angle closure exhibits substantial clinically heterogeneity. However, such approaches are inadequate in their abilities to stratify patients as they do not account for both within-disease and across-disease heterogeneity.

Our work has also identified eight genetic loci associated with PACG; however, they have all been identified using a broad categorisation of PACG. It is hence not known if there are specific genetic variants that confer susceptibility to development of advanced PACG.

In this proposal, we hypothesise that specific anatomical features and rare

variants of moderate to large- effect sizes confer susceptibility on the development of advanced PACG. To address our hypothesis, we aim to:

- (i) Perform comprehensive phenotyping of advanced PACG to identify specific factors associated with severe disease
- (ii) Identify genetic variants that confer susceptibility on advanced disease/blindness by performing targeted sequencing of the known PACG-loci in these subjects
- (iii) Build a multimodal artificial intelligence-driven patient stratification model to identify the individuals at risk of developing advanced PACG disease earlier

It is hoped that this project will lead to improved disease stratification of PACG and facilitate early administration of prophylactic treatments to those at the greatest risk of developing advanced diseases.





**A/Prof  
Tan Ern Yu**

**Senior Consultant,**  
Department of General Surgery,  
Tan Tock Seng Hospital

**Associate Professor,**  
Lee Kong Chian School of Medicine,  
Nanyang Technological University

### Clinical Evaluation of a Novel 20- Gene Signature as a Biomarker and Metabolic Target in Breast Cancer Stem Cells

There is much work on developing strategies to target breast cancer stem cells (CSCs), which exhibit intrinsic resistance to conventional treatments. We have recently identified a novel gene signature comprising 20 genes related to oxidative phosphorylation from

functional CSC assays using patient-derived tumour spheres.

We hypothesise that this signature is a more sensitive CSC marker than existing ones and may predict tumour sensitivity to oxidative phosphorylation inhibitors such as metformin. We also found metformin to be effective in chemo-resistant cells.

Primary objectives are to evaluate this 20-gene signature as an indicator of CSC subpopulation size and to determine the effect of metformin on CSCs.

The secondary objective is to establish patient-derived xenografts for future characterisation. The 20-gene signature will be evaluated in non-diabetic women prior to and after completing neoadjuvant chemotherapy in combination with metformin, and will be correlated with known CSC markers using NanoString technology, and with proliferative and apoptotic markers using immunohistochemistry.

The association with pathological response will also be examined. Analyses will be stratified according

to tumour subtype, to account for variations in chemotherapy regimen.

A similar evaluation will be carried out in diabetic women undergoing neoadjuvant chemotherapy, stratified according to whether they receive metformin for diabetic treatment or otherwise.

The correlation with CSCs will be further validated in 2 cohorts known for CSC enrichment: pre- and post-chemotherapy pairs and primary and matched recurrent tumour pairs.

To validate the association with prognosis, recurrent tumour from the cohort will be compared with matched controls consisting of tumour from women who did not relapse; controls will be matched in terms of disease stage, tumour subtype, histological classification and treatments received. Findings will provide insight into the potential of the 20-gene signature as a CSC marker and as a therapeutic target.



**Dr  
Teo Wan-Yee**

**Clinician Scientist and Assistant Professor,**  
Division of Medicine, KK Women's and  
Children's Hospital & Division of Cellular  
and Molecular Research, National Cancer  
Centre Singapore

*Cancer and Stem Cell Biology Program,  
Duke-NUS Medical School*

**Principal Investigator, Paediatric Brain  
Tumour Research Office, Duke-NUS  
Academic Medical Centre**

**Clinician Scientist and Research Clinician,**  
*Institute of Molecular and Cell Biology*

### Therapeutic Repositioning and Development of Phase I/II Drug OTSSP167 to Target 4 Molecular Subtypes of Medulloblastoma

Paediatric brain cancer is the leading cause of death among childhood cancers. Medulloblastoma (MB) is the most common malignant brain tumour

in children globally. The genomics era has robustly classified paediatric MB into 4 molecular subtypes: sonic-hedgehog-activated MB, Wingless-activated, and less-characterised, more aggressive Group 3 and 4 subtypes.

Recurrent MB is invariably fatal. Our drug discovery platform identifies Phase I/II drug OTSSP167, used in adult cancers, as a compelling therapeutic agent against 4 MB-subtypes, including recurrent/disseminated MB. This proposal aims to therapeutically reposition Phase I/II drug OTSSP167 to target 4 MB-subtypes, and establish a new therapy for aggressive subtypes and recurrent tumour refractory to current regimens.

Specifically, we will evaluate in-vivo therapeutic efficacy of OTSSP167 against a panel of well-characterised, patient-derived orthotopic xenograft (PDOX) Models of 4 MB-subtypes and a pair of primary/recurrent PDOX Models that we have successfully established, to further identify new secondary targets of OTSSP167 for co-determinants of drug response. This will uncover new molecular mechanisms within aggressive Group 3/4 MBs, and treatment resistance in recurrent MB/SHH-MBs.

Based on preliminary findings, our working hypothesis indicates that there exist new secondary targets of OTSSP167, effective against Group 3/4 MBs, and treatment-resistant tumours.

Our established subtype-specific PDOX MB models represent the most complete, patient-relevant MB disease spectrum in the field of neuro-oncology. This serves as an excellent preclinical screening platform to evaluate therapeutic efficacy of OTSSP167.

In terms of feasibility, preliminary studies support that this approach will be effective in predicting clinical trial drug response of OTSSP167 against lethal and treatment-resistant MB.

Our PDOX Models provide immediate, clinically-relevant in-vivo models for preclinical drug positioning, with downstream translation to clinical trials for MB within large international collaborative groups. In turn, this will serve an urgent unmet need for the global paediatric neuro-oncology community.

### Tracking Circulating Tumour Cells and microRNAs in High-risk Breast Cancer

Circulating nucleic acids and circulating tumour cells (CTCs) may potentially be useful for decision-making in breast cancer. Unlike standard tissue-based biopsies, these blood-based biomarkers are non-invasive, and may provide real-time assessment of the evolution of disease biology with changing disease burden better than radiological imaging and other commercial assays.

We hypothesise that, dynamic changes in CTCs and microRNA expression, reflect the tumour burden in breast cancer, and provide insights into mechanisms of resistance. Our objectives are to:

- (i) Determine the potential of serial CTC counts with the microfluidic ClearCell® FX platform for monitoring response and surveillance in high-risk breast cancer patients requiring neoadjuvant chemotherapy.
- (ii) Characterise the CTCs with the 2-gene MMP signature, which has prognostic value in various tumour

- (iii) Identify changes in circulating microRNA signatures with treatment for breast cancer, and correlation with relapse status.

We hope to recruit 60 breast cancer patients undergoing neoadjuvant chemotherapy at 2 centres over a one-year period. Baseline blood tests will be conducted:

- following 6 months of chemotherapy prior to surgery
- within a month, post -surgery
- at 1 and 2-year interval marks, post initial diagnosis

For objective 1, CTCs will be enumerated using the microfluidic platform.

For objective 2 and 3, expression of MMP1 and MMP12 will be evaluated with RNA extracted from single CTCs, and microRNA will be extracted from serum for profiling using the MiRXES IDEALTM miRNA qPCR assays.

The sensitivity of circulating markers at different time points, and correlation with disease relapse status, will be compared using appropriate statistics.

### Dr Yap Yoon Sim



**Senior Consultant,**  
Department of Medical Oncology, National Cancer Centre Singapore

**Assistant Professor,**  
Duke-NUS Medical School

These promising blood-based biomarkers may serve as surrogates for not just tumour response, but more importantly, residual disease burden status, and predict relapse risk.

By refining the risk stratification, breast cancer patients at high risk of relapse can, potentially, be identified for escalation of adjuvant therapies.

Likewise, patients at low risk of relapse, post standard treatments, may be spared from unnecessary toxic treatments.

### The IFIT Family in Breast Cancer: Evaluation of Expression Patterns, Functional Roles and Potential Use as Prognostic Indicators

Breast carcinoma is the most common cancer in women worldwide, and is a leading cause of malignancy-related deaths. In Singapore, its incidence has tripled over 40 years, while its mortality rate has remained relatively unchanged for over the last 25 years.

This then, underlines the need for a deeper understanding of breast cancer, and to discover better markers for patient prognostication. The interferon induced protein with tetratricopeptide repeats (IFIT) family consists of four members. Previous studies have mainly focused on their roles in immune response to viral infections.

During our preliminary findings, we found that silencing IFIT1 or IFIT3 in human breast cancer cells decreased tumour cell migration and invasion through Matrigel. Furthermore, elevated IFIT1 or IFIT3 in breast cancer tissue was associated with reduced patient survival and increased risk

of tumour recurrence. Contrastingly, knocking down IFIT5 increased the migratory and invasive characteristics of breast cancer cells.

This project aims to determine the:

- (i) Differential biological roles of IFITs in breast Cancer
- (ii) Identify candidate downstream signalling mechanisms
- (iii) Evaluate the potential use of IFITs as prognostic indicators in breast cancer patient survival and disease relapse

Knockdown/knockout and overexpression of IFIT members will be performed to investigate functional roles in vitro using human breast carcinoma cells, and in vivo using a SCID mouse model.

Transcriptomic and proteomic studies will be performed using microarrays and mass spectrometry analyses to identify downstream pathways, which will then be selected for experimental verification.

Expression of IFITs in breast cancer tissue samples will further be examined and analysed for associations with clinicopathological features. Survival analysis will evaluate the potential use of IFITs to predict patient survival and breast cancer recurrence.

Together, the study will deepen our knowledge on IFITs in breast cancer and, assess the potential use of IFITs in prognostication for breast cancer patients.

### A/Prof George Yip



**Associate Professor,**  
Department of Anatomy,  
National University of Singapore



## TRANSITION AWARD RECIPIENTS



**Dr  
Chua Horng  
Ruey**

*Senior Consultant,  
Division of  
Nephrology, National  
University Hospital*

*Assistant Professor,  
Department of  
Medicine, Yong  
Loo Lin School of  
Medicine, National  
University of  
Singapore*

### Pre-empting Renal Injury Ensuing Drugs by Elucidating microRNA and Proteomics of Renal Tubular Dysfunction at Its Earliest (PRE-EMPTII study)

Drug-induced acute kidney injury (AKI) develops in 13% of patients on nephrotoxic therapy and predisposes them to chronic kidney disease. AKI is diagnosed by serial increase in serum

creatinine, itself a late biomarker of renal dysfunction.

Our preliminary studies demonstrate that urinary KIM1, clusterin,  $\beta$ 2-microglobulin, MCP1, and more recently, select urinary microRNAs, are elevated prior to AKI onset in patients versus non-AKI controls, while receiving aminoglycosides or vancomycin.

We propose to advance our research by refining the biomarker panel that intercepts drug-induced renal tubular dysfunction, well before AKI is evident

First, we propose an exosome analysis of the above-identified protein biomarkers, to determine if the distinction in levels between cases and controls could be exemplified at >3 days prior to drug-induced AKI, using our biobank urine samples.

Next, the selected microRNAs discovered will be correlated to inducible injury microRNAs in vitro, to examine them for reproducibility, using a microfluidic, human renal proximal tubule cell-model with nephrotoxic insult from antimicrobials, calcineurin-inhibitors, and anti-cancer drugs.

The area under receiver operating characteristic curve of these more

selective protein and microRNA biomarkers, or their combination for AKI prediction at its earliest, will be determined in our current, 130-patient cohort, to derive better performing biomarkers.

Concurrently, we propose to recruit 150 patients over a 1-and-a-half-year period, and prescribe similar drugs to them. Urine samples will be collected at intervals, guided by known AKI trajectories from commenced use of respective drugs.

These samples will be batch-analysed, against the refined biomarker panel for AKI prediction for further validation.

The refined biomarker panel will be implemented for real-time analysis, allowing fluidity of detecting patients at highest risk of AKI during nephrotoxic therapy.

This will be examined in a clinical trial to triage patients for pre-emptive drug cessation or dose reduction, to effectively prevent drug-induced AKI.



**Dr  
Jacqueline  
Chua**

*Senior Clinical  
Research Fellow,  
Ocular Imaging  
Research Group,  
Singapore Eye  
Research Institute*

*Assistant Professor,  
Ophthalmology &  
Visual Sciences  
Academic Clinical  
Programme, Duke-  
NUS Medical School*

### Improved Detection of Glaucomatous Structural Damage using Wide-Field Optical Coherence Tomography

Glaucoma is the leading cause of irreversible blindness worldwide. Diagnosis of early glaucoma remains challenging. By the time the current method of visual field testing detects glaucoma, at least 25% of retinal ganglion cells (RGCs) are lost.

Optical coherence tomography (OCT) imaging is commonly used to aid glaucoma diagnosis in clinical settings. However, its diagnostic ability for detecting early glaucoma remains inadequate, given the considerable overlap of retinal nerve fibre layer (RNFL) thickness measurements between normal and glaucoma affected eyes.

Some of this overlap is due partly to variations in ocular anatomical parameters such as, optic disc size and shape, and the anatomy of the retinal vascular tree, which in itself an important source of measurement error.

We propose a method to mitigate the influence of anatomical ocular parameters on OCT-derived measurements. Our studies have already shown that this anatomy-based compensation method, narrows the variability of RNFL measurements in healthy subjects, and reclassified half of eye patients from the 1% high-risk category (with very thin RNFL) to the normal category.

The primary objective of this proposal is to compare wide-field optical coherence tomography (WF-OCT), combined with compensation for anatomical parameters (termed as WF-OCT plus) and standard OCT, in relation to detecting early glaucomatous structural damage and progression in a clinical setting.

We hypothesise that WF-OCT plus will significantly improve diagnostic performance in early detection of glaucomatous damages and optimise the role that OCT imaging plays in glaucoma management.

Early glaucoma diagnosis is essential to improving patient outcomes. Early treatment can prevent or delay disease progression, and so preserve patients' visual functions.

Given that glaucomatous damage irreversibly leads to blindness at late stage diagnosis, the outcome of this study, presents a novel method to advance glaucoma diagnosis, that will significantly impact the prevention of glaucomatous blindness, not only in Singapore but across the world.



**Dr  
Evelyn Law  
Chung Ning**

**Assistant Professor,**  
Department of Paediatrics, Yong Loo Lin  
School of Medicine, National University of  
Singapore

**Consultant,**  
Department of Paediatrics, Khoo Teck Puat  
- National University Children's Medical  
Institute, National University Hospital

**Principal Investigator,**  
Translational Neuroscience Programme,  
Singapore Institute for Clinical Sciences

### Neurocognitive Development and Human Capital: The Influence of Digital Media Consumption on Young Children in Singapore

This study aims to define the timing and extent to which young children are most vulnerable to digital media consumption and gain clarity on the neural mechanisms. We hypothesise that the brain is most sensitive to

digital media before 12 months. At this early age, we anticipate that processes underlying the maturation of the brain networks are impaired.

Our methodology will tap the Singapore population-based GUSTO (Growing Up in Singapore Towards healthy Outcome) birth cohort to examine the trajectories of digital media use in children from 0 to 36 months.

We will determine the relationships of media exposure at 4 time points (12, 18, 24, and 36 months) to neurocognitive developmental outcomes, including intelligence, school readiness, and social-emotional skills.

Group differences in outcomes between children with excessive use of digital media and those without will be quantified with effect sizes. Using autoregressive time series models, the bidirectional effects between media exposure and cognitive characteristics of children will be explored.

The raw, pre-processed neurophysiology data (i.e.: eye tracking, EEG with event-related potential) from infancy will be cleaned and carefully interpreted.

We propose to employ mixed model, repeated-measure analysis of covariance (ANCOVA) to examine:

- (i) Primary effects
- (ii) Interactions between age and degrees of media exposure on brain waveform and networks.

Greenhouse-Geisser correction will be applied.

This study will be among the first to capture longitudinal developmental profiles and neurobiological mechanisms occurring in young children on early introduction exposure to digital media.

The scientific evidence has the potential to be translated into public policy for the entire paediatric population in Singapore.



