

# FUTURE OF HEALTHCARE THROUGH RESEARCH

ANNUAL REPORT FY2017





### 1 NMRC Governance and Portfolio

- 4 Message from Chairman
- 6 About NMRC
- 8 NMRC Board

### 10 NMRC RIE2020 Funding Portfolio

# 12 Human Capital & Talent Development Programmes

- 13 Nurturing a Vibrant Community of Clinician Scientists
- 14 Human Capital Awards
- 29 Talent Development Programmes
- 31 Clinician Scientists in the Spotlight

### **36 Research Grants**

- 37 Funding Translational and Clinical Research
- 38 NMRC-Funded/Managed Grants
- 40 Open Fund Grants

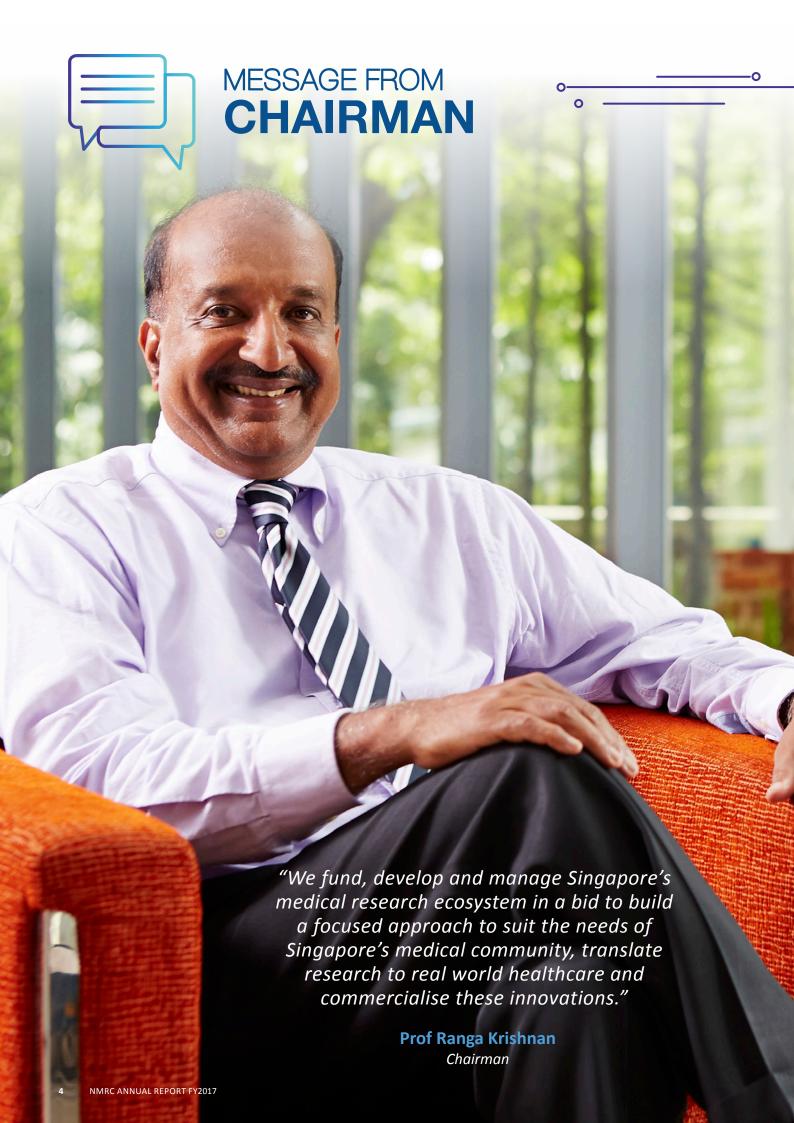
### 46 Events

- 47 National Medical Excellence Awards 2017
- 54 Health and Biomedical Sciences International Advisory Council Meeting 2017
- 55 Overview of Fund Commitment in FY2017











### PAVING THE WAY FOR A BRIGHTER FUTURE WITH TRANSLATIONAL RESEARCH

Since 1994, NMRC has been a major driver of research infrastructure of healthcare institutions in Singapore. Our passion for improving the health of the nation through medical innovation, discovery and translation to the real world in a timely and cost-effective manner has always been constant and enduring.

Not only does NMRC provide crucial research funding for trainees, early career researchers and senior researchers, we also administer large-scale infrastructure and centre grants to public healthcare and medical institutions in Singapore.

We seek to further elevate Singapore's vibrant and rapidly growing presence in medical research by the translation of research into industry, and through developing the necessary infrastructure to reach said goals. However, bridging the gap between research and practice is not a walk in the park. Greater efforts have been taken to quantify and qualify

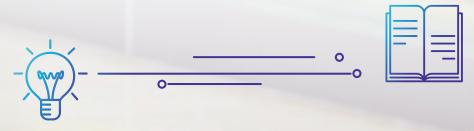
research achievements and their implementation in healthcare, ever since national investment in the biomedical landscape in 2006 and subsequent years.

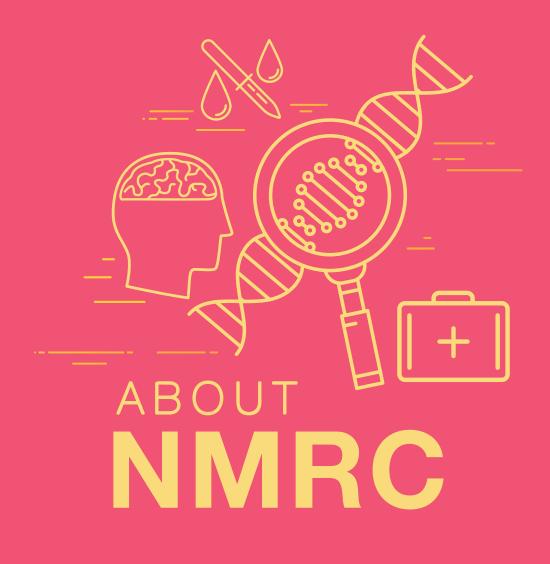
The year 2018 marked the midterm of the RIE2020 funding tranche. Within the framework of the RIE2020 mid-term review, we concluded the impact mapping exercise that has demonstrated the impact of the Health & Biomedical Sciences (HBMS) investments from publicly funded research. Funding shifts and reprioritisation were proposed in due course and endorsed to build transformative capabilities from the short to long term.

In accordance with the public sector transformation initiative, the Integrated Grants Management System (IGMS) was implemented — a onestop platform for research grant management across multiple funding agencies such as the National Research Foundation (NRF), Ministry of Health (MOH), Ministry of Education (MOE) and Agency for Science, Technology

and Research (A\*STAR).
IGMS allows a coordinated and organised approach for participating agencies to harmonise grant management processes, facilitate sharing of research grant information and improve the experience of researchers and stakeholders applying and managing the research grants.

Singapore's biomedical landscape has drastically evolved over the years, and it remains an important contributor in Singapore's manufacturing economy. We look forward to the years ahead where the plan is to develop an ecosystem that better enables translation of research to improve health outcomes, place emphasis on Health Services Research to contain healthcare costs, and transform and enhance the efficiency of health services delivery. A strong core and pipeline of researchers, clinician scientists, innovators, entrepreneurs and investors will be the driving force to pave the way for a brighter medical future in Singapore.







Established in 1994, the National Medical Research Council (NMRC) oversees the development and advancement of Translational and Clinical Research (TCR) in Singapore. It provides competitive research funds to publicly funded healthcare institutions, awards competitive research funds for programmes and projects, supports the development of core clinical research infrastructure, is responsible for the development of clinician scientists through awards and fellowships, and fosters interactions and knowledge exchange among researchers.

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. 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 entire Biomedical Sciences (BMS) community, including private and public research performers, hospitals and government agencies. NMRC spearheaded these investments to realise long-term health and wealth outcomes.

Under the RIE2020 Plan¹, 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). This helped NMRC reinforce its mandate as the champion for translational clinical research in Singapore.

NMRC spearheads MOH's vision for healthcare research to deliver better health and wealth outcomes for Singaporeans. Five therapeutic areas of focus have been identified by MOH, in which NMRC will complement the top-down directed strategic research by funding research proposals received by the various competitive grants and

awards administered. In 2014, the National Health Innovation Centre (NHIC) was established to coordinate across the industry cluster to support a vibrant ecosystem comprising local enterprises, start-ups and multinational corporations.

Human Capital plays a key role in the success of Singapore's TCR industry. Having a critical mass of clinician scientists is crucial for improving human health by providing thought leadership and driving the translation of bench discoveries to bedside applications. As such, NMRC actively supports clinician scientists with funding through research grants, human capital awards and talent development programmes. NMRC has stepped up its efforts to boost the number of clinician scientists in Singapore.

<sup>&</sup>lt;sup>1</sup> RIE2020 info from NRF Website: http://www.nrf.gov.sg/research/rie2020





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. By overseeing the implementation of the research programmes approved by MOH and the HBMS Executive Committee, the Board ensures that the Council is being effectively managed to meet its mission and key performance targets. The Board also ensures that governance frameworks are in place, such that NMRC's budget is appropriately managed and optimally utilised. In FY2019, the NMRC Board consists of 18 members.



Prof Ranga Krishnan Chairman National Medical Research Council



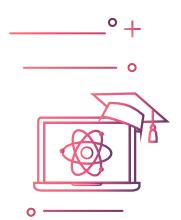
A/Prof Tan Say Beng Covering Executive Director National Medical Research Council



Prof Edward Holmes
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Prof Ivy Ng
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A/Prof Benjamin Ong
Director of Medical Services
Ministry of Health



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



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



Dr Cheong Wei Yang Deputy Chief Executive Officer National Research Foundation



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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



A/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 and talent development programmes, research grants, and enablers and infrastructure.

## Human Capital Awards & Talent Development Programmes



- Singapore Translational Research (STaR) Investigator Award
- Clinician Scientist Award (CSA)
- Transition Award (TA)
- Clinician Scientist & Clinician Investigator Salary Support Programme (CS/CISSP)
- NMRC Research Training Fellowship
- MOH Healthcare Research Scholarship Master of Clinical Investigator (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 (HSR-NIG)

#### **Open Fund**

- Large Collaborative Grant (LCG
- Individual Research Grant (IRG)
- Voung Individual Research Grant (VIRG)

# Knowledge Enablers & Infrastructure Initiatives

- Bioethics Advisory Council (BAC)
- Centre of Biomedical Ethics Clinical Research (CBmE)
- Coordinators (CRC) Funding Initiative
- HSA National Cell Therapy Facility
- Institutional Review Boards (IRBs)

- Investigational Medicine Units (IMUs)
- National Health Innovation Centre (NHIC)
- National Large Animal Research Facility (NLARF)
- Research Space Funding
- Singapore Clinical Research Institute (SCRI)



# HUMAN CAPITAL & TALENT DEVELOPMENT

**PROGRAMMES** 



Manpower is one of the three cross-cutting programmes under the RIE2020 framework. Singapore aims to nurture a sustainable pipeline of skilled clinician scientists who will advance its strategic goals in RIE2020's health and biomedical sciences domain.

Clinician scientists play a critical role in translational and clinical research: their first-hand interaction with patients enables them to identify gaps in the detection, diagnosis and treatment of diseases, while their scientific experience and expertise allow them to frame these clinical insights as 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 will translate into impactful health outcomes.

To help Singapore nurture a vibrant community of clinician scientists, NMRC has put in place various human capital awards and talent development programmes aimed at supporting individuals in their research and career progression.

These awards and programmes include:

### **Human Capital Awards**

- Singapore Translational Research (STaR) Investigator Award
- Clinician Scientist Award (CSA)
- Transition Award (TA)
- Clinician Scientist/Clinician Investigator Salary Support Programme (CS/CISSP)

### Talent Development Programmes

- NMRC Research Training Fellowship
- MOH Healthcare Research Scholarship Master of Clinical Investigation (MCI)





### Singapore Translational Research (STaR) Investigator Award

The prestigious Singapore Translational Research (STaR) Investigator Award is the highest level of NMRC's Human Capital Awards. Designed to recruit and nurture world-class clinician scientists to undertake cutting-edge translational and clinical research in Singapore, the STaR Investigator Award includes five-year funding for the researcher's salary, an annual budget for research support and a one-time start-up grant.

### Clinician Scientist Award (CSA)

The Clinician Scientist Award (CSA) is structured to develop local research talent and give clinician scientists valuable protected time to focus on their research. The Senior Investigator (SI) level of the CSA offers funding for up to five years, catering to senior doctors who are already actively involved in highly productive research. The Investigator (INV) level offers funding for three years and targets younger doctors with the potential to become independent investigators. The CSA provides funding for salary support, together with a competitive research grant.

