NMRC **National Medical Research Council**
Singapore

Innovation
for a Future of Excellence

ANNUAL REPORT FY2019/2020

CONTENTS

MESSAGE FROM
CHAIRMAN

OVERCOMING CHALLENGES AND SCALING NEW HEIGHTS

The COVID-19 pandemic has hit Singapore and many parts of the world hard. The battle is far from won and the pandemic is still raging around the world. While we continue to confront and overcome these challenges, the pandemic has since stimulated growth in our Research & Development (R&D) capabilities in biomedical sciences and infectious sciences, triggered innovation and accelerated technological trends.

The Singapore R&D journey started three decades ago and investment in biomedical research started in 2000. Today, we have built up a vibrant research and innovation ecosystem. Research has not only created new value for our economy, but also informed better policy. The launch of the Research, Innovation and Enterprise 2025 (RIE2025) is a significant milestone in Singapore's R&D landscape, as it is testament to Singapore's investments in RIE over the past years and signifies Singapore's continued investments for the next five years. I have had the privilege to be involved and observe the changes in the R&D scene, especially in terms of the growth of capabilities, talent and collaborations.

NMRC's portfolio has also grown over the years since its establishment in 1994 and even more rapidly in recent years with Singapore's increased investments in biomedical sciences. The intended outcome of NMRC's work has been raised to the next level especially since the RIE2020 funding tranche under the Health and Biomedical Sciences (HBMS) domain where greater emphasis has been placed on attaining the healthcare and economic outcomes.

NMRC is also uniquely positioned as a department under the Ministry of Health (MOH), and one of the main funding agencies receiving RIE funding to drive the RIE objectives under the biomedical sciences domain, termed the Human Health and Potential (HHP) under RIE2025.

In the past year, several national-level platforms have been set up to more effectively serve the needs of the research and clinical community in Singapore, and to bring together the key strengths across Singapore to create internationally competitive peaks in translational research efforts in various strategic areas. They are the Singapore Translational Cancer Consortium (STCC), Precision Health Research, Singapore (PRECISE) and Advanced Cell Therapy and Research Institute Singapore (ACTRIS). Together with existing initiatives, Singapore Clinical Research Institute (SCRI) and National Health Innovation Centre Singapore (NHIC), these have been housed as business units under the Consortium for Clinical Research and Innovation Singapore (CRIS) which collectively aim to contribute to research and clinical translation within the public healthcare family.

Achieving the results in translational clinical research, sustaining efforts and raising existing standards require a long-term commitment. NMRC will continue to dedicate its work to achieve successful outcomes, and towards transforming its health system to deliver better health and healthcare outcomes for Singaporeans.

Prof Ranga Krishnan
Chairman, NMRC
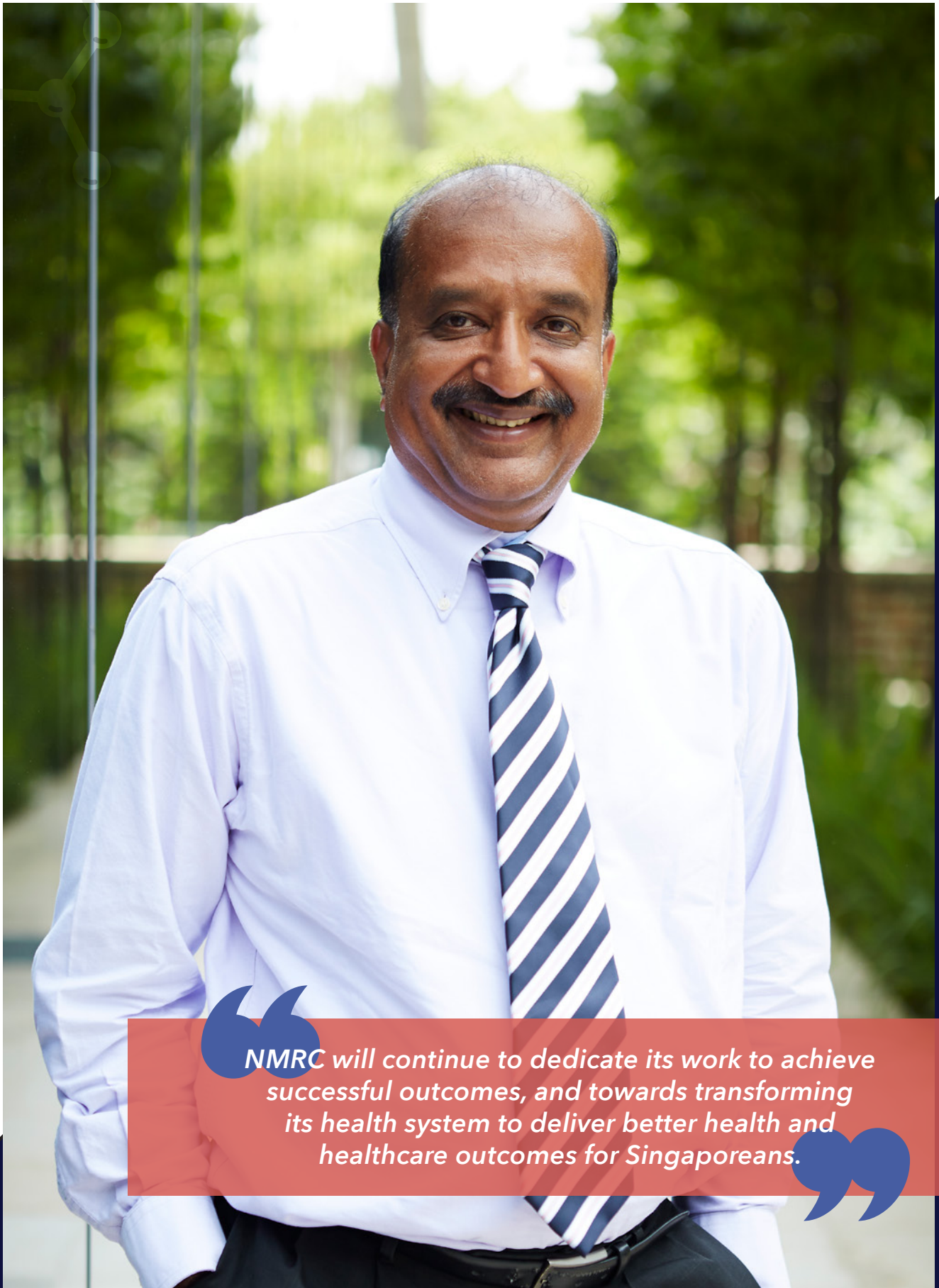
> *NMRC will continue to dedicate its work to achieve successful outcomes, and towards transforming its health system to deliver better health and healthcare outcomes for Singaporeans.*