**A/Prof  
Victor Lee  
Kwan Min**

**Associate  
Professor and  
Senior Consultant,**  
Department of  
Pathology,  
National University  
Health System

### Wnt Pathway in Synovial Sarcoma: Implications for Therapy

Sarcomas are difficult to treat due to a lack of efficacy of conventional chemotherapy drugs. Drugs that target specific tumorigenic pathways offer the potential of having less patient morbidity and more therapeutic efficacy.

Our preliminary work has demonstrated that synovial sarcoma (SS) may be dependent on the Wnt signaling pathway for survival and growth. In other sarcomas, the Wnt pathway may have an inhibitory effect on angiogenesis.

My mentor's lab has developed an upstream Wnt Inhibitor (ETC159) that is currently in clinical trials. Understanding the role of the Wnt pathway in these sarcomas will allow this new drug for clinical use in more cancers.

We hypothesise that SS is driven by an upstream Wnt pathway mutation and can be curtailed by an upstream Wnt inhibitor (ETC159). ETC159 inhibits SS by direct inhibition of tumour cell viability as well as disrupting the tumour's angiogenic potential.

We propose to:

- (i) Investigate how SSX-SS18 upregulates the Wnt pathway in SS
- (ii) Demonstrate the efficacy of ETC 159 in the treatment of synovial sarcoma; and
- (iii) Investigate the effects of Wnt modulation on angiogenesis in sarcomas.

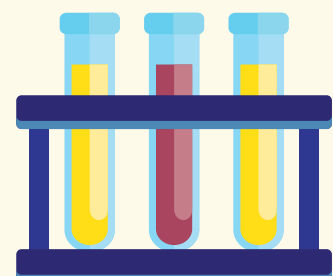
Co-immunoprecipitation of SSX-SS18 will identify the key Wnt proteins that bind to SSX-SS18. Overexpression/

knockdown of these proteins will allow us to investigate the Wnt signaling pathway in SS.

Treatment of synovial sarcoma murine xenografts with ETC159 will allow us to investigate the effects of Wnt modulation on the tumour phenotype as well as transcriptional changes.

We will also investigate the effects of ETC 159 on angiogenesis by immunohistochemistry analysis of the treated tumour specimens, as well as the chicken chorioallantoic membrane angiogenic model.

Understanding the role of the Wnt signalling pathway in driving sarcomas will allow us to develop a new, locally developed treatment modality for these cancers.





**Dr  
Adeline Ng  
Su Lyn**

**Consultant Neurologist,**  
Department of Neurology,  
National Neuroscience Institute

**Assistant Professor,**  
Duke-NUS Medical School

### Alpha-synuclein Gene Promoter (Rep1) Polymorphism and Cognitive Decline in Parkinson's Disease

Parkinson's disease (PD) is a neurodegenerative disorder characterised by cytoplasmic alpha-synuclein aggregates in the substantia nigra. The alpha-synuclein gene (SNCA) is implicated in familial PD; while polymorphism of the SNCA promoter region (Rep1), i.e. variation in Rep1 allele length, is associated with increased PD risk in multiple studies.

The frequencies of Rep1 genotypes in our PD population are ~30% for the shortest allele (allele 0), and ~40% and ~30% for the longer alleles (alleles 1 and 2 respectively). Increased risk of PD may occur via variation in transcriptional regulation of SNCA expression, with longer Rep1 allele lengths displaying increased SNCA expression in both mouse and human brain tissue.

Furthermore, clinical studies have shown that longer Rep1 allele carriers show greater motor decline and neuropsychiatric complications compared with shorter allele carriers.

However, the association of Rep1 with cognition remains unknown. To address this gap, our primary aim is to investigate the association of Rep1 allele-lengths with cognitive decline in mild- to moderate-stage PD (Hoehn & Yahr score  $\leq$ 3).

We hypothesise that longer Rep1 allele carriers (alleles 1, 2) will show greater decline in cognition based on the Montreal Cognitive Assessment (MoCA)

test over 2 years, compared with shorter Rep1 allele carriers.

A secondary aim is to determine if peripheral SNCA expression levels at the baseline are associated with cognitive decline in longer Rep1 allele carriers.

An exploratory aim is to study longitudinal changes in brain structure (grey matter volumes, cortical thickness, and white matter microstructure) and functional connectivity in longer vs shorter allele carriers.

We hypothesise that longer allele carriers will show greater decrease in these measures over a 2-year period compared with shorter allele carriers. These will add evidence to the link between Rep1 polymorphism and cognitive dysfunction in PD, identifying Rep1 as a novel therapeutic target for neurodegeneration in PD.



**Dr  
Pua Yong Hao**

**Senior Consultant,**  
Department of  
Physiotherapy,  
Singapore General  
Hospital

**Assistant Professor,**  
Duke-NUS Medical  
School

### Innovative Tele-monitored Home- Based Program for Post Total Knee Replacement Rehabilitation: A Noninferiority Randomized Controlled Trial

With an ageing population and increasing prevalence of obesity and knee osteoarthritis, the number of total knee replacement (TKR) surgeries will increase with time. In Singapore, although hospital-based outpatient rehabilitation is standard-of-care for patients post TKR, outpatient rehabilitation is costly and inconvenient for patients and their caregivers.

A monitored home-based exercise programme provides the best access to care and is an alternative for patients who do not require intensive "hands-on" rehabilitation.

We have developed a tele-monitored home-based rehabilitation programme, and aim to compare the clinical trial- and cost-effectiveness of this innovative programme with that of standard hospital-based rehabilitation among post-TKR patients in a randomised controlled trial (RCT).

We hypothesise that an 8-week home-based exercise programme, combined with tele-monitoring, will not be clinically inferior to an 8-week hospital-based rehabilitation programme at 6 months post TKR.

In terms of improving physical functional outcomes, the home-based programme will be more cost-effective than a hospital-based rehabilitation programme.

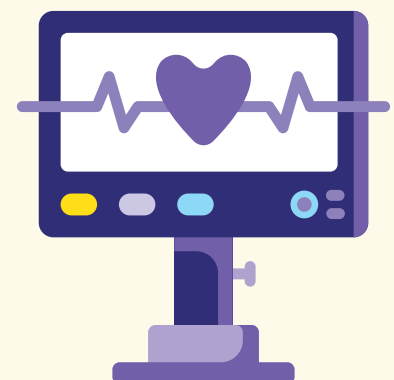
This will be a single assessor-blinded, parallel design RCT. 130 patients with TKR will be randomly assigned to either an 8-week hospital-based, physiotherapist-supervised rehabilitation programme or an 8-week tele-monitored home-based programme.

To monitor patients' functional recovery, the home-based programme will use rehabilitation tools and monitoring devices that have been validated for use by patients post TKR.

Outcome measures will be collected preoperatively, at 1, 3, and 6 months post TKR. The primary outcome will be physical function. Secondary outcomes include healthcare costs, knee pain intensity, knee impairments, and quality of life.

This study is the first in Singapore to examine an innovative and affordable solution for delivering post-TKR rehabilitation services.

If successful, the home-based programme has the potential to serve as a model for managing knee osteoarthritis and other costly, chronic musculoskeletal conditions to which exercise therapy is beneficial.





## Dr Shweta Singhal

**Consultant,**  
*Department of Neuro-  
Ophthalmology,  
Singapore National  
Eye Centre*

**Assistant Professor,**  
*Ophthalmology &  
Visual Sciences  
Academic Clinical  
Programme, Duke-  
NUS Medical School*

### A Study to Identify Markers of Early Retinal Cell Fate Commitment in Pluripotent Stem Cells in Vitro.

Clinical trials in patients with age-related macular degeneration (AMD) have now shown that stem cell-based retinal cell replacement therapy can successfully restore visual function.

However, production of clinical-grade retinal cells from pluripotent stem cells (PSC) is a complex, time-consuming and formidably expensive process. As a result, retinal stem-cell therapy remains inaccessible to most patients.

To produce retinal cells, mixed PSC are subjected to retinal differentiation conditions until retinal cells are formed. This is followed by an extensive purification process to remove non-retinal cell impurities, which escalates the time and cost of cell production.

This purification process could be eliminated from the cell production protocol if committed retinal progenitors were selectively isolated from mixed PSC before differentiation. It has not been possible to use this approach thus far due to lack of selective surface markers of early retinal progenitors.

Using an in vitro model of retinal development and single-cell RNA sequencing analysis, we have now identified a list of cell surface targets

that are differentially expressed in early committed retinal progenitors.

Through this work, we propose to validate these cell surface targets as early committed retinal progenitor markers, by evaluating their ability to yield pure retinal cells in vitro if used for selective cell isolation from mixed PSCs.

We have also identified novel transcription factors differentially expressed in early retinal progenitors.

Part of this proposal aims to understand the significance of these genes in early retinal cell fate commitment.

Not only will this work enhance our understanding of retinal development; successfully validated cell surface markers of early retinal progenitors, will pave the way for automation and up-scaling retinal cell production.

Effectively, bringing down costs and making retinal stem cell therapy accessible to the growing cohort of patients who need it.



## Dr Tham Huiwen Elizabeth

**Consultant, Khoo Teck Puat-National University Children's Medical Institute, National University Hospital**

**Assistant Professor,**  
*Department of Paediatric Medicine, Yong Loo Lin School of Medicine, National University of Singapore*

### The Skin Microbiome in Early Childhood Atopic Dermatitis

Atopic dermatitis (AD) is a chronic, incurable skin disease afflicting 20% of children in Singapore, and is often associated with allergic rhinitis, asthma and food allergies.

Studies suggest that prophylactic administration of emollients from birth in infants with a family history of atopy might prevent AD development in a small proportion.

It is, unclear if there are predictive non-invasive skin biomarkers of

AD present in early life that could precisely identify infants at risk of AD and the atopic march, for whom preventive interventions might be tailored for.

The primary aim of this study of this study is to identify unique characteristics of a newborn's skin microbiome at 7 days of life that predict development of AD and its severity, allergen sensitisation and allergic rhinitis by 18 months of age in comparison to healthy controls.

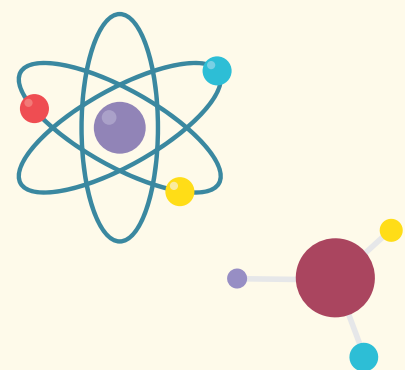
Secondary aims are to elucidate the relationship between the newborn's skin microbiomes in relation to the mode of delivery, to correlate this with the development of AD by 18 months of age.

Additionally, the secondary aim is to define maturation patterns of healthy infant skin microbiome by age, tracking the skin microbiome signatures of healthy infants longitudinally from birth to 18 months of age.

Clinical data collection, skin tape stripping, AD examination and skin prick tests will be performed for mother-offspring dyads in the ongoing Singapore PREconception Study of maternal and child Outcomes (S-PRESTO) cohort at multiple time points from birth to 18 months.

Whole metagenome sequencing and bioinformatics analysis will be carried out for skin microbiome analysis.

Identification of predictive skin biomarkers in the pre-disease phase will identify at-risk infants, who would may benefit from implementation of early interventions, such as prophylactic emollients from birth in high-risk infants or modification of the skin microbiome for the primary or secondary prevention of atopic dermatitis and its associated co-morbidities.





**Dr  
Tham Yih Chung**

***Clinical Research  
Fellow, Ocular  
Epidemiology  
Research Group,  
Singapore Eye  
Research Institute***

***Assistant Professor,  
Ophthalmology &  
Visual Sciences  
Academic Clinical  
Programme, Duke-  
NUS Medical School***

**Community-based Screening for  
Pathological Visual Impairment  
among Elderly Residents using  
Artificial-Intelligence Integrated  
Retinal Imaging**

Visual impairment (VI) is a major public health concern, associated with reduced quality of life and increased frailty risk. Globally, 400 million suffer from VI.

Among them, pathological VI (poor vision due to eye diseases, not refractive error) accounts for 60%.

In Singapore, 12% of individuals aged ≥60 (~90,000) suffer from pathological VI. This number will increase as Singapore’s population ages.

Most causes of pathological VI such as cataract and diabetic retinopathy, when detected early, can be treated from worsening to become severe visual/functional loss. As such, screening for pathological VI is crucial for healthy ageing and productive longevity.

Currently, as part of the Ministry of Health (MOH)-initiated functional screening programme, community vision screenings are conducted among elderly Singaporeans.

The screening model is a 2-tier process, conducted over different dates and sites, involving multiple tests and requires skilled manpower and substantial time to identify pathological VI cases.

These factors limit the capacity and coverage of the current model. It is challenging for the current model to operate sustainably to meet the long-term demand of nationwide annual vision screening for the elderly. With this in mind, a simple, effective and efficient modality for screening pathological VI is critically needed in Singapore.

Artificial intelligence (AI) technology offers unique opportunities to revolutionise the current screening model.

We propose a novel vision screening modality, integrating retinal photography and an AI-based algorithm, to detect pathological VI.

In this proposed project, we aim to refine and validate a newly developed modality, pilot its implementation and performance in a “real-world” community outreach screening setting for elderly Singaporeans.

This model provides a “one-stop shop” screening solution using a single only one test objective, and is cost-effective, time and, labour-efficient. and cost-saving.

Importantly, this aligns to MOH’s long-term approach to preventive care for Singapore’s elderly - to streamline health and healthcare costs (beyond healthcare to health), built along a sustainable model (beyond quality to value).



## CLINICIAN INNOVATOR DEVELOPMENT AWARD RECIPIENTS

### Reducing the Harm of Mechanical Ventilation by Using Dialysis to Remove Carbon Dioxide in the Form of Bicarbonate

Each year, mechanical ventilation is provided to approximately 20 million intensive care patients across the globe. Although life-saving, mechanical ventilation causes lung injuries that may develop into acute respiratory distress syndrome, which affects more than 20% of ventilated intensive care unit (ICU) patients.

Low tidal volume ventilation reduces lung injuries, but often leads to harmful carbon dioxide (CO<sub>2</sub>) accumulation. Today, CO<sub>2</sub> can only be removed directly from the blood using extracorporeal

CO<sub>2</sub> removal (EC CO<sub>2</sub>R) devices, which are complex, expensive, require placement of large bore catheters, and are not widely available. And so, there is an unmet need for simple, widely available, minimally invasive CO<sub>2</sub> removal devices.

In contrast to EC, CO<sub>2</sub>R, dialysis equipment is found in most ICUs. Supported by NMRC-TA funding, we have developed a low bicarbonate dialysate that removes CO<sub>2</sub> in the form of bicarbonate, and have shown that this dialysate lowers arterial CO<sub>2</sub> levels in a hypo-ventilated porcine model.

However, our prototype dialysate exposed recipients to a high dialysis dose. This was because our dialysate still contained some bicarbonate to ensure it had a biocompatible pH, preventing maximisation of the dialysis gradient.

Funded by a NHIC Joint Medtech grant, we created a large nanoparticle that can control dialysate pH and does not cross the dialysis membrane allowing us instead us, to create a novel dialysate containing no bicarbonate.

In this proposal, we aim to test the hypothesis that our novel dialysate will remove >90 ml/min of CO<sub>2</sub> without exceeding a conventional dialysis dose.

We will test this in a large animal model of dialysis to demonstrate that; conventional dialysis systems can be successfully modified to remove clinically important quantities of CO<sub>2</sub>, essentially bringing EC CO<sub>2</sub>R to all ICUs capable of providing dialysis.

**Dr  
Matthew Cove**



*Senior Consultant,  
Division of Respiratory and Critical Care  
Medicine, National University Hospital*

*Research Director and Assistant Professor,  
Department of Medicine, Yong Loo Lin  
School of Medicine, National University  
of Singapore*



**A/Prof  
Ng Wai Hoe**

*Medical Director,  
National  
Neuroscience  
Institute*

*Deputy Group  
Chairman,  
SingHealth Medical  
Board*

*Senior Consultant,  
Department of  
Neurosurgery,  
National  
Neuroscience  
Institute*

*Associate  
Professor,  
Duke-NUS Medical  
School*

### Artificial Intelligence Software for Emergency Neuro-radiological Diagnosis

Radiological scans need to be reported rapidly, accurately and automatically to help expedite medical treatment, improve patient outcomes, and reduce healthcare costs.