### Transition Award (TA)

The Transition Award (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 by facilitating their transition to a stable, independent research position, which in turn will enhance their ability to successfully obtain independent research support later on. The TA is non-renewable, as awardees are encouraged to apply for national-level independent research grants after they have completed this award.

### Clinician Scientist/Clinician Investigator Salary Support Programme (CS/CISSP)

The Clinician Scientist/Clinician Investigator Salary Support Programme (CS/CISSP) supports clinical research by providing funding for clinicians' research time in the form of salary support or full-time-equivalent (FTE). In recognition of the support from clinical departments for their clinicians' time and participation in clinical research, the awarded funding is channelled to the respective departments, which are given flexibility in using the funds to support clinical research.



### SINGAPORE TRANSLATIONAL RESEARCH INVESTIGATOR AWARD RECIPIENTS



### Clinical and Translational Research in Movement Disorders

Essential Tremor (ET) and Parkinson's disease (PD) are two of the most common movement disorders and have underlying genetic aetiologies. Identification of disease pathogenic variants, followed by studies of these variants in human and animal models will shed light on the key molecular pathways which are involved in disease pathogenesis and can potentially lead to identification of new treatment targets. Here we propose to establish a resource containing prospective clinical and genetic data for different subsets of ET patients from our Asian population. From these data and specimens, we will develop human derived cell lines and animal models of ET. In addition, we will create live three-dimensional human brain organoid disease models. From all these models, we will unravel the pathophysiologic disease pathways and search for new therapeutic targets. Separately, we will also conduct clinical studies to study the motor and non-motor effects between PD patients who are carriers of risk and protective variants. We will also aim to identify new drug targets from studying the neuroprotective variants in both human derived cell lines and animal models.

### T-Cell Receptor Mediated Immune Therapy in Chronic Hepatitis B and Hepatocellular Carcinoma

Hepatitis B virus (HBV) infection is predominantly an Asian health problem; of the 350 million people with chronic HBV infection (CHB) worldwide, approximately 75% live in Asia. We aim to understand the immune pathogenesis and develop immune-based therapies to cure this chronic viral infection and its major complication, hepatocellular carcinoma (HCC). Our research relies on state-of-the-art methods to find ways to overcome the immunological defects that cause viral persistence in CHB patients and spread of HBV-related HCC. We developed techniques and unique tools that allow us to engineer functional T lymphocytes bearing T-cell receptors (TCRs) capable of recognizing and destroying HCC cells or inhibiting HBV replication. We have started clinical trials to assess the efficacy of this specific T-cell immunotherapy. My goal is to consolidate the results obtained so far in the characterization, production and clinical use of TCR-redirected T-cells, thereby offering new and more effective treatment options to patients with CHB infection and HBV-related HCC. Because the T-cellbased immunotherapy strategy that we are pursuing is also applicable to other infectious and neoplastic diseases, success in this endeavour should have repercussions beyond HBV, and significantly contribute to strengthen immune-based T-cell therapies in Singapore.



### CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR) RECIPIENTS



### A Prospective Study to Develop a Genomics-Phenomics Platform Approach for Precision Medicine in Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world but the second most important cause of cancer death. Because of its highly heterogeneous nature, the current approach to identifying druggable targets has not delivered efficacious therapies in HCC and is a main reason for the high case fatality. Even when surgical resection is potentially curative in early disease, tumour recurrence remains high and long-term survival poor because of the absence of useful adjuvant therapy. We have shown through multi-region sampling of freshly resected HCC and phylogenetic analysis, that significant intra-tumoral heterogeneity exists and have identified the specific positions of known clonal drivers. Such heterogeneity may further be

elucidated at the level of genome/ epigenome/transcriptome, as well as at the metabolome and clinical phenotype levels, where interaction between the genes and the environment is played out. We hypothesise that an integration of genomic heterogeneity with multiple downstream layers/datasets (e.g. epigenetics, transcriptomic, immunomics, metabolomics and clinical phenotypes) will allow a more coherent understanding of molecular pathways, tumour evolution and disease progression. We aim to combine these approaches to overcome the challenges posed by intra-tumour heterogeneity and to guide the development of therapeutics and precision medicine in HCC.

A Randomised Trial on the Impact of External Counterpulsation Therapy on Cerebral Hemodynamic Parameters in Patients with Symptomatic and Severe Steno-Occlusive Disease of Intracranial Internal Carotid or Middle Cerebral Artery and Impaired Cerebral Vasodilatory Reserve

Narrowing of the arteries in the brain (intracranial stenosis) is widely prevalent among ischemic stroke patients in Singapore (seen in up to 50% patients). Despite a high risk of stroke recurrence, the treatment options remain suboptimal and controversial. Enhanced External Counterpulsation (EECP) therapy appears to be a possible adjuvant treatment option for patients with severe intracranial stenosis. In this project, we aim to identify patients with severe and symptomatic severe stenosis of intracranial Internal Carotid Artery (ICA) or

Middle Cerebral Artery (MCA) and randomised to receive best medical therapy alone or best medical therapy plus EECP for seven weeks. Detailed clinical, imaging and neuropsychological assessments would be performed by blinded assessors at four months. This project intends to reduce the short-term risk of stroke recurrence; generate data for designing a large, well-planned efficacy study; and open a new therapeutic option for patients at very high risk of cerebral ischemic events.





### Associate Professor Louis Tong

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### Translational Program in Ocular Surface and Dry Eye

Dry eye is a group of conditions that affects 300 million people globally and up to a third of the adults in Asian countries. In severe cases, the complication of dry eye may result in blindness. In the ongoing CSA, ending in late 2017, the research group has impacted some clinical practice, published more than 72 peer-reviewed papers, and become one of the top three international groups publishing in the dry eye domain. Reputation of the clinician scientist has increased, resulting in invitations to international expert panels, regional expert councils, invited lectures and industry advisory boards. Current treatment of dry eye is unsatisfactory (not effective or has adverse effects). To improve patients' lives, we aim to build on the existing achievements and

further develop treatment based on specific molecules already identified in previous projects. Through interconnected, highly complementary projects, we will investigate a group of patients with very severe, sight-threatening dry eye, additional inflammation-related molecules, treatment outcomes using state-of-the-art technology, stored human plasma as eyedrops, and patient acceptance in new antiinflammatory drugs. The proposed continuation of funding will support the clinician scientists and members of his trained research team, and maintain the valuable, unique dry eye clinical database.



### CLINICIAN SCIENTIST AWARD (INVESTIGATOR) RECIPIENTS



### Simultaneous Profiling of Circulating Tumour Cells and Tumour in Relation to Immunotherapeutic Response in Cancer

Immunotherapy is promising in cancer patients but responses are difficult to predict. Tumour re-biopsies are limited by tissue and access issues. Sensitivity or resistance to immunotherapy may be due to the underlying tumour or to the individual patient. This proposal seeks to integrate analysis of Circulating Tumour Cells (CTC) and tumour to predict outcomes from immunotherapy treatment underpinned by a clinical study: TCIMMUNITY. In patients undergoing immunotherapy for cancer, blood samples will be enriched for CTCs,

clusters of CTC and Peripheral Immune Cells (PICs) and analysed in response to immunotherapy treatment. We will also examine the patient's DNA to investigate for specific genetic variations that predict for resistance. In doing so, we hope to be able to derive genetic signatures that predict for resistance or sensitivity to these drugs and better select patients who would benefit from them.

### Sex Chromosome Aneuploidy Associated Infertility: A Paradigm for Investigating the Determinants of Germ Cell "Identity"

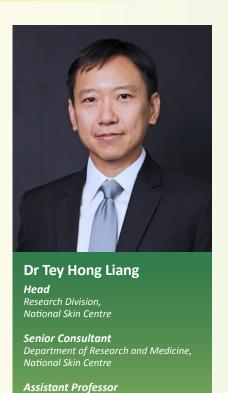
In mammals, females have two X chromosomes (XX) while males have one X and a Y (XY). The presence of the Y chromosome determines male development. Abnormalities in sex chromosome number (i.e. sex chromosome aneuploidy), such as Turner's syndrome (XO females), which affects about one in every 2,000 females and Klinefelter syndrome (XX males), which affects around one in every 660 males, are the most common class of aneuploidy in humans. These syndromes are also associated with infertility. Germ cells develop differently in males and females and give rise to sperm and eggs respectively. During their development these cells express different genes and methylation profiles. We have demonstrated

previously that sex chromosome aneuploid germ cells display imbalanced X chromosome dosages. We have further evidence that a mismatch in the X chromosome number and phenotypic sex can also distort the "identity" of germ cells - with XX males misexpressing "female" genes and XO females misexpressing "male" genes. Our research is aimed at understanding the mechanisms that underlie how the X chromosome number influences gene expression and methylation in germ cells. The research is clinically significant and is aimed at providing a better understanding of the biology underlying sex chromosome disorders and infertility.









Lee Kong Chian School of Medicine, Nanyang Technological University

### Three-Dimensional Imaging in Ex Vivo Skin and Non-Invasive Skin Imaging: Novel Clinical Applications in Skin Cancers and Hypohidrotic **Sweat Disorders**

The aims of the project are to establish platforms for threedimensional visualization and data analysis in the management of skin diseases. The current practice of twodimensional analyses in histology and skin imaging are prone to sampling error and are deficient in providing information on tissue architecture, structure and cellular interaction. Our 3D approach will be used to analyse skin surgical specimens and images obtained from a non-invasive bedside imaging modality, namely, the Optical Coherence Tomography.

These techniques will be validated and applied to skin cancer and disorders of deficient sweating, respectively, to evaluate their clinical utility. These platforms can be expanded to other diseases in the future. We envision that such novel approaches will significantly improve the understanding of the pathology and accuracy of diagnosis of these important diseases and thereby enhance patient management outcomes.

### **Exploring the Inflammatory Signatures** Underlying Progression of Knee Osteoarthritis: A Prospective Study

Knee Osteoarthritis (OA) is common and leads to disability. Currently, no drug seems to work because: 1) the pathogenesis of OA is not well understood; and 2) different knee OA subtypes should be treated differently. An inflammatory subtype of knee OA may respond better to anti-inflammatory drugs. The project aims to build a follow-up cohort of patients with early knee OA to evaluate the inflammatory signals that predict worsening of knee OA. 139 patients with early knee OA were recruited and they gave us detailed symptoms, knee imaging (X-Ray and magnetic resonance imaging, MRI); urine, blood and joint fluid. We will follow-up with these patients after four years to identify patients with

worsening X-rays and MRIs. We will evaluate which inflammatory signals predict worsening. We will also use cutting-edge technologies to find out the exact inflammatory mechanism causing knee OA. We start with a detailed investigation of the cells and their function in the joint fluid, followed by hunting the immune targets in the blood. This project will give insight to the pathways and mechanisms of inflammation underlying knee OA. This will guide doctors to select an inflammatory subgroup of knee OA, who may respond better to specific antiinflammatory treatment.





### Evaluation of a Hepatitis B Virus Minichromosome Disruption Strategy Using CRISPR/dCas9-Fokl Nuclease Delivered by Modified Polyethyleneimine Polymers, in Combination with Nucleotide Analogue Therapy

There is no cure for chronic Hepatitis B Virus (HBV) infection to date. That is due to a highly stable reservoir of circularized HBV DNA within the liver cell nucleus, known as minichromosome, which can become active whenever the antiviral therapy is stopped. We propose to apply the latest DNA editing technology known as the CRISPR/dCas9-FokI system, which can recognize specific viral DNA sequences and disrupt the minichromosome. Such systems require a "carrier" to move their components into the liver cells.

Teaming with other scientists from A\*STAR, we will be synthesizing polymers using nanotechnology, which can act as a carrier to deliver the components of the targeted antiviral systems into liver cells efficiently. These polymers have been shown to block HBV from entering the cells. We hope to combine the DNA editing therapy, blocking virus entry, and the best antiviral drugs already in the market, to achieve a HBV cure with therapy of under one year's duration.