> *We need to recognise that there will be a new normal that we must all adapt to, including the need...for research funding to be sustainable...*

MESSAGE FROM EXECUTIVE DIRECTOR

COPING WITH COVID-19 AND MOVING FORTH

The year 2020 will always be remembered for COVID-19 and the way in which it has impacted Singapore and the world. For NMRC, it was a year of extreme challenges, but also many opportunities.

As part of the MOH, the NMRC team stood alongside MOH colleagues and many Singaporeans to support the battle against COVID-19. Regular NMRC work had to be reprioritised and deferred as much as possible, with about half the NMRC team volunteering and being deployed to support different aspects of COVID-19 planning and operations.

With support from the National Research Foundation Singapore (NRF), NMRC introduced special grant schemes to support research in COVID-19. A total of three grant calls were developed and rolled out within time frames unprecedented in the history of NMRC. This involved setting up a special system of expedited reviews as well as direct engagements between research performers, policymakers and funders. A total of 49 proposals were supported (at the time of writing) with particular emphasis placed on proposals that could quickly be implemented to support the fight against COVID-19.

Although COVID-19 took priority, many aspects of regular NMRC work still had to continue. With so many members of the team deployed to support COVID-19 operations, those who remained had to shoulder all the regular work of NMRC. Research work in non-COVID-19 areas remained important and had to be supported, research talent had to be looked after and research infrastructure maintained. The year also saw the planning for RIE2025 go into full swing, with NMRC playing a key role particularly in developing the healthcare research aspects of the RIE2025 schemes. Several exciting changes were introduced as part of RIE2025, including placing greater emphasis on research in population health, having greater differentiation between types of clinician scientists, and tapping on the full potential of data science in supporting biomedical research.

The fight against COVID-19 is not over, but there is clear light at the end of the tunnel. Research worldwide has played a critical role in the fight against COVID-19. From developing and testing vaccines with unprecedented speed, to coming up with new diagnostic kits and innovations. The Singapore research community has been involved in many aspects of this work. As we transition into the post-COVID-19 world, NMRC and the research community must build upon the many advances and good practices that came about as part of COVID-19. We need to recognise that there will be a new normal that we must all adapt to, including the need, now more than ever, for research funding to be sustainable, particularly given the impact of COVID-19 on the global and Singapore economy. NMRC will continue to play its part, to refine and streamline our systems and processes, to ensure that we remain good stewards of the research funding entrusted to us while supporting the community to deliver impactful research.

I thank the NMRC team for their outstanding contributions and service in the past year. I also thank MOH colleagues and those in the wider healthcare family and the research community for all your support and collaborations. We look forward to working closely with you in the years ahead.