Human clinicians are intrinsically limited by experience, time and fatigue, but they can be assisted by artificial intelligence (AI) algorithms.

Convolutional neural networks (CNNs) are AI algorithms that have demonstrated dramatic successes in computer vision, beating human experts. CNNs can be applied to analyse medical images and read radiological scans.

The first aim of this study is to develop and optimise a three-dimensional CNN (3D CNN) that can analyse Computed Tomography (CT) brain scans for emergency neurological conditions such as stroke and traumatic brain injury. The second aim of this study is to deploy the developed 3D CNN in a large tertiary care hospital.

This proposal translates our prior laboratory work on 3D CNN to a clinical setting. We hypothesise that 3D CNN can be used to assist clinicians in the management of neurological emergencies by detecting and triaging abnormal scans.

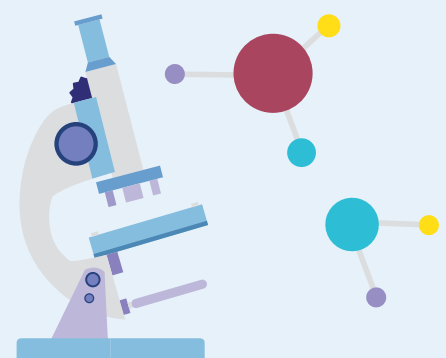
In the first training stage, incoming CT brain data from patients who are scanned emergently at National Neuroscience Institute (NNI) will be collected for three months.

This data will be used to train and optimise the 3D CNN to recognise common neurological emergencies such as acute intracranial hemorrhage.

In the second evaluation stage, the 3D CNN software will be deployed alongside radiologists, and its ability to detect and triage abnormal CT brain scans will be measured.

As rapid and accurate diagnosis of CT brain scans are critical to radiological diagnosis in acute neurological emergencies; this work can improve patients' clinical outcomes in survival, morbidity and quality-adjusted life, and reduce overall healthcare costs.

This work can be used for any organ where CT and magnetic resonance imaging (MRI) scans are required.





**Dr Jessica Quah Lishan**

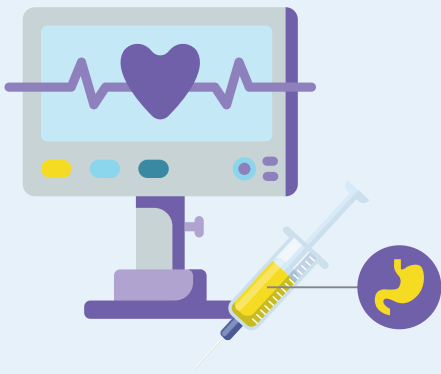


**Consultant,**  
Department of Respiratory and Critical Care  
Medicine, Changi General Hospital

**Adjunct Senior Lecturer,**  
Singapore University of Technology  
and Design

**Clinical Lecturer,**  
Yong Loo Lin School of Medicine,  
National University of Singapore

**Adjunct Teaching Faculty,**  
Lee Kong Chian School of Medicine,  
Nanyang Technological University



**Development of a Programmable Chest/Abdominal Drain Fluid Regulator to Reduce Morbidity, Care Requirements and Improve Outcomes**

Pleural effusions and ascites occur in many disease states, resulting in poor symptom control and quality of life in sufferers. Removal of these collections of fluid via chest/abdominal drainage alleviates symptoms rapidly, but are associated with complications such as re-expansion pulmonary oedema and systemic hypotension when unregulated.

We proposed the creation of an automated device that can volume and rate-control this process.

The aim of this grant proposal research is the creation of 4 device prototypes that can be adapted to existing chest/abdominal drains. The prototypes would be based on a prior patent co-invented by the grant applicant. The hypothesis is that the prototypes would be able to automate rate of fluid drainage over a range of fluid volumes, pressures and viscosity, accurately and precisely.

The prototypes will be developed in 2 phases to meet Class II requirements for devices per Federal Drug Administration (FDA) stipulations.

The phase-1 prototype assembly, comprising 3 subsystems, will be undertaken by collaborating engineers. These subsystems will consist of a drainage mechanism, user interface and failsafe mechanisms.

In phase 2, bench tests will be performed, simulating real-life conditions in pleural effusions and ascites. The prototypes will demonstrate accuracy and precision in volume and rate control of drainage, over a range of fluid volumes, pressures and viscosity.

Refinements will be factored for and performed during bench tests to produce 4 new prototypes that will meet regulatory requirements for first-in-man pivotal studies.

The device is anticipated to generate annual cost savings of S\$2.4 million for the nation and reduce inpatient hospital stays. It will allow a reduction in time to symptom alleviation for patients, as well as, lower physician and nursing workloads.

Ultimately, the device aims to enhance home palliation of pleural effusions and ascites, easing the transition of care from hospital to community in terminally ill patients.

**Development of a System Comprising a Digital Exhaled-breath Carbon Monoxide Self-monitoring Device Linked to Virtual Smoking Cessation Coaching and Virtual Network of Quit-Supporters via Social Media**

Cigarette smoking is the leading cause of preventable death and a major public health threat. Current smoking cessation approaches have sub-optimal quit rates, accessibility and scalability.

We propose to provide smokers access to a personal device to self-monitor their quit smoking efforts, linking them to a virtual smoking cessation coaching programme, and network of quit supporters on social media, to help grow the overall quit rate.

The proposed innovation aims to:

- (i) Develop a quit smoking platform comprising a digital exhaled-breath carbon monoxide self-monitoring device (STEADES-2), which integrates a virtual smoking cessation coaching programme and network of trained quit supporters;

- (ii) Conduct a feasibility study of STEADES-2 using mix research methods to gather feedback and assess user acceptability and utilisation.

We have developed a prototype device to measure exhaled breath carbon monoxide (eCO) with comparable accuracy to commercially available devices.

The second version (STEADES-2) will include facial and individual recognition functionality to mitigate fraudulent usage.

The accompanying STEADES mobile application will allow transmission of eCO data via social media to an online smoking cessation coaching programme and network of quit supporters.

The virtual platform will be developed alongside the device in relation to existing quit smoking programmes run by HPB and polyclinics.

The entire STEADES platform will be assessed for user-acceptability and utilisation in a feasibility study group



**Adj A/Prof Tan Ngiap Chuan**

**Director (Research), Senior Consultant and Family Physician,**  
SingHealth Polyclinics

**Vice-Chair (Research),**  
SingHealth-Duke NUS Family Medicine  
Academic Clinical Programme

comprising 20 smokers, 10 coaches and 10 virtual quit smoking supporters.

Participant feedback will be solicited through questionnaire surveys, individual and group interviews.

The quantitative and qualitative results will be used to:

- Enhance the STEADES' platform
- Design a randomised controlled trial protocol to determine proof of value in the next development phase

# TALENT DEVELOPMENT PROGRAMMES

## NMRC RESEARCH TRAINING FELLOWSHIP

The NMRC Research Training Fellowship provides doctors and health science professionals with the training necessary to become clinician scientists.

Medical doctors registered with the Singapore Medical Council, dental surgeons registered with the Singapore Dental Board, health science professionals and biostatisticians are all eligible to apply.

The fellowship covers overseas research training and graduate research degree programmes at local and overseas institutions. Awardees on local graduate degree programmes will be funded on salary and tuition fees, while those on overseas research programmes, will additionally receive allowances and other benefits in line with host institution's guidelines.

## NMRC RESEARCH TRAINING FELLOWSHIP

11 recipients were awarded the NMRC Research Training Fellowship.

Name	Institution and Type of Training	Project
<b>Dr Troy Puar Hai Kiat</b>	<b>Changi General Hospital</b> <i>Part-time local PhD</i>	Primary Aldosteronism in Singapore: A Curable Cause of Hypertension
<b>Dr Raghav Sundar</b>	<b>National University Hospital</b> <i>Part-time local PhD</i>	Investigating the role of Epigenomic Alternative Promoter Isoforms in Modulating the Immunogenicity of Gastric Cancer
<b>Dr Diana Chan Xin Hui</b>	<b>Singapore General Hospital</b> <i>Part-time local PhD</i>	Regulation of Chronic Pain and its Co-morbidities by Targeting Intraseptal Nerve Growth Factor (NGF) Pathways and Synaptic mechanisms in the Forebrain Medial Septum.
<b>Dr Chan Lai Gwen</b>	<b>Tan Tock Seng Hospital</b> <i>Part-time local PhD</i>	Multimodal Characterization of the Impact of Sleep Disturbances on Traumatic Brain Injury Outcomes
<b>Dr Chia Po Ying</b>	<b>Tan Tock Seng Hospital</b> <i>Part-time local PhD</i>	The Role of Endothelial Glycocalyx Mast Cells and Vascular Nitric Oxide in the Pathogenesis of Dengue
<b>Dr Lee Wei Jie Jonathan</b>	<b>National University Hospital</b> <i>Full-time Overseas Attachment</i>	Treating Non-alcoholic Fatty Liver Disease through Modification of Microbiome-modulated Metabolites
<b>Dr Liu Yu-Chi</b>	<b>Singapore Eye Research Institute</b> <i>Part-time local PhD</i>	The Application of Terahertz Scanning System on the Evaluation of Corneal Opacities
<b>Dr Nei Wen-Long</b>	<b>National Cancer Centre Singapore</b> <i>Part-time local PhD</i>	Somatostatin Receptor Theragnostic in Nasopharyngeal Cancer
<b>Dr Yam Gui Jie Michael</b>	<b>Tan Tock Seng Hospital</b> <i>Part-time local PhD</i>	S.P.A.R.T.A.N trial - Sarcopenia Prevention and Reversal with Physical Training and Nutrition in Distal Radius Fracture Patients
<b>Dr Tan Yijia, Bryan</b>	<b>Tan Tock Seng Hospital</b> <i>Part-time local PhD</i>	Collaborative Model of Care between Orthopaedics and Allied Healthcare Professionals (CONNECT)
<b>Dr Lam Chih Chiang, Benjamin</b>	<b>Khoo Teck Puat Hospital</b> <i>Full-time local PhD</i>	Investigation of Environmental, Genetic and Gut Microbial Factors Underlying Obesity amongst Chinese, Malay and Indians in Singapore

## MOH HEALTHCARE RESEARCH SCHOLARSHIP – MASTER OF CLINICAL INVESTIGATION (MCI)

This scholarship aims to encourage clinicians to pursue advanced clinical research training through the MCI programme at the Yong Loo Lin School of Medicine, National University of Singapore. The scholarship covers both tuition and research fees for the programme.

## NATIONAL OUTSTANDING CLINICIAN SCIENTIST (CS) RESIDENT AWARD

This award is given to a CS Resident who excelled in the clinical training, made significant research contribution with actual or potential translational application to improve clinical care and showed exemplary behavior during residency. The winner receives a \$500 book prize.

## MOH HEALTHCARE RESEARCH SCHOLARSHIP (MCI)

13 recipients were awarded the MOH Healthcare Research Scholarship - Master of Clinical Investigation (MCI)

Name	Institution and Type of Training	Project
<b>Dr Chew Linghui Justin</b>	<b>Tan Tock Seng Hospital</b> <i>Department of Geriatric Medicine</i>	Fat-muscle Crosstalk: The Association of Circulating Adipo-myokines with Frailty and Physical Performance in Sarcopenic Obesity
<b>Dr Goh Xueying</b>	<b>National University Hospital</b> <i>Department of Otolaryngology</i>	Nasopharyngeal Carcinoma: Defining patients who will benefit from surgical intervention to overcome post-radiation middle ear effusion
<b>Dr Ho Wei Loong Sean</b>	<b>Tan Tock Seng Hospital</b> <i>Department of Orthopaedic Surgery</i>	Syndesmotic Injuries in Ankle Fractures: A randomized controlled trial of one versus two-point dynamic fixation in treatment
<b>Dr Kaan Hung Leng</b>	<b>National University Hospital</b> <i>Department of General Surgery</i>	Comparison of outcomes for patients undergoing Colonoscopy with and without sedation
<b>Dr Low Jia Ming</b>	<b>National University Hospital</b> <i>Department of Paediatrics</i>	Chronic Inflammation and Alveolar disruption observed BPD: WJSC administered intravenously in neonatal rodent model study
<b>Dr Ng Jun Jie</b>	<b>National University Hospital</b> <i>Department of Cardiac, Thoracic and Vascular Surgery</i>	Placement of Adhesion Barrier around the Juxta-anastomotic Segment of the AVF to Reduce the Incidence of JAS Formation and Improve Maturation Rates
<b>Dr Ng Pei Lun Sue-Ann</b>	<b>Singapore General Hospital</b> <i>Department of Rheumatology and Immunology</i>	Investigation of Early versus late Systemic Sclerosis (SSc) by cMRI
<b>Dr Tay Khwee Soon Vincent</b>	<b>Singapore General Hospital</b> <i>Department of Plastic, Reconstructive and Aesthetic Surgery</i>	The Use of Cell Surface Markers for Dose Standardization of Uncultured Adipose Stromal Vascular Fraction for Reliable Cellular Therapeutics
<b>Dr Wang Fuqiang</b>	<b>National Cancer Centre Singapore</b> <i>Division of Radiation Oncology</i>	Investigating the Role of Spatially Fractionated Radiotherapy (GRID) in the Treatment of Cancer Patients
<b>Dr Judith Wong Ju Ming</b>	<b>KK Women's and Children's Hospital</b> <i>Children's Intensive Care Unit</i>	The Association between Pulmonary Matrix Metalloproteinases and Clinical Outcomes in Paediatric Acute Respiratory Distress Syndrome
<b>Dr Wu Chun Ho Clement</b>	<b>Singapore General Hospital</b> <i>Department of Gastroenterology and Hepatology</i>	Comparison Levels of Circulating Tumour cells between the Portal Venous and Peripheral Circulations in Pancreatic Cancer
<b>Dr Yang Peiling</b>	<b>National University Hospital</b> <i>Division of Endocrinology</i>	Re-differentiation of Radioiodine-refractory Metastatic Thyroid Cancer
<b>Dr Yau Ying Wei</b>	<b>National University Hospital</b> <i>Department of Emergency Medicine</i>	Using the aiTRIAGE Device to Predict Major adverse Outcomes in ED Patients with Suspected Sepsis

## NATIONAL OUTSTANDING CLINICIAN SCIENTIST (CS) RESIDENT AWARD

There are 2 recipients for the National Outstanding Clinician Scientist (CS) Resident Award.

Name	Cluster and Clinical Specialty
<b>Dr Kok Yee Onn</b>	<b>Singapore Health Services</b> <i>Plastic Surgery</i>
<b>Dr Soh Yu Qiang</b>	<b>Singapore Health Services</b> <i>Ophthalmology</i>

# CLINICIAN SCIENTISTS IN THE SPOTLIGHT

## Professor Toshio Suda

### — STAR AWARD RECIPIENT —

Senior Principal Investigator,  
Cancer Science Institute of  
Singapore

Professor,  
National University of  
Singapore

*“Research is to facilitate reason – with increased international collaboration and systematically educating investigators, more translational studies can come to the fore”*

Professor Toshio Suda began his journey as a paediatrician, and began to search for answers in potential treatments of leukemia. Having spent more than 30 years in multiple countries studying hematopoietic stem cells (HSCs) and the HSC niche, his energy is echoed in his enthusiasm in nurturing and educating more young investigators.

Prof Suda's past work encompasses the study of the intrinsic and extrinsic regulation of HSCs, purification of potent HSCs, analyses of cell differentiation processes, identification of cytokine signaling in hematopoiesis, and the characterization of HSC niches. Hoping to provide novel insights to the development of niche therapy, his focus is firmly on the areas of stem cell niches, stem cell aging and cancer stem cell, and looks to translate his team's findings into clinical settings, which would contribute to stem cell transplantation as well as treatment of hematological diseases.