### validaTing biomARkers of myocardial fibrosis and investiGating thErapies To regress FIBROSIS (TARGETFIBROSIS)

Heart failure is a global pandemic. Despite advances in therapies, the burden of heart failure remains high. Myocardial fibrosis (scarring of the heart muscles) occurs commonly in heart failure from a variety of causes. Non-invasive methods of assessing myocardial fibrosis (blood and imaging) can potentially identify heart failure patients who will be at higher risk of future adverse cardiovascular events, and serve as targets for novel therapies to regress fibrosis. In three separate

studies, we aim to examine markers of myocardial fibrosis to monitor disease progression in a pre-heart failure condition (hypertensive cardiac disease), improve risk stratification of heart failure patients and also to assess treatment response of a novel anti-fibrotic medication. Ultimately, our overall goal is to improve patient care and outcomes through personalised diagnosis and treatment targeted at myocardial fibrosis.









### Genomic and Epigenomic Correlates of Radioresistance in Nasopharynx and Prostate Cancers

Human cancers continue to represent a major health burden in Singapore. Half of all cancer patients will require radiotherapy (RT), and therefore, it is crucial to identify patients who are less likely to respond to RT; these individuals can then be recommended combinatorial treatment intensification. Here, we propose to investigate a potential clinical assay of RT-resistance. First, we have identified a group of nose cancer patients who have relapsed in the nose, despite high-dose RT. In this cohort, we aim to test if the cancer cells present in the recurrence in fact existed in the original tumour. If so, this supports a Darwinian "survival of the fittest" model for cancer

recurrence post-RT. Characterising these cells using next-generation sequencing will thus help define the molecular fingerprint of RT-resistant cancer cells. We will then validate our findings against controls (without relapse), and with a cohort of RTresistant prostate cancers. Together, this should yield a preliminary RTresistant signature to further test in other clinical cohorts. Finally, using a variety of RT-resistant cancer cell lines, we will investigate for potential molecular vulnerabilities of these RTresistant cells that may be exploited by combining RT and novel targeted therapies, including immunotherapy.

### Brown fat activation and browning Efficiency Augmented by chronic COld and Nutraceuticals for Brown adipose tissue-mediated Effect Against Metabolic Syndrome (BEACON BEAMS Study)

The role of Brown Adipose Tissue (BAT) in regulating the metabolism in health and disease has become a topic of high interest. The amount and activity of BAT may be important in regulating body weight, adiposity, insulin resistance and the risk of metabolic syndrome and diabetes. A non-drug approach based on cold exposure and natural functional foods in activating BAT will be investigated for their efficacy to increase metabolic rate. We will evaluate chronic BAT-activating stimuli based on a control group of people with pre-existing BAT and compare that against those initially BAT-negative, followed by a washout to assess for durability and reversal of any metabolic benefits. The

browning of White Adipose Tissue (WAT) into beige fat among BATnegative individuals is of particular interest because this turns the body's own excess fat into a 'fat burning furnace'. We will employ infrared thermography, fat fraction MRI, positron emission tomography and whole-body calorimetry to study BAT mass and activity. This research will offer insights into the dynamic nature of BAT and WAT, and establish the safety and efficacy of chronic cold exposure and functional foods in controlling adiposity through BAT. This aligns well with our nation's priority in addressing obesity and our war waged against diabetes.









### A Randomised Controlled Trial Evaluating a Novel Individualised Treatment Strategy for Carbapenem-Resistant Gram-Negative Bacteria Infections

Antibiotic resistance is a major global medical challenge. Doctors can no longer fall back on "last-line" and non-toxic antibiotic (carbapenems), as many superbugs are increasingly resistant to them. Against these types of superbugs, there is no new antibiotic currently available, and extremely few new antibiotics are in the developmental process. Doctors had to use old, toxic polymyxins or antibiotics combination therapy blindly as a "last-resort" option for such difficult-to-treat infections as routine treatment. However, some antibiotics combinations are useful and some are useless. The goal of the study is to use a "gold standard" method-randomised control trial to evaluate a new treatment strategy by leveraging on the latest technology (which we have developed) that can identify useful antibiotics combinations to kill such superbugs. This test will provide "guided antibiotics combination therapy" to the study subjects and compare the effectiveness to the comparator arm of subjects who will receive standard treatment. This proposal is unique and of high significance as there is no study in the world that compares guided antibiotics combination therapy to standard treatment. The study findings may open a new paradigm in treatment approaches against these superbugs until new potent antibiotics are developed against them.

### Identifying Distinct Immune Cell Subpopulations in Colorectal Cancer Using Single Cell Transcriptomics and Evaluating their Spatio-Biological Interactions in Fixed Tissues

At a microscopic level, cancers comprise many different cell types (e.g. immune, tumour, blood vessel cells and supporting tissue cells) ecologically interacting with one another. Termed the tumour microenvironment, the overall tumour architecture influences clinical behaviour of the cancer. The interactions between tumour and immune cells are attractive drug targets in cancer. Immune checkpoint inhibitors have dramatically improved treatment outcomes in many cancers, but not Colorectal Cancer (CRC), where these drugs have not worked. There is an unmet need to unravel the mediators of the immune milieu in colorectal cancer. Single-cell RNA Sequencing (scRNA-seg) is a new technology that allows one to understand the contribution of different types or

states of immune cells within the tumour micro-environment. We have entered into an academic-industry collaboration to generate single-cell transcriptomes from over 6,000 cells per patient from 50 CRC patients. We will describe the diversity of immune cell subpopulations in colorectal cancer and how they relate to clinical behaviour and patient outcomes. We will also measure several proteins simultaneously in fixed tumour tissue. Together, we seek to understand the immune tumour microenvironment to improve existing treatments, discover predictive biomarkers, and develop novel immune-therapeutic strategies in colorectal cancer.



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#### **Dr Chester Drum**

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

#### Consultant

Department of Cardiology / Medicine, National University Hospital

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### Applications and Development of a Thermostable Protein Nanoparticle

In the treatment of human disease, different types of materials are commonly used to match a disease with a therapy. Small molecules are the most common form of medicine, however their small size and need for chemical synthesis often means a very long process to treat a disease that is highly specific to an individual patient. Antibodies and "biological" drugs can be developed more quickly to address specific mutations or other precision targets. However, antibodies also have their limitations in functional use. Expanding the repertoire of platform technologies

which can deliver and produce novel therapies is critical if medical science is to keep pace with the rapidly increasing "precision medicine" definitions of disease. In our previous proposal, the NMRC funded a new idea for a class of biological molecules that could provide completely new therapeutic options. The work was published and we now seek funding to take the discovery to the next step: by testing animal models of cancer and discovering new forms of treatment using DNA and RNA.

### Characterization of Immune Evasion in NK/T-Cell Lymphoma

Extranodal NK/T-cell Lymphoma (NKTL) is an aggressive tumour associated with Epstein-Barr Virus (EBV) and it is more common in Southeast Asia than other countries. Chemotherapy is ineffective and new treatment methods are urgently required. The use of immuneoncology for cancer has become widespread recently and it involves activating the body's immune system to fight cancer. Some proteins (called immune checkpoint proteins, ICP) which are present on the surface of normal immune cells can help cancer cells escape being killed by the body's normal immune cells, a process known as immune evasion. Recent studies have shown that drugs inhibiting one of the many

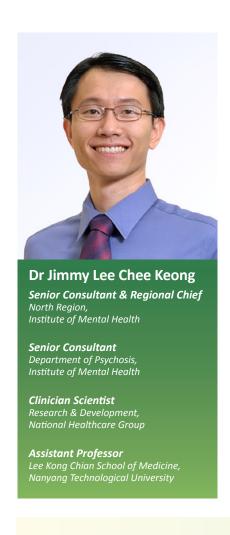
immune checkpoint pathways (e.g. programmed death 1, PD1) may be effective in NKTL. How this occurs and the role of EBV in immune evasion is unknown. In part I of this study, we plan to measure the expression of different types of ICP on the surface of tumour cells and surrounding immune cells because our previous study data indicated that these genes may be important in NKTL. In part II, we will study if EBV is important in the immune evasion of NKTL. This knowledge will help in selecting and designing the correct immune-oncology therapy for NKTL patients.



Associate Professor & Senior Consultant Department of Pathology, Yong Loo Lin School of Medicine, National University of Singapore

Department of Pathology, Cancer Science Institute of Singapore





### Evaluating the Clinical Utility of Immune Phenotypes in Schizophrenia

Schizophrenia has a lifetime prevalence of about 1% of the population but the understanding of its aetiology remains incomplete. A third of patients with schizophrenia could be resistant to current antipsychotic treatment, thus identification of these subpopulations is crucial for development of appropriate treatment regimes. Increasing reports on schizophrenia and immune dysregulation have led researchers to distinguish unique immunology profiles for subgroups of schizophrenia. Findings from our preliminary studies are consistent with literature and encourage further examination on the association between immune system dysregulation in schizophrenia. The primary aim of the study is to identify differences in immune profiles

between people with schizophrenia and healthy controls. Further, we will examine if these differences within people in schizophrenia are related to their clinical improvements. We aim to recruit 200 participants. Immune profiling via flow cytometry and immunoassay tests will be performed on samples collected from study participants and analysed. Results from this study will provide the identification of unique immunology profiles for the subgroups of schizophrenia. This information allows the advancement in personalized treatment management in psychosis and provides the necessary evidence for new immune treatments in schizophrenia.

### Effects of Dapagliflozin and Metformin on Vascular (DMVascular) Function in Newly-Diagnosed Treatment-Naïve Type 2 Diabetes – A Randomised Controlled Trial (DMVascular Study)

The DMVascular study aims to study the impact of medical treatment on vascular complications of diabetes. Our central hypothesis is based on the fact that diabetes causes complications by damaging the blood vessels (small and large). This process is initiated very early and even before the diagnosis of diabetes. It has been seen that Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) provide benefits to large vessels. The primary aim of this study is to see how this medical treatment in comparison with other standard medication affects the vascular

function. This approach is significant as the results have the potential to identify individuals who will benefit most from these medications and uncover new targets for treatment, which may change clinical practice in terms of early diabetes management. This approach is innovative as we are studying non-traditional outcomes, in terms of integrated vascular function (from small vessels to large vessels), using developed and some novel methods developed by our team.





#### **Dr Catherine Ong**

#### Consultant

Division of Infectious Diseases, Department of Medicine, National University of Singapore

### Assistant Professor and

Clinician Scientist Yong Loo Lin School of Medicine, National University of Singapore

Honorary Clinical Research Fellow Infectious Diseases and Immunity, Imperial College London

### Diabetes Mellitus and The Dysregulation of Host **Proteases in Tuberculosis**

Tuberculosis (TB) is still a global health emergency and Singapore faces a rise in both TB incidence rates and an increasing prevalence of Diabetes Mellitus (DM). DM worsens TB, with patients more likely to remain infectious for a longer duration, more likely to have treatment failure and more likely to die. However, the mechanisms driving this condition in DM-TB are undefined. We hypothesise that DM affects the human defence mechanism, leading to the worse clinical outcome in DM-TB. We aim to investigate a group of human

proteases both in conditions of high sugar and normal sugar levels in a cell model, and further validate our findings in a group of healthy volunteers, DM, TB and DM-TB patients. We will further dissect the intracellular signalling pathways that lead to the dysregulation of proteases. This study is at the translational interface and can potentially identify targets for therapy that can further optimise the management of DM-TB.



### **TRANSITION AWARD RECIPIENTS**



### Investigating Paracrine STAT3 Signalling in Colorectal Peritoneal Carcinomatosis to Derive Novel Therapeutic Strategies

Colorectal cancer is the third most common cancer and the fourth most common cause of cancer death globally, accounting for 1.4 million new unique forms of metastasis confined in the abdomen in 15% of colorectal cancer patients. Previously uniformly fatal, radical surgery and use of local chemotherapy has improved the survival of patients. Despite this, the clinical outcome of patients is still suboptimal and much more can be done if we understand the biology of this disease. Our study aims to identify what drives the

growth of these tumours to devise rational novel therapeutic strategies. Work in our laboratory has already identified a critical signalling pathway that is activated by fluid that is present in the abdomen of patients with Peritoneal Carcinomatosis (PC). We are planning to decipher the mechanism of how this occurs and to test our therapeutic strategy experimentally before embarking on clinical trials to treat patients.

### Cancer Cell Metabolism and the Development of Oxidative Phosphorylation Inhibitors as Cancer Therapy

Rapidly dividing cancer cells need more energy than normal cells. Traditionally, their energy production was thought to depend on "glycolysis". In contrast, normal cells largely depend on mitochondria (the "cell powerhouse") for energy production. It was originally proposed that mitochondria were defective in cancers, whereas we now know that they are fully functional. Certain cancers may even depend exquisitely on a key mitochondrial energy-generating process, Oxidative Phosphorylation (OXPHOS). Inhibiting OXPHOS in these particular cancers may result in cell death. Moreover, pathways of energy production are intricately linked to other cancersignalling pathways. Hence, inhibiting OXPHOS may effectively block these other pathways too. Our industry

partner, Otsuka Pharmaceuticals, has successfully developed an oral OXPHOS inhibitor, which has been shown to be safe in humans. This is the first time an oxidative phosphorylation inhibitor is being investigated specifically as anticancer therapy. We are currently conducting a clinical trial at National University Hospital (NUH) to determine the effectiveness of this therapy in selected patients predicted to respond to OXPHOS inhibition. Moreover, we are performing laboratory research to define the role of this novel class of agents in cancer therapy and are using state-of-theart technology to design markers to select patients who will benefit from this novel treatment.



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### Effects of Selinexor in Combination with ICE (Ifosfamide, Carboplatin, Etoposide) and other Chemotherapy Agents in Relapsed or Refractory T-Cell Lymphomas

Patients with T-Cell Lymphoma (TCL) have poor treatment outcomes. Ifosfamide, Carboplatin, Etoposide (ICE) is a chemotherapy regimen commonly used when TCL patients relapse but patients respond poorly to this regimen. Selinexor is a novel agent used in the treatment of cancers including non-Hodgkin's lymphoma. To improve the outcomes of ICE in patients with Relapsed or Refractory (R/R) TCL, we combined selinexor with ICE in a dose-finding phase I study and found high response rates. We thus propose a follow up study in another 10 patients to understand the safety of this combination. If four or more patients show a complete response,

we will proceed to recruit another 18 patients to obtain further data for clinical efficacy of selinexor-ICE in patients with R/R TCL. To get an idea of how selinexor-ICE compares to ICE, we will perform a retrospective review of databases from several large academic centres to obtain data for the clinical efficacy of ICE alone in R/R TCL. We will also test selinexor and chemotherapy in laboratory models of R/R TCL and interrogate mutations from patient's tumours and blood samples to determine if we are able to track the patient's disease by monitoring these mutations in the patient's blood samples.

### Obesity-Related Glycine Deficiency: Investigating a Longstanding Metabolic Paradox Using Bench and Bedside Approaches

Obesity causes abnormalities in the regulation of various nutrients such as amino acids. The amino acid, glycine, helps maintain normal health and is used to produce the anti-oxidant, Glutathione (GSH) that protects our body against oxidative damage, which is known to increase in obesity. We recently found that glycine is deficient in obese individuals; however, the reason for glycine deficiency in obesity is unknown. Moreover, there currently is no specific treatment to prevent obesity-induced oxidative damage. In this project we hope to better understand the reasons why glycine is low in obesity and through which we may discover new treatments to prevent obesity-related complications. We hypothesize that low blood glycine in obese individuals is due to a greater demand for GSH to combat against obesity-induced oxidative damage. These abnormalities are expected to return to normal following weight loss. We plan to recruit 20 severely obese subjects who are scheduled for bariatric surgery and 20 matched lean controls. Subjects undergoing surgery will be studied at baseline and six months following surgery. The pathways responsible for glycine deficiency will be studied by the infusion of various metabolic tracers. We will also perform cell culture experiments to validate findings from human studies.





### Diet-Derived Metabolites and the Risk of Colorectal Cancer: A Nested Case-Control Study in a Population-Based Cohort, the Singapore Chinese Health Study

Colorectal Cancer (CRC) is the most common cancer and one of the main causes of cancer-related deaths in Singapore. More than 90% of the risk of CRC can be attributed to environmental and lifestyle factors, including diet. However, current studies evaluating diet and CRC risk have yielded inconsistent results. Metabolites are the downstream metabolic products of food composition and may reflect the effects of diet more precisely. The overall objective is to evaluate the association between diet-derived metabolites that have been linked to CRC development and the risk of CRC among Chinese in Singapore. No previous similar

study has been done locally. Our aim is to compare blood levels of dietderived metabolites between 500 subjects with CRC against subjects without CRC, within the Singapore Chinese Health Study. We will also examine if the association differs by location (colon versus rectum). Furthermore, we will identify the subtype of CRC that depends on these metabolic pathways for cell growth. The findings will allow deeper understanding of the biological pathways leading to CRC development and may potentially lead to the development of novel therapeutic interventions to reduce CRC recurrence and improve patient's survival.





### NMRC Research Training Fellowship

The NMRC Research Training Fellowship aims to provide 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 both overseas research training and graduate research degree programmes at local or overseas institutions. Awardees of the fellowship receive funding for salary and tuition fees for local graduate degree programmes, or allowances and other benefits in line with the host institution's policies for overseas research attachments.

### MOH Healthcare Research Scholarship – Master of Clinical Investigation (MCI)

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

### National Outstanding Clinician Scientist (CS) Resident Award

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

### NMRC Research Training Fellowship

12 recipients were awarded the NMRC Research Training Fellowship.

Name	Institution and Type of Training	Project
Dr Sabrina Wong	NHGP Part-time local PhD	Development of a Patient Centred-Approach to Improving Outcomes of Patients with Multi-Morbidity in Primary Care
Dr Mo Yin	<b>NUHS</b> Full-time overseas PhD	Preventing Emergence of Antimicrobial Resistance in Intensive Care Units
Dr Amit Jain	NCCS Part-time local PhD	Cell Based Therapy in Lung Cancer
Dr Melvyn Zhang Weibin	IMH Part-time local PhD	A Framework for the Development, Evaluation and Implementation of M-Health Data Collection
Dr Francis Wong Keng Lin	<b>NUHS</b> Part-time local PhD	Evaluating the Efficacy of Exosomes Derived from Human Mesenchymal Stem Cells in Promoting Osteochondral Regeneration for Osteoarthritis
Dr Tiew Pei Yee	<b>SGH</b> Full-time local PhD	Linking Chronic Obstructive Pulmonary Disease Clinical Phenotypes to Endotypes for Possible Disease-Modifying Targets in Asia
Dr Wong Chee Wai	<b>SERI</b> Part-time overseas PhD	Liposomes as a Drug Delivery Mechanism for the Treatment of Proliferative Vitreoretinopathy
Dr Yang Ming	<b>NUH</b> Full-time overseas PhD	Neurorestoration after Spinal Cord Contusion with Cocktail Cell Transplant Therapy
Dr Alvin Tan Wai Kit	TTSH Part-time local PhD	Interactions between Insulin Resistance, Osteocalcin and Skeletal Muscle in Older Chinese Males with Type 2 Diabetes Mellitus
Dr Jason Chan Yong Sheng	NCCS Part-time local PhD	Metagenomic Discovery and Clinical Characterization of HHV-7 in Human Angiosarcoma
Dr Mayuri Bhargava	<b>NUH</b> Part-time local PhD	Retinal Cell Therapy for Age-Related Macular Degeneration
Dr Chan Gek Cher	<b>NUH</b> Overseas research attachment	Failure of Podocyte Regeneration Underlies Diabetic Kidney Disease

### MOH Healthcare Research Scholarship (MCI) 22 recipients were awarded the MOH Healthcare Research Scholarship – Master of Clinical Investigation (MCI).

Name	Institution and Department	Project Title
Dr Bolem Nagarjun	NUHS (MOHH) Dept of Surgery	Proteomics in Glioma Resection: A Mass Spectrometric Approach
Dr Cai Zhengyang Elijah	NUHS (MOHH) Dept of General Surgery	Orbital Cavity Morphometry Determines Fracture Outcome
Dr Chan Hiang Ping	NUHS (MOHH) Dept of Respiratory & Critical Care	Paired Sputum and Blood Transcriptomic Signatures for Assessment of Tuberculosis Disease
Dr Chew Chu Shan Elaine	<b>KKH</b> Dept of Paediatrics	Pilot Evaluation of a Mobile Health Intervention to Identify Early Responders to Treatment in Adolescent Obesity as a Triage Approach
Dr Claire Alexandra Chew Zhen	NUHS (MOHH) Dept of Surgery	Identification of Proteomic-Based Biomarkers in HCC Using Imaging Mass Spectrometry
Dr Chia Kai Ann Daryl	NUHS (MOHH) Dept of Surgery	Granulocyte-Colony Stimulating Factor (G-CSF) Improves FLR Growth and FLR Maturity in Mice Undergoing ALPPS
Dr Goh Yonggeng	NUHS (MOHH) Dept of Diagnostic Radiology	Evaluating Embolic Potential of Carotid Artery Atherosclerotic Plaques Using Contrast Enhanced Ultrasound (CEUS)
Dr Arshvin Kesavan	NUHS (MOHH) Dept of Urology	A Needle Guiding Device for Percutaneous Nephrolithotomy to Improve Procedure Success Rates
Dr Lee Hsien Ren Shawn	NUHS (MOHH) Dept of Paediatrics	T-Cell Receptor Repertoire Diversity and Clonality in Children with B-Cell Acute Lymphoblastic Leukaemia
Dr Li Yunkai Andrew	<b>NUHS</b> Dept of Respiratory & Critical Care	Use of Indirect Calorimetry in the Intensive Care Unit
Dr Lim Si Jing Joline	<b>NUHS</b> Dept of Haematology-Oncology	Targeting IRAK1 in Breast Cancer
Dr Lim Yijuan Yvonne	<b>NUHS</b> Dept of Paediatrics	Bioengineered Probiotics Delivering Anorexigenic Gut Hormones to the Gut as a Potential Treatment for Obesity
Dr Ong Ching Ching	<b>NUHS</b> Dept of Diagnostic Imaging	To Evaluate the Clinical Utility of CT Derived Fractional Flow Reserve
Dr Quah Lishan Jessica	<b>CGH</b> Dept of Respiratory & Critical Care Medicine	Impact of Cognitive Stimulation Using Virtual Reality on Cognitive Impairment Post-Critical Illness
Dr Geoffrey Sithamparapillai Samuel	<b>SGH</b> Dept of Rehabilitation Medicine	Isolation Rehabilitation – Patients Under Isolation Precautions have Longer LOS and are at Greater Risk of Adverse Outcomes
Dr Seow Cherng Jye	TTSH Dept of Endocrinology	Trabecular Bone Score in Postmenopausal Singaporean Women with Type 2 Diabetes Mellitus-A Cross Sectional Study
Dr Soh Yu Sen Alex	NUHS (MOHH) Dept of Gastroenterology & Hepatology	Changes in Oral and Faecal Microbiome in Diarrhoea Predominant Irritable Bowel Syndrome Before and After a Low FODMAP diet
Dr Raghav Sundar	<b>NUHS</b> Dept of Haematology-Oncology	Interrogating Immunotherapy in Gastro-Intestinal Cancers
Dr Tay Wy Keat	NUHS (MOHH) Dept of Urology	Use of Multi-Photon Microscopy (MPM) Imaging in Improving the Diagnostic and Prognostication Value of Histology in Renal Cell Carcinoma
Dr Tsai Shih Hsiang Andrew	<b>SNEC</b> Dept of Ophthalmology	A Longitudinal Study on the Structural-Functional Correlations of Perifoveal Capillary Network Integrity in Diabetes Using Optical Coherence Tomography Angiography
Dr Wang Yu Tien	SGH Dept of Gastroenterology & Hepatology	Effect of Antibiotic Treatment on Colonic Fermentation and its Association with Colonic Microbiota in Non-Constipated Irritable Bowel Syndrome.
Dr Yang Liying	<b>SGH</b> Dept of Obstetrics & Gynaecology	Accuracy of NIPT for Differentiating Between Benign and Malignant Ovarian Cysts

### National Outstanding Clinician Scientist (CS) Resident Award Four recipients were presented the National Outstanding Clinician Scientist (CS) Resident Award.

Name	Cluster and Clinical Specialty	Year of Award
Dr Feng Jiajun	<b>SHS</b> Plastic Surgery	2016
Dr Vincent Tay Khwee Soon	<b>SHS</b> Plastic Surgery	2016
Dr Ku Chee Wai	SHS Obstetrics and Gynaecology	2017
Dr James Mok Wan Loong	SHS Plastic Surgery	2017



### STUDYING THE BRAIN AND STIMULATING THE MIND

Professor Tan Eng King has dedicated his career to neurological research in his pursuit of greater knowledge. "The brain is the most complicated and intricate organ in the body," he enthused. "Trying to understand the functions of the brain is essentially like trying to unravel the mysteries of the universe."

And with the renewal of his Singapore Translational Research (STaR) Investigator Award, Prof Tan is excited and delighted to go forward with uncovering the neurological enigmas that are Essential Tremors (ET) and Parkinson's Disease (PD).