A previous recipient of the Japanese Society of Hematology (2013) and Donald Metcalf Award by International Society of Experimental Hematology (2014), the Senior Principal Investigator at the Cancer Science Institute of Singapore (CSI) is appreciative of the renewal of his Singapore Translational Research (STaR) award. Under the previous STaR project, Prof Suda and his team have discovered that the micro environment directly alters hematopoietic stem cell (HSC) metabolism and their fate – either to self-renew or to differentiate into mature cells. With data suggesting that appropriate regulations of the metabolic state of hematopoietic stem cells (HSCs) may allow HSCs to self-renew and expand, he proposes to build on existing findings, and expand the following areas that will impact clinical implications in terms of HSC expansion for application in disease setting with this STaR project renewal.

Excited for the path moving forward, he believes that his research might provide insights in disease prevention, and more impactful in various segments such as in the pre-leukemic state. Prof Suda looks to ensure that these studies will elucidate the pathophysiology of diseases and would provide critical clues to develop novel treatment and preemptive measures for the diseases.



## Mentoring the Path Forward

Outside of his research efforts, Prof Suda is a firm believer in the importance of mentorship, as well as the educating and nurturing of young minds that are interested, who will become the next generation of investigators. He believes in the need for more “face-to-face time in the mentor-student relationship, and treating them as family in order to systematically build up a pipeline of future researchers and investigators.” Especially in an aging society, where research has to be a core component of healthcare, he also emphasises the need for learning basic methodologies during youths' formative years.

Deeply appreciative of Singapore's institution's drive to promote international collaboration, he credits the availability of academia and industry in creating more opportunities for driving top-level research. Echoing the oft-repeated adage, he believes that “In areas with not much natural resources, we have to engage in noteworthy research in order to stand out on the Asian and world stage.” With clear demarcations between academic interest in research, where projects like his own may take a decade or two, collaboration can create far more innovation in these fields; while industry may benefit from more translated studies and new treatments that are made more quickly available.

For his extraordinary dedication and distinguished contributions in developing and advancing the field of hematology, Professor Toshio Suda receives the Singapore Translational Research Investigator Award.



## Professor Carolyn Lam Su Ping

### — CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR) —

**Senior Consultant,**  
Department of Cardiology,  
National Heart Centre  
Singapore

**Director,**  
Clinical and Translational  
Research Office, National Heart  
Centre Singapore

**Professor,**  
Cardiovascular Academic  
Clinical Program, Duke-  
NUS Medical School

“*As a clinician scientist, saying no is one of the hardest and most important lessons I’ve had to learn, before picking the correct and precious opportunity to harness a worthy effort.*”

Winner of three NMRC human capital awards, Professor Carolyn Lam is no stranger to dedicating her time to world class research. Echoing the words of Steve Jobs, “People think focus means saying yes to the things you have to focus on. But that’s not what it means at all. It means saying no to the hundreds of other good ideas that are out there”.

A senior consultant at the Department of Cardiology, and director of the Clinical and Translational Research Office at the National Heart Centre Singapore, as well as Professor of Cardiovascular Academic Clinical Programme at Duke-NUS Medical School, Prof Lam is no stranger to having to delicately balance the demands upon her time. Amidst an overwhelming multitude of undertaking, she believes that this award is critical in providing the protected time she needs for research.

The renewal of the award comes as a natural progression in Prof Lam’s research. Her first Clinician Scientist Award helped set up a nation-wide observational study in Singapore while the second enabled her to extend the observational study to 10 other countries in Asia. With this third award, Prof Lam looks to enable progression from observational to interventional studies across the established Asian network.

With her cardiology specialization as well as her training in advanced cardiology and heart failure, Prof Lam has had her eye firmly on going bringing the impact of her research to bear. As cardiovascular disease is the main cause of death, hospitalisation and disease burden among patients with diabetes, she exhorts that the prevention is critically important to patients, healthcare providers and systems of care. Looking to her research to yield results to show that, the simple pragmatic approach of intensification of readily available medications can prevent cardiovascular events in a cost-effective way, it has the potential to change medical practice not only in Singapore but across Asia.



## The Heart of the Matter

Prof Lam’s work has been focused on heart failure since the beginning. When her work showed the presence of a unique Asian phenotype of lean diabetic heart failure (with preserved ejection fraction) – one which that was no proven treatment, she decided to go upstream in addressing this huge public health problem by focusing on prevention of heart disease in patients with diabetes. Once efficacy is established, she hopes to progress with cost-effectiveness analyses.

As Prof Lam juggles clinical, research and academic duties, she believes that key next steps for her include learning to manage, mentor, and inspire people. She credits Duke-NUS and the Stanford Executive Programme in imparting invaluable management lessons, as well as helping her hone her focus and leadership abilities. She is also personally grateful for the inclusion of the establishment of an Asian network of investigational partners and sites and being able to leading the A\*STAR funded multi-institutional ATTRaCT platform.

On top of everything Prof Lam has done, she has also served on the global steering committees of multiple multinational clinical trials and international consensus guideline committees; and contributed as an associate editor of the world’s top cardiovascular journals. For her, the achievements closest to her heart are balancing family and work life, while growing her work family of mentees and beloved colleagues.

For her outstanding contributions in developing observational and interventional studies in for cardiovascular events, and incredible dedication in resolving public health issues, Professor Carolyn Lam receives the Clinician Scientist Award (Senior Investigator).

## Associate Professor Ng Oon Tek

### — CLINICIAN SCIENTIST AWARD (INVESTIGATOR) —

**Senior Consultant,**  
National Centre for  
Infectious Diseases

**Associate Professor,**  
Lee Kong Chian School  
of Medicine, Nanyang  
Technological University

**Senior Consultant,**  
Department of Infectious  
Disease, Tan Tock Seng Hospital

*“If you want to go quickly, go alone.  
If you want to go far, go together.”*

A/Prof Ng received his MBBS from the National University of Singapore. He completed Internal Medicine training with the Singhealth cluster, and obtained the conjoint MRCP (UK) and M Med (Internal Medicine) in 2004, with the Siah Cheng Siah Gold medal for best Internal Medicine candidate.

During speciality infectious disease training, it was apparent that the integration of public health, laboratory science and clinical medicine was vital to addressing many infectious disease issues of our time. In an initial foray into grant-funded research, A/Prof Ng worked with collaborators in A\*STAR and other institutions to develop a point-of-care HIV viral quantification device. A spin-off from this project was the implementation of a cost-effective HIV viral load test and genotypic resistance test which was used for patient care at the former CDC HIV national referral clinic and other hospitals.

As a recipient of the NMRC Overseas Research Fellowship, A/Prof Ng completed his Master of Public Health degree at Johns Hopkins followed by a year-long research attachment with a US NIH funded group led by Prof Thomas Quinn. Once back in Singapore, his research efforts were further supported by the NMRC Transition Award (TA), Clinician-Scientist Award (CSA), NMRC IRG and NMRC Collaborative Centre Grant together with US NIH funding via the Treat Asia HIV Network.

A major focus of A/P Ng's current research involves antimicrobial resistance especially multi-drug resistant Gram-negative (MDR GN) infections, the highest priority WHO bacterial antimicrobial resistance threat. In the last decade, political and policy leaders and the healthcare community have become increasingly concerned with



the rise of the antimicrobial resistance threat with this issue being raised as the latest health issue discussed at the United Nations General Assembly. His first CSA award involved working on integrating whole-genome sequencing to inform infection prevention efforts targeting MDR GN. Much of this work is done in the context of the Carbapenemase-Producing Enterobacteriaceae in Singapore (CaPES) Study Group, a network involving infectious disease physicians and clinical microbiologist from all restructured hospitals in Singapore.

In the current CSA renewal, the study team plans to extend the research focus from observational and implementation focused work to an interventional study involving the use of faecal microbiota transplantation (FMT) for intestinal decolonisation of MDR GNs. FMT is a proven treatment modality for *C. difficile* infection with encouraging pilot studies suggesting the ability of FMT to hasten gut microbiome recovery and reestablishment of colonisation resistance to MDR GN carriage.

All the above research and translational work would not have been possible without the involvement of colleagues and mentors from the infectious disease community, both in Singapore and overseas. Additionally, the enabling environment for biomedical research in Singapore has also been a great blessing.



## Dr Tham Huiwen Elizabeth

### — TRANSITION AWARD —

**Assistant Professor,**  
Department of Paediatric Medicine,  
Yong Loo Lin School of Medicine,  
National University of Singapore

**Consultant,**  
Khoo Teck Puat-National University  
Children's Medical Institute, National  
University Hospital

*“Look to problems you face in clinical practice as the basis for research ideas, which would then translate to clinically relevant interventions for research.”*

As a young clinician, Dr Elizabeth Tham was struck by the immense psychosocial, emotional and financial burden that severe Atopic Dermatitis (AD) had, not only on infants and children afflicted by this terrible, chronic skin disease, but also their whole family. A significant proportion of children with severe AD also develop other allergic disorders like food allergies, allergic rhinitis and asthma in later life (atopic march) which compounds the burden incurred by this group of disorders. This inspired her to pursue research into ways to prevent and treat severe AD – an incurable disease which is only permanently resolved when the child outgrows it on his/her own conventional therapy is based around only controlling the symptoms of the disease.

Dr Tham graduated with MBBS from the Yong Loo Lin School of Medicine, NUS in 2007 and was awarded the Jane Prize in Paediatrics. She received her specialist training in Paediatrics and Neonatology at NUH and Kangar Kerbau Women's and Children's Hospital (KKWCH). She went on to undertake the Master of Clinical Investigation (MCI) degree in 2016–2018 under the Ministry of Health (MOH) Healthcare Scholarship, which equipped her with essential skills in hypothesis generation, study methodology, grant and manuscript writing.

Equipped with the basic foundations in research, Dr Tham continued to embark on the NMRC Research Training Fellowship, which provided her the opportunity to gain skills in basic laboratory techniques and benchwork enhanced her scientific writing skills and provided her opportunities for international collaborations. She is currently on the Clinician-Scientist tenure track in National University of Singapore Yong Loo Lin School of Medicine (NUS YLLSoM) and will be soon be pursuing a PhD. She also believes that receiving the Transition Award is an important next step in her development, providing her with the unique opportunity to spend protected time researching the mechanisms behind AD and its prevention.

Dr Tham's work involves elucidating unique signatures of the neonatal and infant skin microbiome which would predict AD development and persistence, and how maternal and environmental factors play a role in modulating AD risk. It is embedded in a large preconception birth cohort in Singapore – the Singapore PREconception Study of long-Term maternal and child Outcomes (S-PRESTO).



With the protected time from securing the TA, she looks to have her work yield valuable insights into the pathogenesis of AD in Asian children and identify endophenotypes of AD compared to healthy children. This would in turn help to develop interventions to modify the microbial and environmental risk factors for AD which could prevent AD onset or attenuate its course and reduce the healthcare burden of AD and its comorbidities.

Very honoured and grateful to be a recipient of this prestigious award, Dr Tham is very excited about the opportunities that this award will provide towards furthering her research into strategies which could help treat and prevent atopic dermatitis, food allergies and other allergic disorders in children.

Dr Tham exhorts other clinicians to start instilling a love for research early, and get trained in research skills as part of their curriculum – a better time to master crucial basics. When equipped with the core research skills and a language for communication with basic scientist collaborators, potential future researchers can develop innovative and clinically translatable research even during clinical training and later clinical practice.

For her unwavering commitment towards improving the lives of children and their families, and unequivocal support for shaping care, Dr Elizabeth Tham receives the Transition Award.

## Adjunct Associate Professor Tan Ngiap Chuan

### — CLINICIAN INNOVATOR DEVELOPMENT AWARD RECIPIENTS —

**Director (Research),**  
SingHealth Polyclinics

**Vice-Chair (Research),**  
SingHealth-Duke NUS Family  
Medicine Academic Clinical  
Programme

**Senior Consultant,**  
Family Physician

*“Family physicians play a pivotal role in optimising the health of the population in the community. We are in a strategic position to address clinical issues across all ages of the population that we care for, and such oversight allows us to design person-centred innovations to improve quality care.”*

As a practising Family Physician, A/P Tan Ngiap Chuan’s professional interests are multivariate – ranging from person-centered care and ageing related research, to the development of mobile applications, serious games and virtual reality in primary healthcare setting. “Research and innovation should be relevant to the bulk of the population,” he explained, establishing his firm belief on research that caters to the majority.

A/P Tan was appointed as the Director of Research at SingHealth Polyclinics (SHP) in October 2012, after serving as a Clinic Director of SHP-Pasir Ris since 2002. As a facilitator for the in-house research training, he also runs basic and qualitative research workshops regularly for the multidisciplinary staff at SHP and FM ACP. He coaches medical students and novice primary care researchers via platforms, such as Research Master Hour and Research Consultation Clinics. He also mentors the SHP and Family Medicine Academic Clinical Programme (FM ACP) Fellowship trainees in the College of Family Physicians of Singapore.

A/P Tan is a firm believer in the power of networks and consistently collaborates with local academic institutions, including Institute of Technical Education, Polytechnics, local universities, SingHealth institutions and other ACPs. On top of this, he is also a key member of the SingHealth consortium, which has recently been awarded the AI-SG Grant, leveraging on artificial intelligence to develop predictive risk model and to enhance evidence-based person-centered care.

### Preventing Major Public Health Threats

With cigarette smoking being the leading cause of preventable death and a major public health threat, A/P Tan saw that the current smoking cessation approaches have sub-optimal quit rates, accessibility and scalability. With this, he aspires to develop a system comprising a digital exhaled-



breath carbon monoxide self-monitoring device, linked to virtual smoking cessation coaching and virtual network of quit supporters via social media, for smokers to access. This may encourage and aid in the process of quitting smoking.

A/P Tan and his team has since developed a prototype device to measure exhaled breath carbon monoxide (eCO) with comparable accuracy to commercially available devices. The virtual platform will be developed alongside the device in relation to existing quit smoking programmes run by the Health Promotion Board (HPB) and the polyclinics.

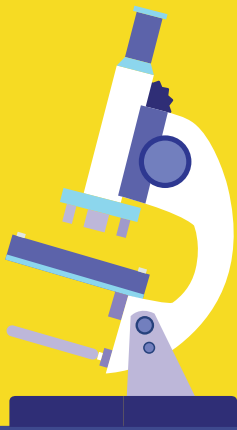
### Clinician Innovator Development Award

A/P Tan is extremely honoured and humbled as one of the first Family Physicians to receive the award. With this funding, he believes that the protected time would be invaluable, because time is of the essence. “When we take the time to recognise, reflect, respond and research, we can move beyond just the usual scope of medicine.”, he adds, looking forward to see other aspiring Family Physicians taking up the mantle of research and innovation.

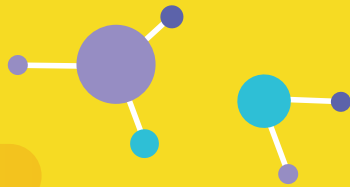
For his unwavering commitment to the family medicine and public health, as well as tireless efforts in giving back to society, Associate Professor Tan Ngiap Chuan receives the Clinician Innovator Development Award.



**RESEARCH**



**GRANTS**



# FUNDING TRANSLATIONAL AND CLINICAL RESEARCH

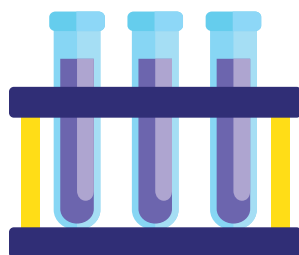
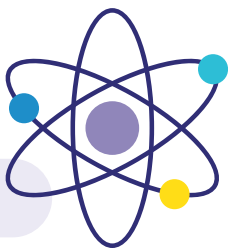
Funding of translational and clinical research is one of the core pillars of NMRC's mandate. In line with this, NMRC offers several grants to support small to large-scale, Singapore-based research initiatives across the biomedical science spectrum. To ensure the best possible use of research funding, all grants are peer-reviewed and awarded competitively.