The first STaR award had already led to the identification of new molecular targets. These are currently being further developed in partnership with other organisations.

According to him, the focus of the research with the aid of the second STaR award is "to develop humanised and animal models which will assist in identifying new molecular targets and pathways that result in the dysregulation of the neurological circuit." Following which, he will attempt to control the dysregulation by devising a treatment.

Fundamentally, Prof Tan set about his research in order to improve the quality of life for patients with movement disorders. "The primary aim is to try to improve patient outcome and patient management, develop early patient diagnosis, figure out how to reduce patients' symptoms and progression, identify risks of drug complications, and

allow patients to integrate back into society," he said.

"It is very tough to be a doctor and conduct research at the same time, so ultimately it has to be the passion that drives you," he advised earnestly. "If you have the passion, the interest, a good mentor, a strong drive and a deep desire to help the many suffering patients, then I think that this track will be very satisfying in the long run."

#### Nurturing the Minds of Future Medical Professionals

A man of many hats, Prof Tan holds various appointments. Among them is Research Director at National Neuroscience Institute, Senior Consultant Neurologist at the National Neuroscience Institute (Singapore General Hospital Campus), and Professor at the Duke-NUS Medical School.

Beyond his research efforts, Prof Tan speaks of the deep passion he has for nurturing young minds. He draws immense satisfaction from grooming the future generation of medical research professionals, and seeks to "create a system that will empower younger clinician scientists to grow and prosper in a clinical and academic environment" while "enthusing them in their area of research."

He is grateful not only for the funding from STaR award, but also for the opportunity to contribute to the pipeline of national talent, particularly clinician scientists and researchers.

"I see the STaR award as partly giving back to the system through mentoring, through trying to improve the system rather than just focusing on an individual research."



### SINGAPORE TRANSLATIONAL RESEARCH INVESTIGATOR AWARD

#### **Professor Tan Eng King**

**Director** Research, National Neuroscience Instituto

**Deputy Medical Director** Academic Affairs, National Neuroscience Institute

Senior Consultant Neurologist Department of Neurology, National Neuroscience Institute (SGH Campus)

**Professor**Duke-NUS Medical School

Embarking on the path of clinician scientists is not easy and given the unique nature of his statuses, both as an established clinician scientist and existing academic appointments at SingHealth-Duke NUS and the Ministry of Health, he is able to continue his mentorship to contribute to the pipeline of leaders in the area of healthcare research.

### STRENGTHENING IMMUNE-BASED T-CELL THERAPIES IN SINGAPORE

Modern diseases are often regarded as recent developments. However, studies have found evidence that the Hepatitis B Virus (HBV) has been around since the Palaeozoic Era, with strains of the virus appearing in birds of that time. This is indicative of a resilient pathogen that has mutated over several million years – and is not so easily beaten.

Today, out of the 350 million people worldwide who have been diagnosed with Chronic Hepatitis B (CHB), approximately 75% of them reside in Asia. It is a predominantly Asian health issue, and Professor Antonio Bertoletti is one such person who has endeavoured to get to its roots. Renowned for his expertise in the pathogenesis and immunological control of HBV, Prof Bertoletti is a Professor of the Emerging Infectious Diseases Programme in Duke-NUS Medical School.

He attributes the success of his recent scientific career to two Singapore Translational Research (STaR) Investigator Awards that he received, for the project titled "T- Cell Receptor Mediated Immune Therapy in Chronic Hepatitis B and Hepatocellular Carcinoma". The first in 2012 gave him a great deal of leverage in building the necessary immunological tools to construct T-cells that are able to target CHB and Hepatocellular Carcinoma (HCC).

The current STaR award enables him to further develop ways to engineer T-cells with increased fitness against the liver cancer.

### Doctoring T-Cells for Immunotherapy

"At the moment, there is no cure for HBV and HCC," Prof Bertoletti acknowledged. "We only have drugs that stop the replication of HBV, but they do not eliminate the virus. Patients have to be on that medication for their entire lives. If they stop, the virus escalates."

He aims to develop a finite therapy that can reach a functional cure through the use of T-cell immunotherapy. This intricate process involves extracting patients' T-cells, modifying the T-cells to recognise and destroy HCC cells or inhibit HBV replication, and then reinserting the engineered T-cells.

Clinical trials have already been established to assess the efficacy of this specific T-cell immunotherapy. Prof Bertoletti is hopeful that the results can offer new and more effective treatment options to patients with CHB infection and HBV-related HCC. If successful, it could potentially be applied to other diseases and make a pivotal impact in the medical field.



For aspiring clinician scientists striving to make similar contributions in the name of health, Prof Bertoletti emphasised that the road is long and grinding. "You need to show a deep knowledge of your field. Clearly, what is important is to have translational knowledge," he pointed out. "Not only do you need to understand the theory, but you also need to fully grasp the patients' needs."

"This STaR Award allows me to practically achieve my research goals. The security of working for five years with secure funding allows you to think of a long-term strategy."

# THE LIFEBLOOD OF INTRACRANIAL STENOSIS THERAPY

Associate Professor Vijay Sharma's career trajectory was inspired by his experiences with intracranial stenosis during medical training. In fact, he discovered a worrying phenomenon among his patients — almost one out of two stroke patients had intracranial stenosis.

Today, he is a Senior Consultant at the Division of Neurology, Department of Medicine at National University Hospital (NUH) and an Associate Professor at Yong Loo Lin School of Medicine in the National University of Singapore (NUS). As one of the recent recipients of the Senior Investigator Level (SI)-Clinician Scientist Award (CSA), he feels that "it is a very big privilege and recognition of my efforts." He added, "It indicates that I have been successful in previous works and it is quite motivating."

With funding from CSA-SI, A/Prof Sharma can develop new modalities of treatment that will provide hope for patients with intracranial stenosis, a disease that is highly prevalent among Asians. This disease carries a high risk for recurrent stroke despite the best medical therapy available. While intracranial stenting is associated with unacceptable periprocedural complications, external carotid-internal carotid bypass surgery is still debatable. Thus, definitive and effective treatments are largely lacking.

Solving the woes of intracranial stenosis patients calls for ground-breaking and non-invasive therapy,

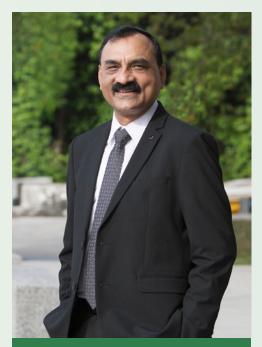
something that he looks to achieve with a technique inspired by the Enhanced External Counterpulsation (EECP) therapy. "Basically," he explained, "this machine functions like a powerful leg massager, and it has worked for patients with stenosis of the arteries of the heart. Hence, I started exploring the possibilities of using the EECP machine for intracranial stenosis."

The technique induces the development of new arteries in the brain, and helps them to mature in order to minimise the risk of bursting (and bleeding). His current clinical trial aims to analyse if this treatment improves perfusion to the brain, reduces the risk of strokes and improves the patients' cognition and memory.

### Intense Scrutiny, but Immense Satisfaction

A/Prof Sharma finds his work challenging enough as it is, and with additional pressure of close scrutiny of the medical community, a career in research comes with much hardship.

"When you are simply a clinician, your only critics are your patients and their families but as a researcher, in addition to the patients and their families, you will be continuously examined by your colleagues both locally and internationally," he confided. "The amount of monitoring and the high expectations that come with research is definitely challenging and stressful. However, if you are



### CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR)

### Associate Professor Vijay Sharma

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

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

National University Health System

prepared to be scrutinised and have your work picked apart, this will be a very rewarding path."

He advises clinician scientists to persevere and listen to the constructive criticisms of their peers, juniors, seniors and mentors as he believes that this will push their research in the right direction.

"Your success balances all the distractions that come with clinical research. Be open to constructive criticisms in order to grow in your research."

### SOOTHING SKIN AILMENTS THROUGH 3D IMAGING

When Dr Tey Hong Liang first began practicing as a dermatologist, he realised that most of his clinical work involved counselling patients with chronic skin disorders. Some of his patients experienced itching so severe that they even contemplated suicide as a desperate means to an end. This tragic phenomenon is such a common incident that he currently runs his clinic next to a psychiatrist's.

As the Head of the Research Division in National Skin Centre, he strives to solve patients' skin problems and give them a new lease of life. The purpose of his research, funded by the Clinician Scientist Award (CSA), aims to better understand and diagnose imperceptible skin conditions.

Through the use of 3D imaging in ex vivo skin and non-invasive skin imaging, Dr Tey will be able to acquire new and highly sophisticated insights to skin conditions, which will in turn enable him to better treat the ailments

"The main crux of it is that we want to go beyond the conventional 2D methods of investigation in current standards of medical practice," he explained. "We want to go beyond histology, which is 2D, into 3D, 4D and in vivo (meaning live tissues). Because we essentially live in a 4D world, but the current standard practice now only utilises 2D."

There are many limitations when it comes to 2D skin analyses, as doctors can only view cross-sections of the

skin. With 3D imaging, dermatologists can immerse themselves within the skin's whole volume and uncover new anatomical knowledge. In the past, 2D analyses portrayed nerves branching out individually like tree branches, but 3D imaging has recently proven the latter false; depicting nerves as distributed like a network with branches interconnected to each other.

The dermatologist drew on a metaphor to explain the situation more succinctly: "Think of the skin's nervous system like the architecture of a building where it can be fully taken in only in 3D. If we just see a slice of the building in 2D analyses, we cannot appreciate the building for what it is."

#### No Rash Decision

After spending a decade in skin research, Dr Tey is heartened to see his efforts paying off with marked improvements to treatment outcomes. He continues moving forward in this direction of bettering his patients' quality of life, and encourages fellow clinician scientists who are in this unique position to deliver and make changes as well.

"Clinician scientists understand the root of the problem and know what needs to be solved," he said. "We must be proactive, patient-centred and problem-centric in order to make improvements to the conditions and the patients' quality of life."



### CLINICIAN SCIENTIST AWARD (INVESTIGATOR)

#### **Dr Tey Hong Liang**

#### Head

Research Division, National Skin Centre

#### Senior Consultant

Department of Research and Medicine, National Skin Centre

#### Assistant Professor

Lee Kong Chian School of Medicine, Nanyang Technological University

"As clinician scientists, our uniqueness and value can serve to plug the gap between science and clinical practice."

# THE ASSOCIATION BETWEEN DIET-DERIVED METABOLITES AND COLORECTAL CANCER

Colorectal Cancer (CRC) is the most common cancer and one of the main causes of cancer-related deaths in Singapore. Despite its high prevalence, no previous study has been conducted that accurately analyses the association between diet-derived metabolites and CRC in Singapore.

Upon receiving the Transition Award (TA), Dr Dawn Chong set out to evaluate the association between diet-derived metabolites and the development of CRC among the Chinese in Singapore within the population-based cohort, the Singapore Chinese Health Study. More than 90% of CRC's risk factors can be traced back to environmental and lifestyle influences, including diet.

The consultant at National Cancer Centre Singapore (NCCS) proclaims her delight at receiving the TA. "I am very grateful to National Medical Research Council (NMRC) for supporting my mission to improve clinical outcomes for CRC patients," Dr Chong enthused. "This award allows me to translate study findings from bench to bedside. It provides funding, protected time for research and an opportunity for me to work with likeminded colleagues."

The entire study cohort comprises only the Chinese ethnic group, given the highest incidence of CRC among the Chinese population compared to other ethnicities in Singapore. The group's lifestyle habits are theorised to be a major factor in the

development of CRC. Since dietderived metabolites (downstream metabolic products of food composition) may reflect the effects of the diet more precisely, Dr Chong decided to focus on them. Thereafter, she aims to identify subtypes of CRC that depend on these metabolite pathways for growth and progression.

The determined oncologist hopes that the findings derived from the study will reveal a deeper understanding of the biological pathways leading to CRC development, and potentially enable the development of novel therapeutic interventions to reduce CRC recurrence and mortality rates.

### A Holistic Approach to Managing Cancer

Dr Chong's interest in cancer was piqued during her housemanship (an internship period for newly qualified doctors who just graduated from medical school) when she developed a holistic approach to managing cancer patients.

She goes beyond the call of duty to improve patient care outside of basic clinical care, and has a genuine passion for getting to know her patients and their families — all for the goal of better alleviating their hardship as best as she can.

"Many patients feel that cancer is a devastating disease. Beyond the medical aspects of treatment



for colorectal cancer, patients face psychological challenges as well. Many of them may be depressed, or have anxiety issues. These issues affect the patients, and extend to their family members too."

Despite the harsh realities of oncology, Dr Chong finds her work extremely rewarding. "The reward that you reap at the end when you see your research findings benefiting the greater good will make all the hard work worthwhile," she optimistically added.

"Always keep an open mind. Be open to opportunities and be receptive to advice and suggestions. Tenacity, good mentorship and strong teamwork are the keys to success in research."



# RESEARCH GRANTS



The funding of Translational and Clinical Research (TCR) is one of the core pillars of NMRC's mandate. To carry out this function, NMRC offers several grant programmes that support small-scale and large-scale Singapore-based research initiatives covering a broad spectrum of biomedical sciences.

To ensure that its limited funds are put to the best possible use by funding the best science, NMRC awards all of its research grants on a competitive, peer-reviewed basis.

NMRC's competitive grant programmes are divided into two main categories:

#### **NMRC-Funded/Managed Grants**

The category supports research on a programme level and different types of investigator-led studies via the following grant 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 category aims 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. Under RIE2020, NMRC will be administering the Open Fund grants on behalf of the HBMS EXCO and the funding agencies (A\*STAR, MOE, MOH, NRF). The category is supported via the following grant schemes:

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



#### **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 CTG includes two schemes:

1. The Industry Collaborative Trials Scheme (ICT) supports clinical trials of strategic industry partnerships that are important for the development of the clinical trials landscape in Singapore. ICTs involve both 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 the 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 up to 30% of the TPC (inclusive of 20% indirect costs). Funding for each project is open and for up to five years. The ICT scheme is open throughout the year.

Year	Proposals Reviewed	Grants Awarded	Total Sum Awarded (\$ millions)
2016	3	3	5.68

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. This may possibly result in foreground Intellectual Property (IP), and collaboration with companies is optional. Funding for each project is up to \$1.5 million (inclusive of 20% indirect costs) for up to five years.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
Nov 2016	10	2	20%	2.13
May 2017	10	1	10%	0.73
Total	20	3	15%	2.86

#### **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.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
May 2017	69	9	13.0%	13.60
Nov 2017	56	9	16.1%	13.60
Total	125	18	14.4%	27.20

#### **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.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
May 2017	31	8	25.8%	1.82
Nov 2017	36	7	19.4%	1.68
Total	67	15	22.4%	3.50

#### **Health Services Research Grant (HSRG)**

The Health Services Research Grant (HSRG) is a MOH research grant which aims to promote the conduct of HSR and enable the translation of HSR findings into policy and practice. HSRG grant calls are open twice a year.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
Jun 2017	41	14	34.1%	13.35

#### **Health Services Research New Investigator Grant (HSR-NIG)**

The New Investigator Grant (HNIG) subcategory of the Health Services Research Grant (HSRG) was launched with the aim to support new HSR researchers. The quantum supported for this new subcategory is \$100,000 over two years. The HNIG grant calls are open twice a year, along with the HSRG grant calls.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$)
Jun 2017	8	1	12.5%	0.12
Nov 2017	12	2	16.7%	0.24
Total	20	3	15.0%	0.36



#### **Open Fund-Large Collaborative Grant (OF-LCG)**

The Open Fund-Large Collaborative Grant (OF-LCG) aims to support the best teams of researchers from public institutions to advance human health and wellness, and create economic value for Singapore and Singaporeans, through the pursuit of excellence in research and its applications.

They represent a unique opportunity to bring together investigators from across all of Singapore with the clinician scientists and clinical investigators in the hospitals and Academic Medical Centres.

#### Key elements include:

- Collaboration within as well as between the basic and clinical research communities, and interdisciplinary collaboration across institutions is important for integrating, coordinating and leveraging on the full spectrum of research capabilities in Singapore, from basic science to clinical research.
- Aim to make significant contributions to the advancement of study of therapeutic areas and help establish Singapore as a global leader.
- Facilitate the discovery and application of basic science ideas for the following, where pathway to impact should be clearly articulated:
  - → Advancement of health, including the translation of clinical findings into practices and policies; and
  - → Supporting industry sectors integral to HBMS economic strategy, including PharmBio, MedTech, Food & Nutrition and Personal Care.

A total of \$275 million has been secured from the National Research Foundation (NRF) Singapore's Research, Innovation and Enterprise (RIE) 2020 Open fund to provide opportunities for new large collaborative programmes to be funded and existing ones to be renewed on a competitive basis. Each grant provides funding of up to \$25 million (inclusive of 20% indirect cost) for up to five years.

The OF-LCG is open to proposals of the highest quality across the breadth of disciplines relevant to its mission. To better realise the goals of Health and Biomedical Sciences (HBMS) in Singapore, the following five therapeutic areas have been identified as national priorities:

- Infectious diseases
- Diabetes mellitus and related metabolic/endocrine disorders
- Cancers
- Cardiovascular diseases
- Neurological and sense disorders





For each grant call, themes will be set in two/three therapeutic areas to focus on issues of particular national interest. The HBMS community is encouraged to address these themes. For the May 2017 grant call, the table below shows the therapeutic areas and set themes emphasised:

Grant Call	Therapeutic Area(s) Emphasised	Set Theme(s)
May 2017	Cancer (e.g. breast cancer, gastrointestinal cancer, haematological cancer, liver cancer, lung cancer, nasopharyngeal cancer)	<ul> <li>Precision Methods for Prevention, Disease Detection and Treatment Stratification</li> <li>Metastasis and Resistance</li> <li>Enhancing Cancer Immunotherapy</li> </ul>
	Cardiovascular Diseases	<ul> <li>Macrovascular Diseases: myocardial infarction and chronic coronary heart disease, stroke, aortic and peripheral arterial disease</li> </ul>
	Neurological and Sense Disorders	<ul> <li>Age-Related Neurological and Eye Disorders (e.g. vascular dementia, Parkinson's disease, age-related macular degeneration and glaucoma)</li> </ul>

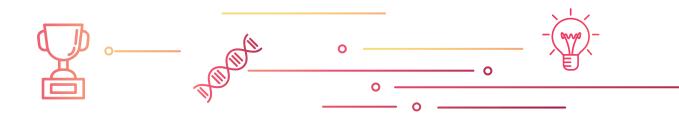
The review process is two-stage – comprising the Letter of Intent (LOI), and Full Proposal (FP) for shortlisted LOI applications. The success rate and details of the awarded programmes for the May 2017 call is tabulated in the table below:

Grant Call	Letters of Intent Received	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
May 2017	15	6	3	20%	59.09



### **Awarded Programmes**

Programme Title	Therapeutic Area(s) Emphasised and Set Theme(s)	Leadership Team (Institution)
The VICTORY (Virus-Induced Cancer: Translational Oncology Research & immunologY) Consortium	Cancer (gastrointestinal, haematological cancer, liver cancer, nasopharyngeal cancer): Enhancing cancer immunotherapy	Corresponding PI:  A/Prof Toh Han Chong (NCCS)  Theme PIs:  Prof Salvatore Albani (TII SingHealth)  A/Prof Subhra Biswas (SIgN A*STAR)  Dr Valerie Chew (TII SingHealth)  Prof Chng Wee Joo (NCIS)  A/Prof John Connolly (IMCB A*STAR)  A/Prof Ramanuj DasGupta (GIS A*STAR)  Prof Goh Boon Cher (NCIS)  Prof Han Weiping (SBIC A*STAR)  A/Prof William Hwang (NCCS & SGH)  A/Prof Paul MacAry (NUS)
Next-Generation Clinical Trials and Integrative Research for Fighting Lung Cancer	Lung Cancer: Precision methods for prevention, disease detection and treatment stratification; metastasis and resistance; enhancing cancer immunotherapy	Corresponding PI:  Dr Tan Eng Huat (NCCS)  Theme PIs:  A/Prof Gopal Iyer (NCCS)  A/Prof Darren Lim (NCCS)  Dr Evan Newell (SIgN A*STAR)  Dr Ng Quan Sing (NCCS)  Dr Ross Soo (NUHS)  Dr Anders Skanderup (GIS A*STAR)  Dr Tam Wai Leong (GIS A*STAR)  A/Prof Daniel Tan (NCCS)  Prof Daniel Tenen (CSI)  Dr Toh Chee Keong (NCCS)  Dr Lisa Tucker-Kellogg (Duke-NUS)  Dr Zhai Weiwei (GIS A*STAR)
TAAP: Translational Asian Age-related macular degeneration Program	Neurological and Sense Disorders: Age-related eye disorders (macular degeneration)	Corresponding PI:  A/Prof Gemmy Cheung (SERI)  Theme PIs:  A/Prof Caroline Chee (NUHS)  A/Prof Cheng Ching-Yu (Duke-NUS)  Prof Ecosse Lamoureux (Duke-NUS & SERI)  Prof Dan Milea (SERI)  Prof Leopold Schmetterer (SERI & LKC)  A/Prof Colin Tan (TTSH & NTU)  Dr Wang Xiaomeng (IMCB A*STAR)  Prof Wong Tien Yin (SERI)  A/Prof Yasuo Yanagi (SERI)



#### **Open Fund-Individual Research Grant (OF-IRG)**

The Open Fund-Individual Research Grant is provided to support the conduct of research proposals in basic and translational clinical research that are relevant to human health and wellness as well as research that looks at the causes, consequences, diagnosis, prevention and treatment of human diseases. The OF-IRG will provide a funding quantum of up to \$1.5 million per project (inclusive of 20% indirect costs) for up to five years.

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
Nov 2016	123	15	12.2%	17.67
May 2017	136	16	11.8%	17.57
Total	259	31	12.0%	35.24

#### **Open Fund-Young Individual Research Grant (OF-YIRG)**

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

Grant Call	Proposals Reviewed	Grants Awarded	Success Rate	Total Sum Awarded (\$ millions)
Nov 2016	67	17	25.4%	5.09
May 2017	66	19	28.8%	5.58
Total	133	36	27.1%	10.67





The National Health Innovation Centre Singapore (NHIC) provides the publicly-funded clinical research sector of Singapore with translational funding and strategic guidance to accelerate healthcare innovation.

Established in 2014, we aim to impact the clinical landscape by accelerating the development of innovative technologies and services to improve healthcare delivery and patient care. By promoting the collaboration of researchers, clinicians and industry, we will better position Singapore to tackle the healthcare challenges of tomorrow.

NHIC funding is specifically aimed to expedite the translation of an innovation (by validating, derisking or developing it) towards a commercially attractive product. Our three funding schemes are for projects which address an unmet healthcare need and have demonstrated 'proof of principle' supported by experimental data.



The NHIC team members have strong track records in the identification and commercialization of intellectual property from academic, clinical and commercial fields. The depth and breadth of this experience is offered under each NHIC award, where their expertise and resources will be applied to the evaluation and nurturing of innovations along the commercialization pipeline.

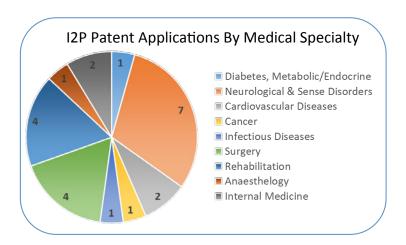
NHIC will add value by adopting an active role in the mentoring of applicants and their respective teams at all stages, from early stage discussions through to the funding of the application and postaward management of projects (including progress against milestones and commercialization). Through this committed involvement, NHIC aims to deliver the significant healthcare impact desired under the schemes.

#### **Notable Highlights of FY2017**

NHIC has funded 23 I2P patent applications and 9 I2D projects for FY2017. In addition, NHIC has cofunded a total of 9 MedTech projects with SingHealth Foundation and NUHS for early-stage development. In total, NHIC has facilitated 7 spin-off companies, 6 licences generated from I2D projects and 8 licences generated from I2P patent applications, reaching in more than \$\$490,000 of licensing revenues for the healthcare clusters.

#### Innovation to Protect (I2P) Grant

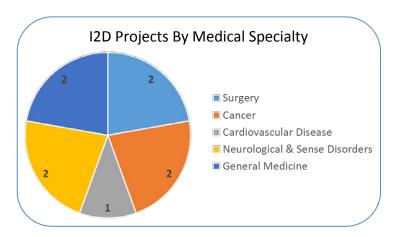
This scheme funds expenses to protect patentable innovations with significant healthcare impact and commercial potential. The I2P funding support is applicable for the following patenting stages: First filing, and Secondary filing such as PCT, NPE, prosecution, grant and maintenance.