These grants are broadly categorised under:

## NMRC-Funded/Managed Grants

This category supports the research of the healthcare community across a range of investigator-led studies and core research capability building through the following schemes:

- Centre Grant (CG)
- Clinical Trial Grant (CTG)
- Clinician Scientist Individual Research Grant (CS-IRG)
- Clinician Scientist Individual Research Grant New Investigator Grant (CS-IRG-NIG)
- Health Services Research Grant (HSRG)
- Health Services Research New Investigator Grant (HSR-NIG)



## Open Fund Grants

The Open Fund grants aim to fund the best ideas, through competition, to support individual and collaborative research that is aligned with RIE2020's vision for the Health and Biomedical Science (HBMS) domain: to be a leading centre that advances human health and wellness, and creates economic value for Singapore and Singaporeans, through the pursuit of excellence in research and its applications.

- Open Fund - Large Collaborative Grant (OF-LCG)
- Open Fund - Individual Research Grant (OF-IRG)
- Open Fund - Young Individual Research Grant (OF-YIRG)

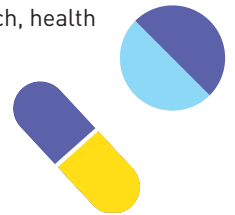
# NMRC-FUNDED/ MANAGED GRANTS



## CENTRE GRANT (CG)

The Centre Grant (CG) funding framework aims to support the public healthcare institutions/clusters to build up their core research capabilities in terms of common research platforms, shared equipment and core manpower. To better realise the RIE2020 healthcare goals, the RIE2020 funding framework further seeks to enhance collaborative and transdisciplinary research productivity.

Under the RIE2020 CG framework, there were two funding opportunities - Main Centre and Collaborative Centre. Applicants were also encouraged to focus on one of the RIE2020-prioritised therapeutic areas of research: cancer, cardiovascular diseases, diabetes mellitus and related metabolic/endocrine disorders, infectious diseases and neurological & sense disorders; as well as address translational medicine & implementation science research, health systems research, primary care research or population health research.



## CLINICAL TRIAL GRANT (CTG)

The RIE2020 Clinical Trail Grant (CTG) includes two schemes:

- 1 The Industry Collaborative Trials Scheme (ICT) supports ICTs which involve both the clinician and company contributing intellectual inputs and funds to conduct the trial and develop novel or pre-existing drugs/medical device/interventions for new indications. The prerequisite for application is Principal Investigator's (PI) ability to obtain industry contribution of at least 70% (cash or in-kind) of the Total Project Costs (TPC). The PI can apply for funding quantum of up to 30% of the TPC (inclusive of 20% IRC) over a period of five years. CTG-ICT is a rolling grant call.

PERIOD	PROPOSALS REVIEWED	GRANTS AWARDED	Total Sum Awarded (\$ millions)
FY2018	1	0 #	0

# Application was withdrawn

- 2 The Investigator-Initiated Trials Scheme (IIT) supports IITs of both early and late phases which are initiated and driven by clinicians who are interested to conduct clinical trials on novel or pre-existing drugs/medical device/interventions for new indications. No minimum company contributions, however, applications with industry contribution would have higher priority. Pls note that from May 2018 Grant Call onwards, CTG-IIT is funded by NRF Central Gap. The funding quantum is up to \$1.5million (without IRC) over a period of three years. Projects with duration of more than 3 years will be evaluated on a case-by-case basis. CTG-IIT grant calls are made twice per year.

*Statistics for the FY2018 grant calls are not available at the time of print and will be published in the next publication.*



## CLINICIAN SCIENTIST-INDIVIDUAL RESEARCH GRANT (CS-IRG)

Clinician Scientist-Individual Research Grants (CS-IRGs) are provided to clinician scientists to enable them to carry out medical research on a specifically defined topic for a period of three years in a local public institution. The focus of the research should be translational and clinical in nature. The quantum supported for CS-IRGs is up to \$1.5 million over a period of three years. CS-IRG grant calls are made twice per year.

PERIOD	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
MAY 2018	52	8	15.4%	13.30
NOV 2018	47	9	19.1%	13.33
<b>TOTAL</b>	<b>99</b>	<b>17</b>	<b>17.2%</b>	<b>26.63</b>

## CS-IRG NEW INVESTIGATOR GRANT (CS-IRG-NIG)

The CS-IRG New Investigator Grant (CS-IRG-NIG) is a sub-category of the CS-IRG that is targeted specifically at new clinical investigators. The CS-IRG-NIG is intended to serve as a career stepping stone, providing new investigators with their first independent national-level grant. Applicants with substantial research experience are not eligible to apply for this grant. The quantum supported for CS-IRG-NIGs is up to \$200,000 over a period of two years. CS-IRG-NIG grant calls are made twice a year.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
MAY 2018	25	7	28.0%	1.60
NOV 2018	25	7	28.0%	1.61
<b>TOTAL</b>	<b>50</b>	<b>14</b>	<b>28.0%</b>	<b>3.21</b>

## HEALTH SERVICES RESEARCH GRANT (HSRG)

The Health Services Research Grant (HSRG) promotes the conduct of HSR and enables the translation of HSR findings into policy and practice. There is no cap in funding quantum or funding duration. HSRG grant calls are made once a year.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
NOV 2017	26	8	30.8%	8.63
MAY 2018	31	8	25.8%	4.80
<b>TOTAL</b>	<b>57</b>	<b>16</b>	<b>28.1%</b>	<b>13.43</b>

## HEALTH SERVICES RESEARCH NEW INVESTIGATOR GRANT (HSR-NIG)

The Health Services Research New Investigator Grant (HSR-NIG) is a subcategory of the Health Services Research Grant (HSRG). Launched with the aim of supporting new HSR researchers, the quantum supported for HSR-NIG is up to \$100,000 over a period of two years. HSR-NIG grant calls are made twice a year.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
MAY 2018	7	1	14.2%	0.12

# OPEN FUND GRANTS

## OPEN FUND-LARGE COLLABORATIVE GRANT (OF-LCG)

The Open Fund-Large Collaborative Grant (OF-LCG) supports the best teams of institutional, investigative researchers to advance human health and wellness, that co-create economic value, through research excellence and application, for Singapore and Singaporeans. It offers a unique opportunity to pair researchers with clinician scientists, and clinical investigators across hospitals and Academic Medical Centres within Singapore.



Collaborative efforts among clinical research communities, interdisciplinary and investigative partnerships across institutions, to leverage the full spectrum of scientific research capabilities in Singapore



Advancements to the study of therapeutic areas that position Singapore in the forefront of biomedical science

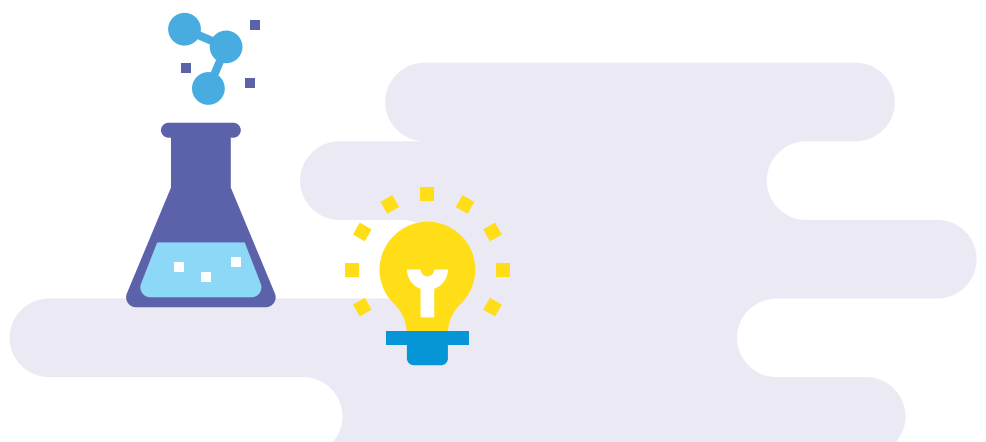


Discovery and application of biomedical science-based ideas with clear impact/bearing to advancement of health, including the translation of clinical findings into practices and policies

To better realise Singapore’s Health and Biomedical Sciences (HBMS) goals, the OF-LCG is open to proposals of the highest quality based on the five therapeutic areas identified as national priorities - infectious diseases, cancers, cardiovascular diseases, diabetes mellitus and related metabolic/endocrine disorders, and neurological and sensory disorders.

Two-tiered funding was also introduced in the May 2018 grant call, with funding (inclusive of 20% indirect cost) of up to \$10 million and \$25 million respectively, for a period of up to five years. For the May 2018 grant call, the therapeutic areas and set themes are detailed in the table below.

Emphasised Therapeutic Area(s) For the May 2018 Grant Call	Set Theme(s)
<b>Cancers</b> (e.g. in Breast cancer, Gastrointestinal cancer, Haematological cancer, *Liver cancer, Nasopharyngeal cancer)	<ul style="list-style-type: none"> <li>Precision methods for prevention, disease detection and treatment stratification</li> <li>Metastasis and resistance</li> <li>Enhancing cancer immunotherapy (excluding*)</li> </ul>
<b>Cardiovascular Diseases</b>	<ul style="list-style-type: none"> <li>Macrovascular diseases: myocardial infarction and chronic coronary heart disease, stroke, aortic and peripheral arterial disease</li> </ul>
<b>Diabetes Mellitus and Related Metabolic/Endocrine Disorders</b>	<ul style="list-style-type: none"> <li>Primary prevention of diseases</li> </ul>
<b>Infectious Diseases</b>	<ul style="list-style-type: none"> <li>Infectious diseases including emerging infectious diseases (EID) (e.g. Respiratory Tract Infection (RTI)), antimicrobial resistance &amp; healthcare-associated infections, dengue &amp; vector control)</li> </ul>
<b>Neurological and Sense Disorders</b>	<ul style="list-style-type: none"> <li>Age-related neurological and eye disorders (e.g. vascular dementia, Parkinson’s disease, glaucoma)</li> </ul>



The review process is two staged, comprising a Letter of Intent (LOI), and Full Proposal (FP) for shortlisted LOI applications. The success rate and details of awarded programmes for the May 2018 call are listed below:

FUNDING TIER	LETTERS OF INTENT RECEIVED	FULL PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
TIER 1	8	4	1	22.2%	82.00
TIER 2	10	5	3		

## AWARDED PROGRAMMES

Programme Title (Funding Tier)	Therapeutic Area(s)	Leadership Team (Institution)
<b>The Singapore SYMPHoma translational study (SYMPHONY)</b> <b>(Tier-1)</b>	<b>Haematological Cancer</b> Precision methods for prevention, disease detection and treatment, stratification, metastasis and resistance, and enhancing cancer immunotherapy	<b>Corresponding PI</b> Prof Lim Soon Thye (NCCS) <b>Theme PIs</b> Prof Chng Wee Joo (NUS), Prof Ong Choon Kiat (NCCS), Dr Anand Jeyasekharan (NUHS), Prof Olaf Rotzschke (SIgN), Prof Steve Rozen (Duke-NUS), A/Prof Ng Siok Bian (NUHS), Dr Tiffany Tang (NCCS), Prof Hong Wanjin (IMCB), Dr Nicholas Grigoropoulos (SGH), Prof Chng Wee Joo (NUS), Prof Takaomi Sanda (CSI), Dr Navin Kumar Verma (NTU), Prof Tan Soo Yong (NUHS), Dr Javed Iqbal (SGH), Dr Khor Chiea Chuen (GIS), Dr Owen Rackham (Duke-NUS), Dr Edward Chow (NUS), Dr Anita Chan (SERI)
<b>Advancing Precision Medicine for Cardiovascular Disease and Diabetes in Asian Populations</b> <b>(Tier-2)</b>	<b>Diabetes Mellitus and Related Metabolic/Endocrine Disorders</b> Primary prevention of diabetes  <b>Cardiovascular Diseases – Macrovascular Disease</b> Myocardial infarction and chronic coronary heart disease, stroke or aortic and peripheral arterial disease	<b>Corresponding PI</b> Prof John Chambers (NTU) <b>Theme PIs</b> Prof Rob Martinus van Dam (NUS), Prof Tai E-Shyong (NUH)
<b>Singapore Gastric Cancer Consortium – Bringing Discoveries to Patients</b> <b>(Tier-2)</b>	<b>Gastric Cancer</b> Precision methods for prevention, disease detection and treatment stratification, metastasis and resistance and enhancing cancer immunotherapy	<b>Corresponding PI</b> A/Prof Yeoh Khay Guan (NUS) <b>Theme PIs</b> Dr Yong Wei Peng (NUH), Dr Matthew Ng (NCCS), Prof Jimmy So (NUS), Prof Melissa Teo (NCCS), Prof Yoshiaki Ito (NUS), Prof Patrick Tan (Duke-NUS)
<b>Singapore PARKinson's disease Translational Clinical Programme (SPARK, Phase II)</b> <b>(Tier-2)</b>	<b>Neurological and Sense Disorders - Age-related Eye Disorders</b> Parkinson's Disease	<b>Corresponding PI</b> Prof Tan Eng King (NNI) <b>Theme PIs</b> Lim Kah Leong (NUS), Ng Huck Hui (GIS), A/Prof Louis Tan (NNI), Prof Zhang Su-Chun (Duke-NUS)

## OPEN FUND-INDIVIDUAL RESEARCH GRANT (OF-IRG)

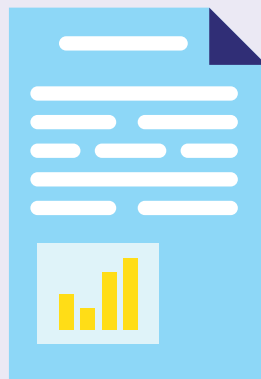
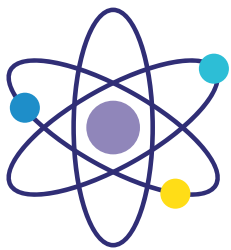
The Open Fund-Individual Research Grant (OF-IRG) supports research proposals in basic and translational clinical research relevant to human health and wellness. It also supports research proposals that look at cause, consequence, diagnosis, prevention and treatment of human diseases. The OF-IRG provides a funding quantum of up to \$1.5 million per project (inclusive of 20% indirect costs) for a period of up to five years.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
NOV 2017	126	12	9.5%	16.28
MAY 2018	124	12	9.7%	17.67
<b>TOTAL</b>	<b>250</b>	<b>24</b>	<b>9.6%</b>	<b>33.95</b>

## OPEN FUND-YOUNG INDIVIDUAL RESEARCH GRANT (OF-YIRG)

The Open Fund-Young Individual Research Grant (OF-YIRG) is a subcategory of the OF-IRG. Launched with the aim of supporting new investigator towards their first independent national level grant, the OF-YIRG provides a funding quantum of up to \$0.3 million per project (inclusive of 20% indirect costs) for a period of up to three years.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	TOTAL SUM AWARDED (\$ millions)
NOV 2017	65	19	29.2%	5.47
MAY 2018	62	17	27.4%	5.08
<b>TOTAL</b>	<b>127</b>	<b>36</b>	<b>28.4%</b>	<b>10.55</b>



# NATIONAL HEALTH INNOVATION CENTRE SINGAPORE



The National Health Innovation Centre Singapore (NHIC) provides Singapore's publicly-funded clinical research sector with translational funding and strategic guidance to accelerate healthcare innovation. Established in 2014, NHIC makes impact upon the clinical landscape by accelerating the development of innovative technologies and services, to improve healthcare delivery and patient care. By promoting collaboration between researchers, clinicians and industry, NHIC enables Singapore to better tackle future healthcare challenges.

NHIC funding expedites the translation of an innovation towards a commercially attractive end-point, by validating, de-risking or supporting its development. NHIC has several funding schemes for projects that address unmet healthcare needs and have demonstrated 'proof-of-principle' supported by experimental data. These schemes are:

## 1 INNOVATION TO PROTECT

This scheme funds expenses to protect patentable innovations with significant healthcare impact and commercial potential. The I2P funding supports first and secondary filing, such as PCT, NPE, prosecution, grant and maintenance.

## 2 INNOVATION TO DEVELOP

The scheme supports the development of a clinically-significant and commercially-viable healthcare innovation.

## 3 INNOVATION TO INDUSTRY

This scheme is for successfully completed I2D projects, where the project requires further co-development with an industry partner, who demonstrates licensing interest.