I2P Grant	Application Received	Grants Awarded	Success Rate	Amount Committed
First Filing	14	13	92.8%	\$95,000
Secondary Filing	10	10	100%	\$250,000

#### Innovation to Develop (I2D) Grant

This funding is for an ambitious, deliverable development plan to take an innovation to a commercially attractive endpoint. This category will provide a funding quantum capped at \$\$250,000 (inclusive of max. 20% indirect costs) awarded to the host institution.



I2D Grant	Proposal Received	Grants Awarded	Success Rate	Amount Committed
April 2017	23	2	8.7%	\$500,000
August 2017	12	4	33.3%	\$999,948
December 2017	15	3	20.0%	\$748,600



# **EVENTS**





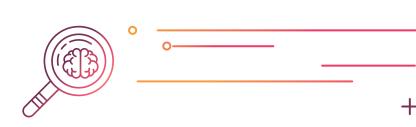
# NATIONAL MEDICAL EXCELLENCE

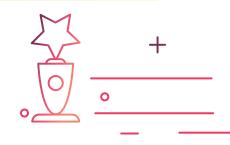
AWARDS 2017

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.

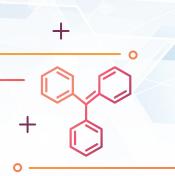
In 2017, the NMEA recognised six individuals for their outstanding contributions to clinical practice, research, mentoring, education and healthcare delivery. The following awards were given out:

- National Outstanding Clinician Award
- National Outstanding Clinician Scientist Award
- National Outstanding Clinician Mentor Award
- National Outstanding Clinician Educator Award
- National Outstanding Clinical Quality Champion Award
- National Clinical Excellence Team Award





### NATIONAL OUTSTANDING CLINICIAN AWARD 2017





#### Professor Christopher Cheng Wai Sam

**Chief Executive Officer** Sengkang Health

**Senior Consultant**Department of Urology
Singapore General Hospital

SingHealth

Clinical Associate Professor Yong Loo Lin School of Medicine National University of Singapore

**Adjunct Professor**Duke-NUS Medical School

With an illustrious career spanning over 30 years, Professor Christopher Cheng is a prominent and well-respected urologist who enjoys strong professional standing in the Singapore and international medical communities. Professor Cheng graduated from the National University of Singapore in 1982 and obtained his FRCS (Surg) in 1986, and FAMS (Urology) in 1993. He was the first urologist in Singapore to be fellowship certified in Uro-oncology at the Mayo Clinic (1990 – 1992).

A fervent advocate of patient safety and quality care, Professor Cheng works tirelessly to ensure patients receive the highest standard of care. He is a firm believer in leveraging on technology advances and medical innovation to transform the delivery of healthcare to better meet patients' needs.

As one of Singapore's leading Urologist and the lead Urologist in the Department of Urology at the Singapore General Hospital, Professor Cheng has been at the wheel of several milestones in the area of urology in Singapore. Among his myriad achievements were the establishment and expansion of the first Urology Centre in Singapore, as well as the introduction of several medical innovations such as prostate biopsy robot (Mona Lisa) and da Vinci robotic prostatectomy. Today, the Urology Centre is ranked among the best in the region, and its uro-oncology services are also widely recognised as among the best internationally.

A dedicated clinician and educator, Professor Cheng spearheaded the development and training in laparoscopic urology by organising the training and services and also performing the first laparoscopic adrenalectomy, nephrectomy and donor nephrectomy in Singapore. These procedures are now performed as a routine standard of care today.

Recognising the need to develop innovative technology for safer and more effective treatment for patients, he drove the development of several diagnostic and therapeutic options for prostate cancer. A pioneer in using robots in surgery, he led the development and introduction of the first in Asia da Vinci robotic prostatectomy with the Health Sector Development Programme grant from the

Ministry of Health. This procedure is now widely adopted in all urological services in Singapore.

Professor Cheng believes in the importance of educating and investing in the next generation of Urologists and has been playing an active role in undergraduate and postgraduate teaching since 2004. Given his passion and inspiring and nurturing demeanour, he has trained many junior surgeons over the years, many of whom are now established Urologists making significant contributions to the field of urology.

With the growing complexity in healthcare and higher expectation from patients, Professor Cheng is leading the design and development of a new model of teambased care for the upcoming Sengkang General Hospital (SKH), slated to open in the second half of 2018. The new model of care focuses on the acuity of care or care themes, where patients will be treated according to their care needs and not just on their condition. Such patient-centric and holistic care will strengthen the delivery of care and enhance patients' experiences.

A strong advocate of research and a visionary leader deeply committed to improving patient care, Professor Cheng drove and promoted a research culture in SKH. A research department has already been set up with several major grant applications receiving favourable reviews.

In recognition of his unswerving dedication and exemplary contributions, Professor Cheng was awarded the Young Surgeon's Award of the Academy of Medicine in 1986, the SingHealth GCEO Excellence - Outstanding Clinician Award in 2011 and the National Day Award - The Public Administration Medal (Silver) in 2015. He is also a two-time recipient of the 'Service with a Heart Award', which bears testimony to the passion that he places in his patients and work. Patient-centric and holistic care remains the core tenet of his clinical practice.

For his extraordinary dedication and distinguished contributions in developing and advancing the field of urology, patient safety and care quality, Professor Christopher Cheng is awarded the 2017 National Outstanding Clinician Award.

### NATIONAL OUTSTANDING CLINICIAN AWARD 2017

Professor Arijit Biswas led the Division of Maternal Fetal Medicine at the Department of Obstetrics and Gynaecology (O&G), National University Hospital (NUH) for 17 years, from 2000 to 2016. Under his leadership, the Department has grown its obstetric service to one of international standards, providing high quality patient care and maintaining an excellent safety record.

Professor Biswas has been instrumental in improving obstetric care for women both antenatally and during labour. He introduced fetal ECG (STAN) monitoring in labour, which has now been incorporated into routine practice in the delivery suites at NUH. He developed and introduced new ultrasound services at the hospital, including the nuchal translucency screening scan and 3-dimensional ultrasound scan. He has also formed vital partnerships with rheumatologists and paediatric cardiologists to initiate new joint clinical services for high-risk women with recurrent pregnancy loss and fetal cardiac abnormalities respectively, allowing these women to benefit from one-stop, multi-disciplinary care.

Professor Biswas also contributed significantly to helping women with highrisk pregnancies or fetal abnormalities receive cutting-edge care by introducing novel and effective treatments with a particular focus on prenatal intervention and fetal therapy procedures. These include in-utero treatment for select cases of fetal hydrops, in-utero blood transfusions for severely anaemic foetuses, and in-utero selective fetoscopic laser ablation of anastomotic vessels for Twin-Twin Transfusion Syndrome (TTTS), among others. Professor Biswas also performed the first radio-frequency ablation procedure for a monochorionic twin pregnancy in Singapore.

Aside from the clinical advances that he has championed, Professor Biswas also ensured that clinical processes in the Division of Maternal-Fetal Medicine at NUH kept pace with time. Professor Biswas designed, developed and implemented the Department's first database of maternity records that allowed for accurate record-keeping and

epidemiological research. Importantly, the database also allowed for the automated calculation of maternity services-related clinical quality indicators that have helped to maintain the hospital's high standards of care.

Professor Biswas continues to support the Department at NUH as the Director of Clinical Services and Head of the Fetal Care Centre. He is a dedicated leader, who personally supervises the running of the Obstetric Services at NUH, provides regular on-the-floor consultant cover, and remains accessible even when he is not on call. The high volume of referrals for second opinions, advanced ultrasound scans and ultrasound-guided invasive procedures that he receives from obstetricians and gynaecologists in Singapore, as well as the region, is testament to his reputation as a highly knowledgeable and experienced clinician.

Professor Biswas is also passionate about teaching and training the next generation of doctors and obstetrics and gynaecology specialists. He continues to be in great demand as a clinical teacher. He is patient with his juniors and displays deep knowledge about the art and science of obstetrics and gynaecology. He has also been an invaluable mentor to many residents and junior colleagues. For his good work with residents, he was awarded the "NUH Postgraduate Teaching Excellence Award" in December 2012.

Professor Biswas is well recognised as an expert in the field of Maternal Fetal Medicine both nationally and internationally. Apart from holding numerous leadership and advisory positions at NUH and NUS, Professor Biswas is the Chairman of both the national O&G Resident Advisory Committee and the Clinical Advisory Group on Zika Virus Infection and Pregnancy at the Ministry of Health and member of the Specialist Accreditation Board, Singapore. He was also previously President of the College of O&G and a Council Member of the Academy of Medicine Singapore. Professor Biswas has also published more than 137 papers in international peer-reviewed journals with a citation count of 1852 and an





#### **Professor Arijit Biswas**

Senior Consultant
Division of Maternal-Fetal Medicine
Department of Obstetrics & Gynecology
National University Hospital

**Professor** Yong Loo Lin School of Medicine National <u>University</u> of Singapore

National University Health System

H-index of 22, and maintains active research interests to date.

For his outstanding contributions and achievements in clinical work that have advanced the safety and quality of obstetric care, Professor Arijit Biswas is awarded the 2017 National Outstanding Clinician Award.

# NATIONAL OUTSTANDING CLINICIAN SCIENTIST AWARD 2017







#### Associate Professor Chong Yap Seng

Senior Consultant
Division of Maternal-Fetal Medicine
Department of Obstetrics & Gynecology
National University Hospital

**Associate Professor** Yong Loo Lin School of Medicine National University of Singapore National University Health System

Executive Director Singapore Institute for Clinical Sciences Agency for Science, Technology and Research Associate Professor Chong Yap
Seng is a clinician scientists with a
special interest in fetal growth and early
development. His research seeks to
benefit population health in Singapore,
both for the current and the future
generations.

Associate Professor Chong and his team set up the Growing Up in Singapore Towards healthy Outcomes (GUSTO) Study in 2009. GUSTO is one of the most comprehensive longitudinal cohort studies ever conducted in Singapore or anywhere else in the world, involving mothers-to-be and their children. GUSTO is aimed at studying the growth and development of individuals from early life to discover new prevention and early intervention strategies to optimise health. The study is a multi-organisational effort that harnesses research talent from the National University Health System, KK Women's and Children's Hospital, A\*STAR's Singapore Institute for Clinical Sciences, and other academic partners locally. GUSTO also collaborates with international researchers from New Zealand and the United Kingdom, among

GUSTO researchers recruited over 1200 Singaporean women who volunteered to participate in the birth cohort study between 2009 and 2010. These volunteers are followed from early pregnancy through delivery and as their children grow up, to provide valuable insight into the early determinants of health and disease. Supported by the Translational Clinical Research Flagship Programme grant from the National Medical Research Council, Ministry of Health, GUSTO has been cited to be one of the leading birth cohort studies in the world with some of the most detailed assessments and analyses of child development, cognition and physical health ever established.

GUSTO has generated over 140 scientific publications since 2012, and the findings have also directly influenced health policy and clinical practice in Singapore. GUSTO researchers discovered that the prevalence of gestational diabetes mellitus (GDM) was much higher than expected and showed that a universal testing policy for GDM would be more cost effective than high-risk screening.

They submitted a white paper to MOH in September 2015, which led to MOH recommending universal testing for GDM to all doctors in Singapore.

GUSTO's research work was expanded further when the Singapore PREconception Study of long-Term maternal and child Outcomes (S-PRESTO) cohort study was funded in 2014. This is one of the first and most comprehensive studies of women planning to conceive to be launched in the world and seeks to understand how the health of women before pregnancy affects both the health of the mothers and their babies.

The sustained influence of the early environment, including maternal health and nutrition over the early life course, forms the basis of the 'developmental origins of health and disease (DOHaD)' paradigm, which has helped shape the foundation of Associate Professor Chong's work in GUSTO and S-PRESTO. Under the DOHaD programme, Associate Professor Chong leads a dynamic, highly-collaborative research group.

Besides research, Associate Professor Chong remains a busy obstetrician who is noted for his efforts to promote natural birth and breastfeeding in Singapore. He also led the Medical Education Unit for 10 years, helping to develop teaching skills and the curriculum in the Yong Loo Lin School of Medicine, where he is currently a Vice-Dean promoting strategic collaborations with academic partners around the world. Finally, Associate Professor Chong is the Executive Director of A\*STAR's Singapore Institute for Clinical Sciences where he is working with the food and nutrition industry to translate some of his team's research into viable products.

For his outstanding contributions towards improving population health in Singapore through the study of health and disease in early life, and its potential impact in later life, Associate Professor Chong Yap Seng was awarded the 2017 National Outstanding Clinician Scientist Award.

## NATIONAL OUTSTANDING CLINICIAN MENTOR AWARD 2017

As an accomplished neurosurgeon, Dr Chumpon has played an essential role in the training of young clinicians and clinician scientists. Through his many decades as an outstanding clinician, he has mentored generations of neurosurgeons from Singapore and the region – many of whom are leaders in the field today.

For those who know Dr Chumpon well, he is a tower of strength for his colleagues, students and patients. His relentless energy to find solutions in his quest to improve surgery and its links to other fields of medicine has made him a leader in neurosurgery. He is one of the foremost mentors for neurosurgery in Singapore.

A pioneer in neurosurgery in Singapore, Dr Chumpon can also be credited for the crucial role he played in the development of the discipline. Under the mentorship of Singapore's founding fathers of neurosurgery, the late Dr Tham Cheok Fai and Dr Gopal Baratham, Dr Chumpon helped set up the department of Neurosurgery in Singapore General Hospital (SGH) in 1990.

As such, Dr Chumpon is one of the foremost mentors for neurosurgery in Singapore and has nurtured many of the nation's leaders in medicine. His mentees include Associate Professor Ang Beng Ti, Head, Department of Neurosurgery (Singapore General Hospital Campus), National Neuroscience Institute and Dr David Low, Consultant, Department of Neurosurgery, National Neuroscience Institute and Head, Neurosurgical Service, KK Women's and Children's Hospital.

As an educator, Dr Chumpon is a fierce proponent for structured and directed training. He was instrumental in leading the advancement of neurosurgical training in Singapore. He was Chairman of the Specialist Training Committee and Chairman, Chapter of Neurosurgeons, Academy of Medicine, during which, an MOU was signed with the Royal College of Surgeons, Edinburgh on the Specialty Fellowship Examination in Neurosurgery in Singapore leading to the FRCSEd (Surgical Neurology) in 2005. This set the beginning for certification of neurosurgical training in Singapore.

With SGH's strategic proximity to many national specialty centres, Dr Chumpon established a multi-disciplinary approach for complex neurosurgical problems. Today, a multi-disciplinary approach has been accepted as good clinical practice. This culminated in the successful separation of the Nepalese conjoined twins in 2001. In this complex case, Dr Chumpon was one of the lead surgeons.

For this mega-feat which projected Singapore and SGH onto the world medical stage, the team was awarded the Excellence for Singapore Award and the Singapore Medical Alumni Association Award.

Dr Chumpon was also the lead clinician in the development of the DextroscopeTM, a 3D virtual reality workbench for planning and training in neurosurgery. This technology has been used to train neurosurgeons locally and worldwide, a prototype of which was used to plan the separation of the conjoined twins.

Dr Chumpon has dedicated his life to neurosurgery because he believes that the best must reside to serve and care for patients in the public healthcare system. He has instilled values of public duty and nurtured many generations of neurosurgeons for Singapore.

For his outstanding contributions and exemplary lifelong dedication in nurturing the past, present and next generation of doctors to address the neurological needs of patients and Singapore's ageing population, Dr Chumpon Chan was awarded the 2017 National Outstanding Clinician Mentor Award.



Dr Chumpon Chan

Senior Consultant
Department of Neurosurgery
National Neuroscience Institute

SingHealth



## NATIONAL OUTSTANDING EDUCATOR AWARD 2017



# Associate Professor Tham Kum Ying

**Education Director**Pre-Professional Education Office
Tan Tock Seng Hospital

**Senior Consultant** Emergency Department Tan Tock Seng Hospital

National Healthcare Group

**Assistant Dean Year 5** Lee Kong Chian School of Medicine Nanyang Technology University



Associate Professor Tham Kum Ying is well known and respected as a teacher par excellence in Singapore's public healthcare, and has been actively involved in the education of medical students, nurses, paramedics, house officers, medical officers and trainees since 1994.

As Associate Dean and Director of Clinical Training from 2007 to 2010, Associate Professor Tham plays an active leadership role in enhancing the teaching and faculty development programmes of the National Healthcare Group (NHG), Tan Tock Seng Hospital (TTSH), and the Yong Loo Lin School of Medicine at the National University of Singapore (NUS). In 2010, she was appointed Assistant Chairman of the Medical Board (Education) to enhance education as a core mission of TTSH. She continues to lead in medical education and training efforts in her current appointment as Education Director of TTSH's Pre-Professional Education Office.

In 2011, Associate Professor Tham became part of the start-up team as Assistant Dean at Singapore's third medical school, the Lee Kong Chian School of Medicine (LKCMedicine). She planned and implemented clinical aspects of the curriculum, customised teaching materials from Imperial College to a curriculum suited to Singapore's needs and relevant in the local context, so that the school's graduates "would be the kind of doctors you and I would want caring for us."

A firm believer that doctors must be able to communicate effectively with their nurses, patients, families and caregivers, Associate Professor Tham was the first clinician educator to introduce a communications course for medical students undergoing clinical training at TTSH. Students were presented with challenging 'real-life' scenarios to hone their skills in empathy and to increase their awareness and sensitivity when handling the patients and their families.

Since 2009, Associate Professor Tham has systematically introduced Workplace-Based Assessment, first to the doctors, and eventually to other professional groups, so as to better integrate competence with performance. She has also worked closely with the Harvard Macy Institute to create and develop a signature programme to equip NHG's policy makers including clinician educators and residency programme directors with the know-how to design, lead, manage and evaluate education programmes. Close to 200 clinician educators in NHG and nationally have since completed the programme, and many have gone on to complete a post-graduate Master's degree in Health Professions Education.

Nationally and regionally, she is a coveted teacher, lecturer and educator in resuscitation, trauma, emergency medicine and medical education. Her current research interests focus on trauma resuscitation and the teaching and learning of medical professionalism. Among her numerous accolades are the Best Teacher Award from TTSH in 2000, the Nanyang Educator Award from NTU in 2015, as well as the commendation as Bilingual Regional Educator from the China-Hong Kong Chapter of the American College of Surgeons in 2016.

Outside of Singapore, Associate Professor Tham contributed to the clinical and educational capacity-building project for emergency medical services in Malang, Indonesia, and continues to lead the capacity-building project for two rural districts in Sichuan, China.

A firm believer in life-long learning, Associate Professor Tham was Singapore's and NHG's first clinician educator to complete her Doctorate of Education (EdD, Dual Award) from the Institute of Education – University of London, UK, and National Institute of Education, NTU in 2016.

For her unstinting passion and outstanding leadership in medical education and training, and for her unwavering commitment to mentor and teach Singapore's doctors of tomorrow, Associate Professor Tham Kum Ying was awarded the 2017 National Outstanding Clinician Educator Award.

# NATIONAL OUTSTANDING QUALITY CHAMPION AWARD 2017

The late Associate Professor Gomez dedicated his life to the most fragile of patients; caring for countless premature and ill newborns over the span of his illustrious career. His commitment to the wellbeing of these young children earned him a loyal following of grateful families who took time to meet up with Associate Professor Gomez, years after their children had graduated from the Neonatal Intensive Care Unit (NICU).

After obtaining his post-graduate degree in Paediatrics from the National University of Singapore in 1986,
Associate Professor Gomez undertook fellowship training at Monash Medical Centre in 1988, and had been practicing Neonatology in KK Women's and Children's Hospital (KKH) ever since.
Associate Professor Gomez was the Head of the hospital's Special Care Nursery from 2002 to 2005 and assumed the headship role at the NICU in 2006.

As Director of Medical Informatics and also Chairman of the Medication Safety Committee at KKH, Associate Professor Gomez had deep appreciation of the power of automation and computerisation in bolstering patient safety. He devoted efforts outside of his clinical duties to participate in and lead workgroups to enhance electronic medical records and medication safety, both within KKH and in the SingHealth Academic Medical Cluster. He was instrumental in the deployment of the Closed Loop Medication Management system in KKH, which was also the pilot site for the SingHealth cluster. In view of his contributions in the area of medical informatics, Associate Professor Gomez was awarded the National Health IT Excellence Award 2015 - Champion for Health IT Excellence.

Associate Professor Gomez had also received national awards and international recognition for his work in clinical quality improvement in other areas such as improving weight gain in very low birth weight infants as well as infection control in the NICU. The Clinical Process Improvement Project - Improving the Nutritional Intake of the Very Low Birth Weight (VLBW) Infant

won the second runner-up award at the Singapore Clinical Quality Forum, National Scientific Poster Competition in 2005. His other project, aimed at reducing the incidence of healthcare associated infection in the VLBW infants, won the first runner-up award at the same National Scientific Poster Competition in 2009.

Associate Professor Gomez demonstrated his passion for medication safety and contributed his expertise at a national level, as co-Chairman of the Ministry of Health's National Medication Safety Taskforce. This was one of his many appointments, at various other workgroups and committees.

Associate Professor Gomez had also imparted his valuable knowledge and skills to successive generations of medical professionals. He was extensively involved in the teaching of medical students, nurses and advanced specialist trainees in Paediatrics and Neonatology since 1986, and was conferred the title of Adjunct Associate Professor by the Duke-NUS Medical School in April 2017.

For his outstanding contributions and devotion in advocating patient safety, clinical quality improvement and medical informatics as well as his inspiring dedication in shaping neonatal care, Associate Professor Gomez was awarded the 2017 National Outstanding Clinical Quality Champion Award.



## Adjunct Associate Professor Joseph Manuel Gomez

**Head and Senior Consultant** Neonatal Intensive Care Unit Department of Neonatology KK Women's and Children's Hospital

# **Director**Medical Informatics KK Women's and Children's Hospital

Chairman Medication Safety Committee KK Women's and Children's Hospital

Adjunct Associate Professor Duke-NUS Medical School

SingHealth

# **Co-Chairman**National Medication Safety Taskforce Ministry of Health







# HEALTH AND BIOMEDICAL SCIENCES INTERNATIONAL ADVISORY COUNCIL

MEETING 2017

On 30 and 31 October 2017, Singapore's Health and Biomedical Sciences International Advisory Council (HBMS IAC) held its annual meeting. Chaired by Sir Richard Sykes, the meeting centred around how HBMS Research, Innovation and Enterprise (RIE) investments support Singapore's national priorities, including strategies to implement Precision Medicine and Smart Health; value capture strategies for Medical Technology (MedTech); and the development of the R&D roadmaps for Singapore's priority areas to capture health and economic value.

The HBMS IAC commended the significant progress made by the various HBMS agencies over the past year. At the same time, the HBMS IAC emphasised that patience was needed, given the long gestation period for HBMS research to be translated to health and economic outcomes. In terms of sharpening its strategies, the HBMS IAC advised Singapore to undertake a deeper analysis of its unique strengths and capabilities and seek to play to them; and recognise its gaps and adopt a portfolio approach to funding HBMS research.

The HBMS IAC also called for a greater level of synergy between the national initiatives involving Ageing, Precision Medicine, Smart Health and MedTech, as all these initiatives require cross-domain capabilities and interdisciplinary expertise, thus entailing collaboration with the Advanced Manufacturing and Engineering (AME), Services and Digital Economy (SDE) and Urban Solutions and Sustainability (USS) domains.

In collaboration with our research partners, NMRC will build on our good progress in RIE2020 and continue to develop and implement mechanisms that facilitate the translation of research outputs into health outcomes, so as to advance human health and wellness and create economic value for Singapore and Singaporeans.







# OVERVIEW OF FUND COMMITMENT



45

**IN FY2017** 





\$157.95

#### NMRC Funded/Managed Grants

cs-irg \$27,2

cs-irg-nig \$3.5

MILLION

HSRG \$13.35

HSR-NIG \$0,36

**ст** \$8.54

#### **Open Fund Grants**

OF-LCG \$59.09
MILLION

OF-IRG \$35.24
MILLION

OF-YIRG \$10.67

2.10%
TALENT DEVELOPMENT

18.52% HUMAN CAPITAL

→ 47.64<sup>%</sup> RESEARCH GRANTS

31.74% KNOWLEDGE ENABLERS & INFRASTRUCTURE

HUMAN CAPITAL

\$61.40
MILLION

STAR \$15.5 2 Awardees MILLION

CSA \$34.5

18 Awardees MILLION

TA \$5.1

5 Awardees MILLION

ci/cssp \$6,3 65 Awardees MILLION

KNOWLEDGE ENABLERS & INFRASTRUCTURE

\$105.22

crc \$35
MILLION

**IMU** \$4.22 MILLION

NHIC \$25
MILLION

NLARF \$7
MILLION

SCRI \$34
MILLION

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#### NATIONAL MEDICAL RESEARCH COUNCIL

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