## 4 INNOVATION TO STARTUP

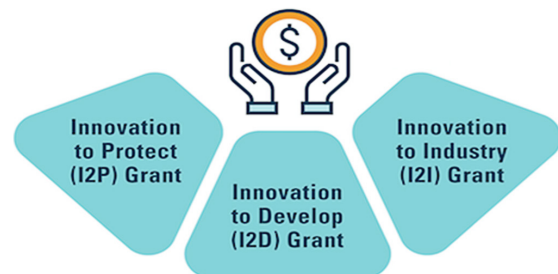
This program is a streamlined funding pathway, which brings together three grant schemes (SMART Innovation grant, NHIC Innovation to Develop and Enterprise Singapore Startup SG Tech), to support medical technology innovation to form a start-up company.

In addition to funding, NHIC also provides guidance to maximise projects' commercial potential. Researchers and clinicians are supported by NHIC team members with the experience in identifying and commercialising intellectual property from academic, clinical and commercial fields. The helps to evaluate and nurture innovations along the commercialisation pipeline.

Each project is assigned an NHIC project mentor, who adopts an active role in overseeing the project from early-stage discussions, to application of funding and post-award management. This improves teams' progress and commercialisation efforts, helping to achieve the desired healthcare impact.

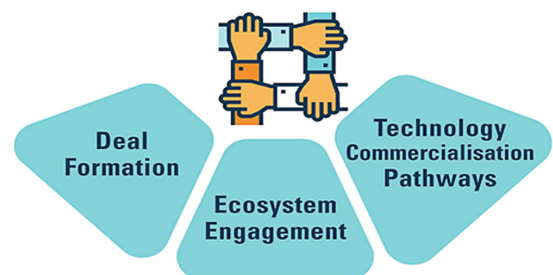
## FUNDING

Three translational funding streams available for innovations addressing an unmet healthcare needs



## MENTORING

We mentor project teams to drive translation of healthcare innovations with commercial potential



## PARTNERSHIP

We partner within Singapore's ecosystem to maximize the impact of our translational funding





## NOTABLE HIGHLIGHTS OF FY18

In FY 2018, NHIC funded the following:

**36** Innovation to Protect (I2P) Patent Applications

**7** Innovation to Develop (I2D) Projects

**2** Innovation to Startup (I2START) Projects

**2** Innovation to Industry (I2I) Projects

**7** Joint MedTech Projects (Co-funded with SingHealth Foundation and NUHS for early-stage development)

In addition, NHIC facilitated the following:

**9** Spin-off Companies

**10** Licenses Generated from I2D Projects

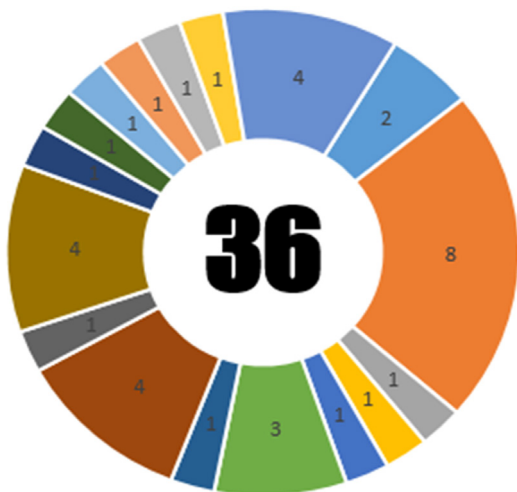
**14** Licenses Generated from I2P Patent Applications

This resulted in more than S\$633,000 in licensing revenues for the healthcare cluster

### INNOVATION TO PROTECT (I2P)

The 36 I2P projects were awarded across a range of medical specialities.

#### I2P Awarded Applications by Medical Specialty

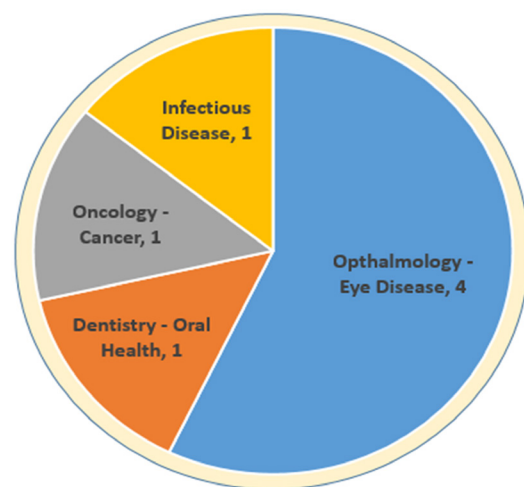


- Neurosurgery/Neurology
- Ophthalmology
- Critical Care Medicine
- Mental Health
- Cardiovascular Disease
- Dermatology
- Urology
- General Surgery
- Interventional Radiology
- Anesthesia/Surgery
- Infection
- Orthopaedic
- Anesthesiology
- Pain Management
- Dentistry - Oral Health
- Rehabilitation
- Others

### INNOVATION TO DEVELOP (I2D)

7 I2D projects were awarded across a range of medical specialities.

#### I2D Awarded Applications by Medical Specialty



- Ophthalmology - Eye Disease
- Dentistry - Oral Health
- Oncology - Cancer
- Infectious Disease

I2D GRANT	PROPOSAL RECEIVED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED
First Filing	18	17	94.4%	\$120,000.00
Secondary Filing	21	19	90.5%	\$520,000.00

I2D GRANT	PROPOSAL RECEIVED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED
April 2018	5	1	20.0%	\$249,600.00
August 2018	10	3	30.0%	\$749,546.80
December 2018	15	3	20.0%	\$749,599.60

# KNOWLEDGE ENABLERS AND INFRASTRUCTURE INITIATIVES

In RIE2020, MOH continues to develop and maintain support for enabling infrastructure that is important as part of the healthcare research strategy and clinical trial landscape. Specifically for 2018, we would like to highlight the progress update from two of our funded initiatives - Centre for Biomedical Ethics and Health Sciences Authority Cell Therapy Facility for FY18 are provided below:

## Centre for Biomedical Ethics (CBmE)

*The CBmE Funding Initiative has since adopted the name Science, Health and Policy-relevant Ethics in Singapore (SHAPES) to reflect their activities, outcomes, and contributions appropriately and comprehensively.*

### 1 Framework for Big Data Ethics in Health and Research

The SHAPES Working Group, consisting of local and international collaborators, successfully published the Big Data Ethics Framework in 2019 as a body of work that includes seven papers and an editorial in a Special Issue of the Asian Bioethics Review 11(3). While SHAPES is pleased to have completed such a large body of work with publications as tangible outputs, their aim in 2020 is to ensure that the Framework

is not only widely publicised but, importantly, widely understood and implemented.

### 2 Gene Modifying Technologies Project

SHAPES has established a Gene Modifying Technologies (GMT) Working Group (WG) comprising international experts of significant standing from a variety of local institutions and experts from the UK, US, Australia, Canada, and Hong Kong. The GMT WG contributed to the *Symposium on the Ethics of Gene Modifying Technologies* on 29-30 April 2019. The symposium was attended by experts and included clinician-scientists, policymakers, and other related researchers. Following the symposium, two full-day intensive working sessions were organised so the GMT WG could set the parameters for the collaborative

work, which will be available for publication in 2020.

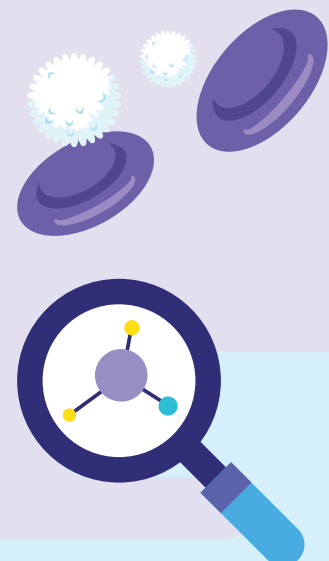
### 3 Research Project to understand Perceptions around IRB processes and functions in Singapore.

SHAPES has completed the analysis of data for the research project: *Perspectives of Singaporean Biomedical Researchers and Research Support Staff on Actual and Ideal IRB Review Processes and Functions: A Quantitative Analysis*. SHAPES is currently in the process of writing up the findings which will help plan workshops for IRB members and researchers in 2020. This research will provide insights into Singaporean researchers' perceptions of IRBs previously not available.

## Health Sciences Authority Cell Therapy Facility (HSA CTF)

The Health Sciences Authority Cell Therapy Facility (HSA CTF) is an accredited facility to manufacture and produce high quality cell therapy products for safe and affordable administration to patients, under International Good Manufacturing Practice (GMP PIC/S) standards and it was funded as a research enabler that provides the infrastructure, scientific know-how, and technical expertise to support the evolving field of cell therapy research. In the process of doing this, it has helped train and built up local expertise in this niche field of therapy and research.

Currently, it does not charge investigators from the public healthcare institutions (PHIs) and public academic groups for the use of its facilities and infrastructure. Other than introducing to them and emphasising the huge potential of cell therapy in novel clinical management of patients, such as the use of dendritic cell vaccines to augment anti-tumour responses in nasopharyngeal carcinoma and the use of mesenchymal stromal cells (MSCs) for immunomodulation in life threatening autoimmune diseases, HSA CTF is also bringing into Singapore cutting edge technology in CAR-T cell manufacture and has established a novel CAR-T product that is distinct from the commercially approved ones from Novartis and KITE Pharma.





# EVENTS





NATIONAL  
*Medical Excellence*  
 AWARDS 2018

16 August 2018  
 GUEST-OF-HONOUR  
 Mr Gan Kim Yong, Minister for Health

Jointly organised by:



Supported by:



# NATIONAL MEDICAL EXCELLENCE AWARDS 2018

The National Medical Excellence Awards (NMEA) is held annually to honour and recognise clinicians, clinician scientists and healthcare professionals who made outstanding contributions in the advancement of healthcare, improvement in standards of patient safety and quality of care, which ultimately improve people's lives.

In 2018, the NMEA recognised 5 individuals and 2 teams for their outstanding contributions to clinical practice and quality, research, education and healthcare delivery.



## NATIONAL OUTSTANDING CLINICIAN AWARD 2018



**Associate  
Professor  
Patrick Tseng  
Seng Kwong**

**Senior Consultant,**  
*National University Centre for Oral  
Health, Singapore*

**Associate Professor,**  
*Faculty of Dentistry  
National University of Singapore  
National University Health System*

Patient-centeredness is at the core of Associate Professor Patrick Tseng's delivery of care. He goes by the adage "always put yourself in your patient's shoes" and strives to deliver treatment in the safest manner possible.

A/Prof Tseng specialises in Endodontics – the dental specialty focused on the diagnosis and treatment of the dental pulp. The prospect of having to undergo endodontic treatment, such as root canal therapy, typically strikes fear in patients. Nonetheless, A/Prof Tseng's skills and proficient management of conditions have resulted in minimal discomfort for his patients.

He has consistently received one of the highest number of compliments as a clinician in the National University Hospital (NUH). His ability to put his patients at ease with the assurance that they are in good hands has garnered him multiple referrals both locally and regionally. Highly commended for his consideration towards his patients, A/Prof Tseng accommodates his patients' schedules as much as possible. He makes every patient feel like a VIP and was presented the NUH Star Award in 2002 and SPRING Singapore's Excellent Service Award in 2007.

A pioneer in Endodontics with 33 years of clinical experience, A/Prof Tseng is always driven to discover safer and more effective treatment methods. In 2001, he was invited by world-renowned Endodontists, Dr Cliff Ruddle and Professor Pierre Machtou, to observe the development of a revolutionary root canal file system in California which was safer, more efficient and produced more anatomically accurate canal shapes.

Capitalising on the advantages of the system, he worked with the Swiss endodontic file manufacturing company, Dentsply-Maillefer, to produce a manual version of the rotary Endodontic file and co-developed the latter. He was instrumental in the testing and modification of the design of the files and handles, which are now widely used in undergraduate teaching programmes across Asia, Europe and in many parts of the world.

Evident of his leadership in Endodontics, A/Prof Tseng receives regular invitations to be a keynote speaker at regional events. Through these opportunities, he has successfully boosted the popularity of the National University of Singapore (NUS) Faculty of Dentistry's three-year Endodontics programme, which in turn has gained a solid reputation in the region.

A/Prof Tseng has made an indelible mark at the institutional, national and international levels. He has served as a committed team member of the National University Health System (NUHS) for three decades, as a dedicated clinician at the National University Hospital (NUH) and an educator at the Faculty of Dentistry at the National University of Singapore (NUS).

He continues to be involved in both undergraduate and graduate teaching, imparting his knowledge to the next generation of dental healthcare professionals since he started teaching in 1991 and was conferred Associate Professorship in 2005.

In 1992, A/Prof Tseng helped to formulate the criteria for Endodontic certification for the Academy of Medicine. He was also involved in the setup of the Faculty's Graduate Programme in 1999. A/Prof Tseng has been a longstanding member of the Specialist Committee for Endodontics of the Faculty of Dentistry, at the National University of Singapore (NUS), which has overseen the training of dentists in the specialty of Endodontics since 2004.

At the national level, A/Prof Tseng was the Chief Dental Officer at the Ministry of Health from July 2006 to April 2018. He has overseen a number of key reforms during his tenure, notably setting up the Dental Specialist Accreditation Board in 2008.

He was instrumental in initiating the registration and regulation of dental specialists, which was much needed for the management of more complex dental cases. A/Prof Tseng also made basic cardiac life support and continuing professional education mandatory for dentists, so that they keep pace with the rapid changes and developments of dental practice.

A/Prof Tseng has also been a member of the editorial board of the Journal of the American Association of Endodontists since 2005, in recognition of his outstanding contributions to the field of Endodontics. He is also involved in research as a member of the editorial boards of the Singapore Dental Journal and the Hong Kong Dental Journal.

All in all, A/Prof Tseng is highly respected in the dental community and the field of Endodontics internationally, for his passion and regard to better patient care. For his exceptional contributions to the advancement of safety and quality in patient care and the field of Endodontics, A/Prof Tseng was conferred the 2018 National Outstanding Clinician Award.





## NATIONAL OUTSTANDING CLINICIAN SCIENTIST AWARD 2018

Associate Professor Toh Han Chong is widely respected and recognised as a leading authority on immunotherapy worldwide. His international accomplishments speak volumes of his dedication towards the war against cancer. Equally deep is his love and devotion to his patients, and his passion for nurturing the next generation of medical students, research technologists, research officers, post-doctoral fellows, clinical fellows and junior faculty members.

A/Prof Toh is among the pioneers of Cell and Cancer Immunotherapy in South-east Asia and has been leading the programme here for over 15 years. The programme was an uphill enterprise, with Singapore then having modest translational cell therapy and cancer immunotherapy capabilities, infrastructure and healthcare talent, and at the same time, facing wide skepticism on the clinical relevance of cancer immunotherapy as a treatment for cancers.

His work on immunotherapy is now widely regarded as one of the standard pillars of cancer treatment and was named "Breakthrough of the Year 2013" by the journal *Science*. Together with co-leader and protégé Dr John Chia, A/Prof Toh launched and established a consortium of over 65 clinical sites across Asia in the landmark global investigator-initiated randomised Phase 3 clinical trial exploring the role of aspirin in an adjuvant setting for colorectal cancer (ASCOLT).

Since 2009, what started as a two-man seed idea at the National Cancer Centre Singapore (NCCS) has grown into a leading, global clinical trial involving 1200 patients. ASCOLT has successfully secured international grants from Switzerland and Australia, in addition to local funding from the NMRC under the Ministry of Health.

This internationally recognised study has been globally cited by key opinion leaders such as Professor Ian Tannock, Sir John Burns and Professor Peter Rothwell. If shown to confer a survival benefit, this trial would have a major impact on the treatment on colorectal cancer, saving costs and millions more lives, globally.

A/Prof Toh has been published extensively in 97 journal publications. In recognition of his excellence in research, he has been invited to speak and lecture at numerous local, regional and global oncology events.

A/Prof Toh currently Chairs the Board of the Sing-Health Investigational Medicine Unit (IMU) and played a major role in the establishment of the Sing-Health IMU. Together with then Sing-Health Deputy Group CEO, Prof Soo Khee Chee and then Sing-Health Group Director of Clinical Research, Prof Fong Kok Yong, A/Prof Toh identified key operational and management staff to establish IMU from its inception.

He also rallied academic clinicians across the Outram campus to conduct their early-phase and proof-of-concept clinical trials in the IMU. The Sing-Health IMU today is one of two early-phase clinical trials units in Singapore. Its reputation is on par with top early-phase clinical trial centres across Asia, including South Korea, Taiwan and Hong Kong.

A/Prof Toh has an extraordinary commitment and passion to teach and mentor the doctors and healthcare professionals of tomorrow. Many of his protégés have gone on to become successful clinicians in their own right.

They include, Dr John Chia who was presented "Best Poster Award" from the European Society for Medical Oncology for his first-in-human clinical trial study for a nasopharyngeal cancer vaccine. Dr Marissa Teo who was conferred the L'Oréal International Women in Science Award for her work in cell therapy at A/Prof Toh's laboratory.

Currently, A/Prof Toh is responsible for developing structure, curriculum and content for Research and Education as the Academic Vice-Chairperson (Education) of the Sing-Health Oncology Academic

Clinical Programme at Duke-NUS Medical School.

His commitment to nurture the next generation of clinicians goes beyond the cluster. A/Prof Toh has been regularly invited to speak at National Healthcare Group Research Preparatory and Study Design Workshops, aimed at gearing up young clinical researchers and potential future clinician scientists.

A/Prof Toh has been feted for his contributions and leadership in Singapore and around the globe. Among his awards, A/Prof Toh has received, the 2009 and 2017 NMRC Clinician Scientist Awards; the 2016 Gordon Research Conference for NPC (Hong Kong) - Outstanding Poster Presentation Award; the Duke-Sing-Health AM-ETHOS Mentoring Award in 2016; the 2008 Duke-NUS Graduate Medical School Best Teacher Award (Molecules and Cells) in 2008 and the National Excellent Service Award (Star Award) in 2004.

More recently, for his outstanding contributions to cancer immunotherapy, work offering hope to patients, Associate Professor Toh was presented the 2018 National Outstanding Clinician Scientist Award.



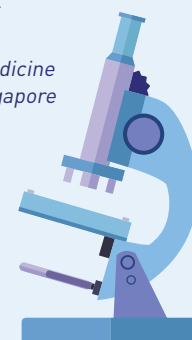
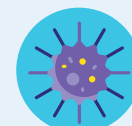
**Associate  
Professor Toh  
Han Chong**

**Deputy Medical Director (Education),**  
*National Cancer Centre Singapore*

**Senior Consultant,**  
*Division of Medical Oncology  
National Cancer Centre Singapore  
SingHealth*

**Associate Professor,**  
*Cancer & Stem Cell Biology Programme  
Duke-NUS Medical School*

**Clinical Senior Lecturer,**  
*Yong Loo Lin School of Medicine  
National University of Singapore*



## NATIONAL OUTSTANDING CLINICIAN EDUCATOR AWARD 2018



**Associate  
Professor  
Chen Fun Gee**

**Director,**  
*Division of Graduate Medical Studies  
Yong Loo Lin School of Medicine  
National University of Singapore*

**Head,**  
*Division of Critical & Intensive Care  
National University Hospital*

**Senior Consultant,**  
*Department of Anaesthesia  
National University Hospital  
National University Health System*



Associate Professor Chen Fun Gee has been involved in medical education since 1987. Teaching countless medical students and officers during their postings to the Department of Anaesthesia, A/Prof Chen has conducted numerous examination preparatory courses and workshops at the National University of Singapore (NUS).

Appointed a member of the Anaesthesia Specialist Training Committee in Singapore in 1996, A/Prof Chen was instrumental to the Master of Medicine Anaesthesia postgraduate programme, and has actively contributed to teaching anaesthetists, both as a trainer and examiner. Additionally, A/Prof Chen was also an examiner for the University of Malaya Anaesthesia Postgraduate examinations, and the Hong Kong College of Anaesthesia fellowship examinations.

In 2002, A/Prof Chen was appointed Chair of the Ministry of Health (MOH) committee to setup the sub-specialty of Intensive Care Medicine in Singapore. As a pioneering member, he was among the first group of examiners instrumental to forming the programme and conduct of Intensive Care Medicine licensing examinations in Singapore.

In 2009, A/Prof Chen was concurrently appointed as Director, Division of Graduate Medical Studies (DGMS) at the Yong Loo Lin School of Medicine, NUS and Co-chair of the Joint Committee of Specialist Training (JCST). As the director of the DGMS, he was responsible for assessment standards for all eleven Master of Medicine examinations, as well as the Master of Science, Speech and Language Therapy examination. During his tenure with DGMS, he worked with domain experts to start the NUS Audiology programme, as well as the Graduate Diploma of Mental Health, and the Graduate Diploma of Palliative Medicine programmes. These graduate diploma programmes help general practitioners to upgrade their knowledge, and equips them with the skills needed to meet Singapore's growing healthcare needs.

As the JCST Co-chair, A/Prof Chen worked with 35 specialties in Singapore in the transition to the American Council of Graduate Medical Education-International (ACGME-I) system of training. Working together with the Ministry of Health and NUS, the existing postgraduate training programmes were modified in line with ACGME requirements.

Likewise, accreditation for non-ACGME programmes were also based on the processes and standards as outlined by ACGME. Together with the American Board of Medical Specialties, US Board examinations were incorporated into the existing assessment systems in Singapore for 11 specialties.

As Chair of the Joint Committee of Family Medicine (JCFM), A/Prof Chen worked in close collaboration with the College of Family Medicine for the training and assessment of Family Medicine specialists in Singapore. In 2012, he worked with the Chief Examiner, Dr Ruth Lim, and her team to revamp the Master of Medicine in Family Medicine course, to ensure that Family Medicine graduates were well equipped to meet the changing needs of patients in their care.

A/Prof Chen also chairs the Graduate Nursing Advisory Committee at the Yong Loo Lin School of Medicine, NUS, which charts the direction of graduate nursing education in Singapore. As a member of several Advanced Practice Nurse committees, A/Prof Chen provides valuable input on curriculum, training, professional practices and licensing examinations for the Master of Nursing and Advanced Practice Nurse internship programmes.

In addition, A/Prof Chen is also working with the Singapore Pharmacy Board to develop tools for the assessment of pharmacy residents. This is still a work in progress, and the first portfolio examinations for pharmacy will commence in 2019.

A/Prof Chen is a practicing specialist in Anaesthesia and Intensive Care Medicine. Since 1992, he has been regularly invited to speak at Anaesthesia and Critical Care Medicine-related conferences. Because of his interest in education, he has also been invited to speak at medical conferences both locally and internationally. For his extraordinary contributions to the nation, A/Prof Chen was conferred the Public Administration Medal (Bronze) at the 2016 National Day Awards.

More recently, for his exemplary dedication and contributions to advance medical education and healthcare standards in Singapore, A/Prof Chen was awarded the 2018 National Outstanding Clinician Educator Award.

## NATIONAL OUTSTANDING CLINICIAN EDUCATOR AWARD 2018

An anaesthesiologist for nearly 30 years, Associate Professor Lim Boon Leng has taken on a wide range of roles in medical education, both nationally and internationally. From mentoring trainee anaesthesiologists for their specialist examinations, A/Prof Lim has also been a member of the National Specialist Training Committee (Anaesthesiology) from 1998 to 2011 and the sub-specialty, Intensive Care Medicine Training Committee (ICU) from 2006 to 2014 to improve the training of both anaesthesiologists and intensivists.

A/Prof Lim is not just dedicated to teaching clinicians, his interest lies in raising the bar for medical knowledge and skills, for the betterment of successive generations of clinicians and educators. He was one of the pioneer intensivists to initiate the Fundamental Critical Care Support Course in 2000, which still runs today, to train anaesthesiologists, respiratory and emergency physicians, nurses and allied health professionals involved in the care of ICU patients.

The programme director for the Duke-NUS School of Medicine's Critical Care Module from 2008 to 2016, A/Prof Lim was actively involved with the planning and execution of the school's critical care programme from its start in 2008. Presently, A/Prof Lim is a Senior Consultant at the Singapore General Hospital's Department of Anaesthesiology.

Following Singapore's transition from the UK-based specialist accreditation system to the current US-based, Accreditation Council for Graduate Medical Education – International (ACGME-I) Residency training system in 2009, A/Prof Lim was appointed Associate-Designated Institutional Official (DIO) from 2010 to 2012. He was subsequently promoted to DIO for Sing-Health Residency programme from 2012 to 2018.

A/Prof Lim led many transformational changes through his career. Successfully attaining accreditation for thirty-four residency programmes, A/Prof Lim also initiated the Essentials in Clinical Education online course to improve the pedagogy of the Sing-Health Residency teaching faculty. Spanning five key domains, the course covers design and planning of learning activities, assessment and feedback to learners. Since its start in 2015, the course has also been extended to nursing and allied health teaching staff.

A/Prof Lim's tenure as DIO marked a period of mentorship and guidance for many. An encouraging and patient mentor, A/Prof Lim was ever mindful of building rapport with the pipeline of budding clinicians and was always on hand to provide guidance on challenging cases.

Attending every Resident event, A/Prof Lim was always on hand to interact with residents, respond to their feedback and discuss challenges they faced during their training.

A/Prof Lim worked closely with the MOH - Medical Education Coordinating Committee, Manpower Standards and Development Division to improve residency programmes. Additionally, he also worked with MOH Holdings' Healthcare Leadership College on plans for the Singapore Chief Residency Programme, this to prepare Singapore's top residents for leadership roles.

In 2017, he initiated the Sing-Health Residency Leadership Programme, with a similar objective to build up a pool of leaders among the residents.

As the Sing-Health Deputy Group Director of Education (Graduate), A/Prof Lim also chaired various MOH committees to help drive healthcare training policy.

Internationally, for his work in educating and training anaesthesiologists in China, A/Prof Lim was appointed Honorary Executive Committee Member of the Chinese Society of Anaesthesiologists in 2004 and conferred the Outstanding Contribution Award in 2009. He was also appointed Honorary Visiting Professor of Xi'an 4th Military

Hospital in 2002, and Qingdao Medical University in 2007 and 2016 respectively.

For his dedication and passion in pushing the boundaries of postgraduate medical education and training, and his outstanding leadership in fostering an environment for teaching and continuous learning, A/Prof Lim Boon Leng was presented the 2018 National Outstanding Clinician Educator Award.



**Associate  
Professor Lim  
Boon Leng**

**Deputy Group Director,  
Education (Graduate)  
Sing-Health Academy**

**Senior Consultant,  
Department of Anaesthesiology  
Singapore General Hospital**

## NATIONAL OUTSTANDING CLINICAL QUALITY CHAMPION AWARD 2018



**Associate  
Professor Wong  
Moh Sim**

**Deputy Group Chief Quality Officer,**  
*National Healthcare Group*

**Deputy Chairman,**  
*Medical Board*  
*(Clinical Quality & Manpower  
Development)*  
*Kho Teck Puat Hospital &  
Yishun Health*

**Head and Senior Consultant,**  
*Laboratory Medicine*  
*Kho Teck Puat Hospital &  
Yishun Health*  
*National Healthcare Group*

A passionate advocate for patient safety and quality care, Associate Professor Wong Moh Sim plays an instrumental role in the overall planning, development, implementation and evaluation of corporate strategies to drive quality, patient safety and clinical risk management within Kho Teck Puat Hospital (KTPH) and the National Healthcare Group (NHG).

A/Prof Wong is no stranger to clinical quality. As the first Patient Safety Officer at Alexandra Hospital (AH), she was responsible for implementing the patient safety and quality improvement framework in AH. A/Prof Wong helped lead AH to achieve its maiden JCI<sup>®</sup> accreditation in 2005 and has continued to play a leading role in subsequent iterations of JCI audits for KTPH. As AH's first Patient Safety Officer, A/Prof Wong helped NHG to establish the Patient Safety Framework, alongside other NHG patient safety officers, and actively participated in numerous patient safety training activities at institutional and cluster levels.

A/Prof Wong is also the lead clinician for the Yishun Health patient safety collaboration with the Cognitive Institute for Speaking-up for Safety. In this role, A/Prof Wong lead efforts to build a strong culture of safety and quality by empowering staff to support each other and normalise two-way, collegial communication to prevent unintended patient harm.

A/Prof Wong is a faculty member of the Singapore Healthcare Improvement Network (SHINe) for the Large-Scale Initiatives to Reduce Harm. She helped develop the change package and measurements for the Healthcare Associated Infections (HAI) Workstream for Institute for Healthcare Improvement (IHI) and local faculty. Under the guidance and mentorship of the HAI Workstream faculty, nine institutions have been coached to implement an evidence-based catheter-associated urinary tract infection (CAUTI) prevention bundle, with seven institutions achieving institution-wide spread of this bundle. More than 350 incidents of CAUTI have been prevented from April 2014 to September 2017 with a cost avoidance of more than S\$1.5 million.

A veteran in laboratory management and workflow, A/Prof Wong has headed the Department of Laboratory Medicine in both AH (2002-2005) and KTPH (2005-to date). Under her leadership, both departments have grown service levels to national

excellence standards — providing cost-efficient, quality laboratory services for better patient care.

Using Clinical Practice Improvement Programme (CPIP) and Toyota Production System methodologies, A/Prof Wong not only improved operational efficiency, she also designed improvement projects for better clinical outcomes. Among her successful initiatives, a turnaround time of less than 45 minutes for 95% of all laboratory results from the Department of Emergency Medicine in 4 months. For this achievement, she was awarded CPIP Project Commendation.

In 2006, A/Prof Wong chaired and led the NHG Critical Laboratory Results Collaborative, to improve the communication of critical laboratory results. As a result of this collaboration, NHG established its own list of Critical Laboratory values, and instituted many processes to ensure reliable communication for appropriate and timely management of patient care. A/Prof Wong was also instrumental in efforts to introduce the concept of open communications to NHG. To date, A/Prof Wong remains an active trainer in the Open Disclosure programme.

Beyond her numerous accolades, A/Prof Wong is a firm advocate of continuous learning. Actively involved in staff training, she encourages her staff to learn and upgrade their skills regularly. In line with this, A/Prof Wong currently teaches at the Department of Pathology at the Yong Loo Lin School of Medicine, National University of Singapore.

At the national level, A/Prof Wong serves on various committees, including the Singapore Association of Clinical Biochemists (SACB) and Technical Advisory Committee for Chemical Metrology at the Health Sciences Authority (HSA), where she chairs the workgroup and advises on the development of local proficiency testing programmes, and feedback on the interpretation of performance of participating clinical laboratories to HSA.

For her exemplary contributions in developing and advancing the field of patient safety and clinical quality improvement, and her dedication in designing clinical interventions to sustain positive change, A/Prof Wong has been awarded the 2018 National Outstanding Clinical Quality Champion Award.





## NATIONAL CLINICAL EXCELLENCE TEAM AWARD 2018

### RESPONSE, EARLY INTERVENTION AND ASSESSMENT IN COMMUNITY MENTAL HEALTH (REACH) PROGRAMME



**Associate Professor  
Daniel Fung Shuen Sheng**

*Chairman, Medical Board  
Programme Director, REACH*

*Senior Consultant,  
Department of  
Developmental Psychiatry  
Institute of Mental Health*



**Ms Geraldine  
Wong Cheng Im**

*Principal Medical Social  
Worker*

*Team Leader, REACH (North)  
Department of  
Developmental Psychiatry  
Institute of Mental Health*



**Ms Grace Li Jiaying**

*Senior Occupational Therapist*

*Team Leader, REACH (South)  
Department of  
Developmental Psychiatry  
Institute of Mental Health*



**Ms Chan Mei Chern**

*Deputy Director, Operations*

*Head of Operations, REACH  
(North & South)  
Department of  
Developmental Psychiatry  
Institute of Mental Health*

In 1995, the World Health Organization put forth the idea that schools play a vital role in reducing health risk. The majority of children and adolescents do not suffer from mental illness. However, there are some who are at risk of developing emotional, behavioural and/or neurodevelopmental issues. When this happens, early identification and intervention will help to alleviate problems as children and their families learn to manage symptoms, and continue to build resilience through childhood and adolescence.

Empirical findings have shown that a community-based model of psychiatric care not only improves accessibility to services, but also reduces the stigma associated with mental illness. With this in mind, the **Response, Early intervention and Assessment in Community Mental Health (REACH)** was set up. Under the auspices of the National Mental Health Blueprint in 2007, REACH supports schools, community agencies and general practitioners in helping children and adolescents below 19 years old with mental health concerns.

REACH is led by the Institute of Mental Health (IMH) in collaboration with MOE, social service organisations, general practitioners (GPs) and the National Council of Social Service (NCSS). It is represented by multidisciplinary mobile teams comprising medical doctors, clinical psychologists, medical social workers, occupational therapists and nurses.

These cross-functional teams provide assessments and interventions to students, as well as support and train community partners.

In 2011, REACH services expanded from one to four mobile sub-teams, with IMH leading two teams in the north and south regions, and KK Women's and Children's Hospital and the National University Hospital leading teams in the east and west regions respectively, in support of all mainstream schools, and by 2014, all Special Education (SPED) schools in Singapore.

The formation of these mobile clinical teams is a major breakthrough in the traditional hospital-based psychiatric care model in Singapore. By bringing services into the community, REACH improves accessibility and timely interventions for children and adolescents to receive care in a holistic environment.

REACH also helps build capability by training community partners (school counsellors, educators, GPs and staff in the social care sector) through a structured mental health training series. This brings about a multiplier effect, to disseminate and impart care knowledge and skills across sectors, which translates to better support for students who may require mental health interventions within the community.

Since its inception in 2007, REACH has supported more than 6,000 students and trained more than 2,000 educators. REACH has also successfully carried out interventions and right-sited care in the community, reducing the number of new referrals to IMH's Child Guidance Clinics (CGC) over the years.

In the last decade, REACH has actively worked to build robust working relationships with all MOE mainstream and SPED schools, and has bridged a strong network of social service organisations and GP partners, to form an integrated mental health support platform for children and adolescents in the community.

REACH has also extended its partnership with the six Madrasahs to provide mental health support to their student population, and as well, to explore working with pre-schools to support the mental health needs of preschoolers.

For their dedication, untold contributions and holistic approach to mental health care for children and adolescents, through extensive cross-sector collaboration, community training, and early detection and intervention strategies, REACH was conferred the 2018 National Clinical Excellence Team Award.



## NATIONAL CLINICAL EXCELLENCE TEAM AWARD 2018

### NUHS VALUE DRIVEN OUTCOMES (VDO)



**Associate Professor Keith  
Lim Hsiu Chin**

*Group Chief Value Officer,  
National University Health System*

*Senior Consultant,  
Department of Radiation Oncology  
National University Cancer Institute,  
Singapore*



**Associate Professor James  
Yip Wei Luen**

*Group Chief Medical Informatics Officer,  
National University Health System*

*Senior Consultant, Department of Cardiology  
National University Heart Centre, Singapore*  
*Associate Professor, Department of Medicine  
Yong Loo Lin School of Medicine  
National University of Singapore*



**Ms Wong Soo Min**

*Group Chief Financial Officer  
Corporate Office Chief of Staff  
National University Health System*

With an ageing population, a growing chronic disease burden and rising healthcare costs in Singapore, the National University Health System (NUHS) Value Driven Outcomes (VDO) team embarked on a mission to achieve better value in healthcare, with a focus on both outcome and cost.

One way to improve value is to be able to measure and compare it against benchmarks. And so, the ability to assign quality measures and attribute costs of care to individual patient encounters is critical for visibility and transparency. By understanding the value of care, identifying deviations versus best practices, clinicians are equipped with data and analytics to drive the right optimisation.

The VDO project was first started in 2016. For each condition, individualised quality indicators from four key dimensions – Clinical Quality and Safety, Appropriateness of Care, Patient Reported Outcomes and Patient Experience – were defined and correlated with cost metrics such as facility utilisation, medication, investigations and manpower cost.

Data visualisation tools were deployed for users to track and analyse outcomes of each quality indicator, cost drivers for each condition, and the percentage of patients with defined care indicators. This then defines quality of care delivered at specific cost.

Driven by insights from the VDO reports, the teams were able to initiate improvement plans such as:

- (a) reduction in unnecessary length of stay;
- (b) improvement in Deep Vein Thrombosis prophylaxis compliance;

- (c) adoption of cost-effective standard implants; and
- (d) standardisation of investigations and medication usage.

NUHS with projects on seven conditions in 2016 and expanded to twenty in 2017 across two hospitals – National University Hospital and Ng Teng Fong General Hospital (NTFGH).

Today, there are 53 ongoing projects across both hospitals and the National University Polyclinics. These projects have resulted in a 4% weighted average increase in the number of patients achieving the defined care and a 6% weighted average reduction in costs of care. Overall, they have resulted in \$11 million in savings to the public healthcare system in areas such as cost avoidance and reduction in tests.

With the expanded NUHS cluster, the VDO methodology was replicated in NTFGH in 2017, with mapping and implementation completed in less than four months, enabling the launch of six VDO projects.

This has enabled both institutions to benchmark the cost of care and outcome indicators, and cross-share best practices to allow for improved costs and outcomes. In addition, the VDO approach pioneered by NUHS has since been adopted by the Ministry of Health and rolled out across Singapore in 2017, with seven VDO projects launched nationwide.

For their outstanding contributions and achievements in the development of a VDO methodology for the benefit of patients and Singapore's public healthcare system, the NUHS VDO team has been awarded the 2018 National Clinical Excellence Team Award.

# NMRC AWARDS CEREMONY AND RESEARCH SYMPOSIUM 2018

In 2018, the NMRC Awards Ceremony and Research Symposium were held concurrently during a one-and-a-half-day event at the Novotel Singapore Clarke Quay on 17 and 18 April 2018.

Attracting key players, and over 400 clinician scientists and researchers in the field of biomedical research, the event recognised clinicians and researchers for their achievements and contributions to the continuous improvement of patient care. The event was a useful networking platform for collaborations among the many individuals across healthcare institutions, academia and industry partners.

With the theme “Research for a Better Future”, NMRC hoped that the event would provide the opportunity for fostering stronger collaborations towards research excellence and better healthcare outcomes for a better future.



## AWARDS PRESENTATION

The NMRC Awards Ceremony is a platform where the recipients under the NMRC Human Capital and Talent Development Programmes, namely Singapore Translational Research (STaR) Investigator Award, Clinician Scientist Award (CSA), Transition Award (TA), MOH Healthcare Research Scholarship – Master of Clinical Investigation (MCI) and NMRC Research Training Fellowship, are honoured and recognised for their significant contributions to advance human health and wellness. The Guest of Honour was Permanent Secretary (Health) Mr Chan Heng Kee.

In 2018, NMRC had the privilege of hosting 4 eminent international experts; Prof Andrzej Krolewski, Joslin Diabetes Centre, Prof Derrick Crook, Nuffield Department of Medicine, University of Oxford and Director of National Infection Service at Public Health England, Prof Andrew Farmer, Nuffield Department of Primary Care Health Sciences, University of Oxford,

and Dr Aby Buchbinder from the Global Drug Development organisation of Novartis, to share their expertise and research work in the area of Diabetes Mellitus, and related Metabolic/Endocrine Disorders, Infectious Diseases, Health Service Research and drug development respectively.

## RESEARCH SYMPOSIUM

The Research Symposium is a platform to promote and inculcate the spirit of translational clinical research in Singapore’s biomedical and healthcare research landscape. In 2018, recipients of NMRC-administered grant programmes, clinicians and researchers in the research and clinical community and industry here, were invited to join the symposium for a two-day knowledge sharing and networking.

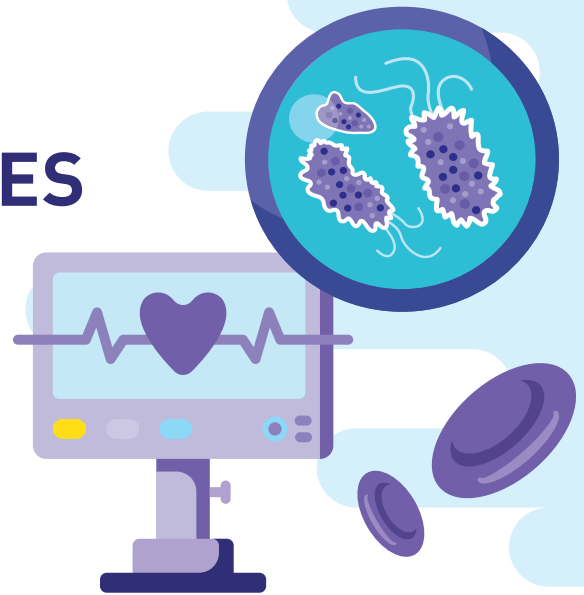
Day One of the concurrent session began with the Awards Presentation, with parallel sessions on Cancer and Cardiovascular diseases, followed by a combined session on clinical research

and industry. The day concluded with a wine and cheese reception, setting the tone for a collegial networking session for participants across the clinical and research community and industry partners to explore collaboration opportunities.

Continuing the session on Day Two, the symposium began with parallel sessions on Diabetes Mellitus, and related Metabolic/Endocrine Disorders, Neurological and Sensory disorders, Infectious Diseases, Health Service Research. Ranging over one and a half days, with 28 local and overseas experts, the symposium covered strategic areas in which NMRC hopes to drive key translational biomedical research.

Beyond the symposium, participants were also presented opportunities to view exhibition booths by the National Health Innovation Centre Singapore, Diagnostics Development Hub, Experimental Biotherapeutics Centre, Health Sciences Authority Cell Therapy Facility, Singapore Clinical Research Institute and SHAPES (by the Centre for Biomedical Ethics) during intervals.

# HEALTH AND BIOMEDICAL SCIENCES INTERNATIONAL ADVISORY COUNCIL MEETING 2018



On 29 and 30 Oct 2018, Singapore's Health and Biomedical Sciences International Advisory Council (HBMS IAC) held its annual meeting. Chaired by Sir Richard Sykes, the meeting focused on the progress and achievements of the HBMS Domain following the Research, Innovation and Enterprise (RIE) 2020 Mid-Term Review (MTR); how the HBMS Domain has addressed the HBMS IAC's previous recommendations through the developments and shifts in strategy for greater health and economic value capture post-MTR; and proposed course adjustments for the remainder of RIE2020 and beyond.

The HBMS IAC commended the progress made by the HBMS Domain and noted the promising outcomes from concerted efforts to increase economic and health value creation. It was observed that HBMS researchers and institutions were collaborating more closely across Singapore, and that the local HBMS ecosystem had reached an inflexion point, with increased vibrancy in the local innovation and enterprise (I&E) ecosystem.

To enhance the healthcare impact of Singapore's HBMS investments, the HBMS IAC recommended that greater focus be placed on developing talent with both strong

domain knowledge and competence in other scientific disciplines, such as data science, engineering, business and social sciences, so as to drive innovation, and the commercialisation and implementation of promising HBMS research findings, as well as on supporting strategic cohorts to generate useful data for the design and implementation of effective public health interventions. The HBMS IAC also acknowledged the important role played by clinician scientists (CSs), particularly in facilitating the translation of research innovations into healthcare, and called for a more holistic support system to nurture existing CSs and build up a robust CS talent pipeline. Further, the HBMS IAC called for greater research investments in ageing and productive longevity, so as to better prepare Singapore for the health, social and financial burden an ageing population would bring in the near future.

Working with our partners in the research community, NMRC looks forward to building on our sustained investments over the years to develop an ecosystem that further enables the translation of research into real-world applications and value capture, so as to deliver better health and wealth outcomes for Singaporeans.

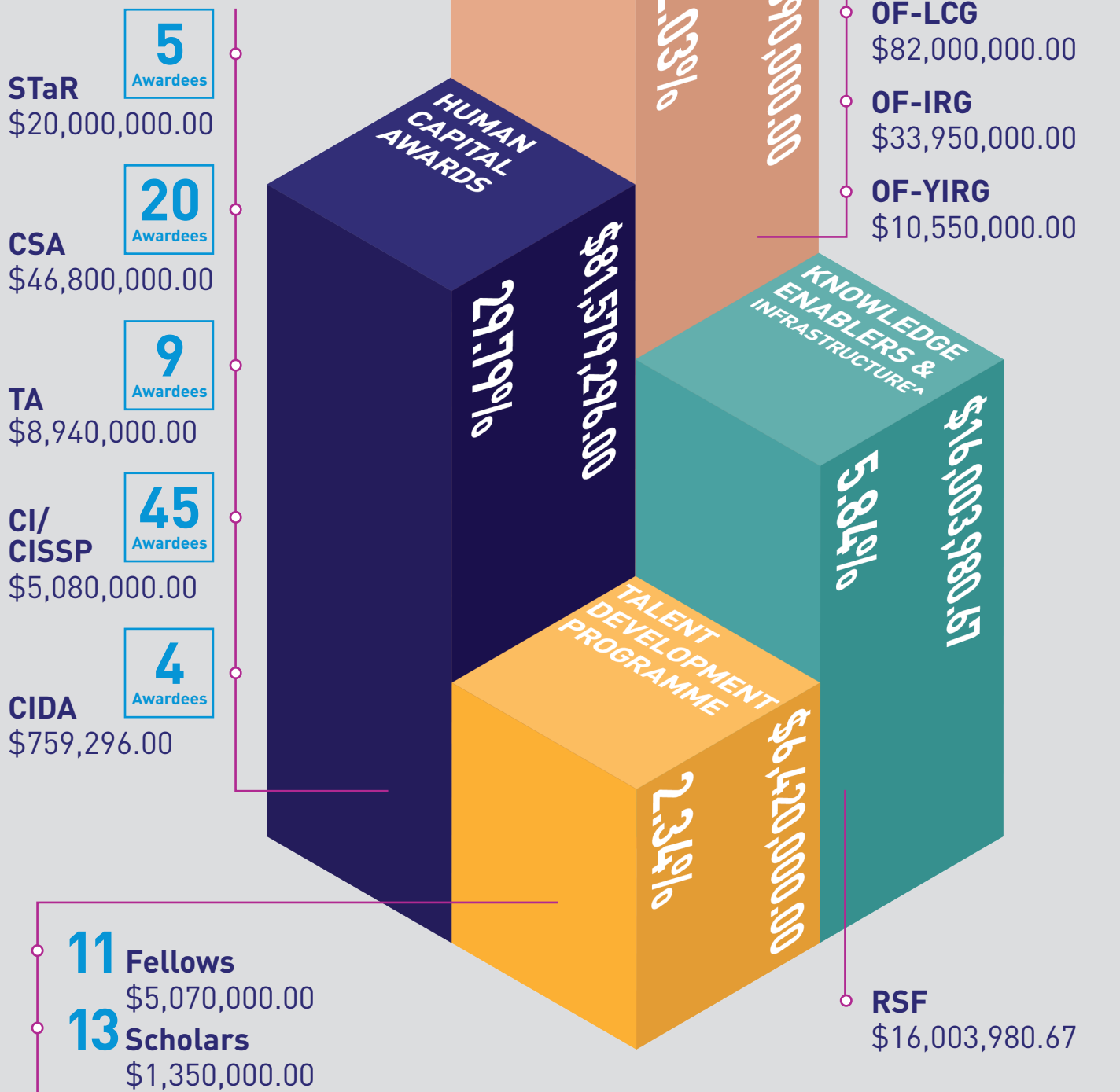




# OVERALL FUNDING DISTRIBUTION

FOR NMRC FUNDING INITIATIVES (FY2018)

Figures presented reflect funding committed in the FY and grant calls completed by the time of print. Figures would be reported in the year funds were committed.



Figures for the KE&E initiatives are reported in the respective years when funds were committed.

**NATIONAL MEDICAL RESEARCH COUNCIL**

#09-66 Harbourfront Centre,  
1 Maritime Square (Lobby C),  
Singapore 099253  
Email: [moh\\_nmrc@moh.gov.sg](mailto:moh_nmrc@moh.gov.sg)