A/Prof Tan Say Beng
Executive Director, NMRC

ABOUT NMRC
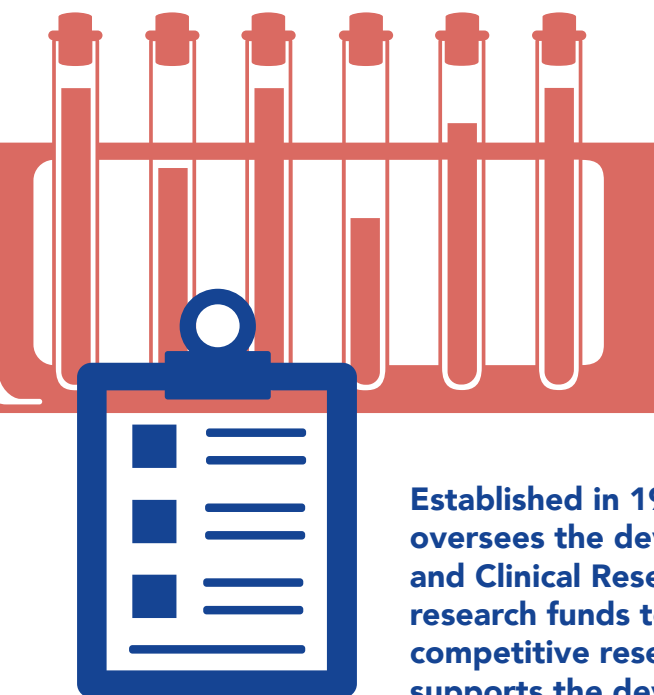
Established in 1994, the National Medical Research Council (NMRC) oversees the development and advancement of Translational and Clinical Research (TCR) in Singapore. It provides competitive research funds to publicly funded healthcare institutions, awards competitive research funds for programmes and 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 ever 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 sector performers, hospitals and government agencies. NMRC spearheaded these investments to realise long-term health and wealth outcomes.

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

in Singapore. NMRC also spearheads the MOH's vision for healthcare research to deliver better health and wealth outcomes for Singaporeans. NMRC will also complement the top-down directed strategic research by funding research proposals received by the various competitive grants and awards administered.

In the next funding tranche under RIE2025, the funding allocation has been increased to $25 billion with continued support for basic research, an expanded scope to better drive economic growth post-pandemic, address our national needs, and strengthen technology translation and enterprise innovation capabilities. The HBMS domain will be expanded into Human Health and Potential (HHP) where it builds on good progress in HBMS and additionally strategises efforts towards enabling Singaporeans to enjoy good health, and to realise their full potential. In alignment with the RIE2025 vision and changing health priorities, there will be key shifts to the MOH's strategic thrusts towards transforming and protecting health. NMRC continues to be one of the major funding agencies and departments under the MOH to support and realise the goals of the HHP and MOH's objectives through the administration of the various infrastructure and grant funding schemes.
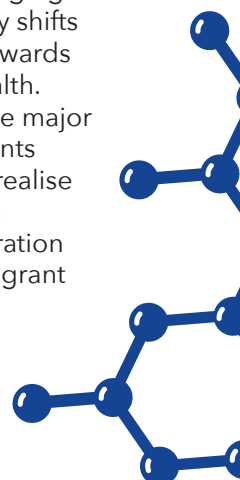
NMRC BOARD

The NMRC Board advises the Council on the formulation of strategies and priorities to promote excellence in translational and clinical research in Singapore, with the objective of improving human health. By overseeing the implementation of the research programmes approved by the 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. As of FY2020, the NMRC Board consists of 18 members.

Prof Ranga Krishnan
Chairman
National Medical Research Council

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

Prof Edward Holmes
Honorary Senior Fellow
Agency for Science Technology and Research

Prof Ivy Ng
Group Chief Executive Officer
SingHealth

A/Prof Kenneth Mak
Director of Medical Services
Ministry of Health

Prof Yeoh Khay Guan
Chief Executive
National University Health System

Mr Beh Kian Teik

Deputy Chief Executive Officer

National Research
Foundation Singapore

Prof James Best

Dean

Lee Kong Chian School of Medicine,
Nanyang Technological University

Mr Jean-Luc Butel

*Global Health Care
Advisor and President*

K8 Global

Prof Chong Yap Seng

Dean

Yong Loo Lin School of Medicine,
National University of Singapore

Prof Thomas Coffman

Dean

Duke-NUS Medical School

Prof John Lavis

*Canada Research Chair in
Evidence-Informed Health Systems*

McMaster Health Forum

Prof Leo Yee Sin

Executive Director

National Centre for Infectious Diseases

Prof Michael Merson

Wolfgang Joklik Professor

Global Health, Duke University

Prof Ng Huck Hui

Assistant Chief Executive

Biomedical Research Council, Agency
for Science Technology and Research

Prof Benjamin Seet

*Deputy Group Chief Executive
Officer (Education and Research)*

National Healthcare Group

Prof John Wong

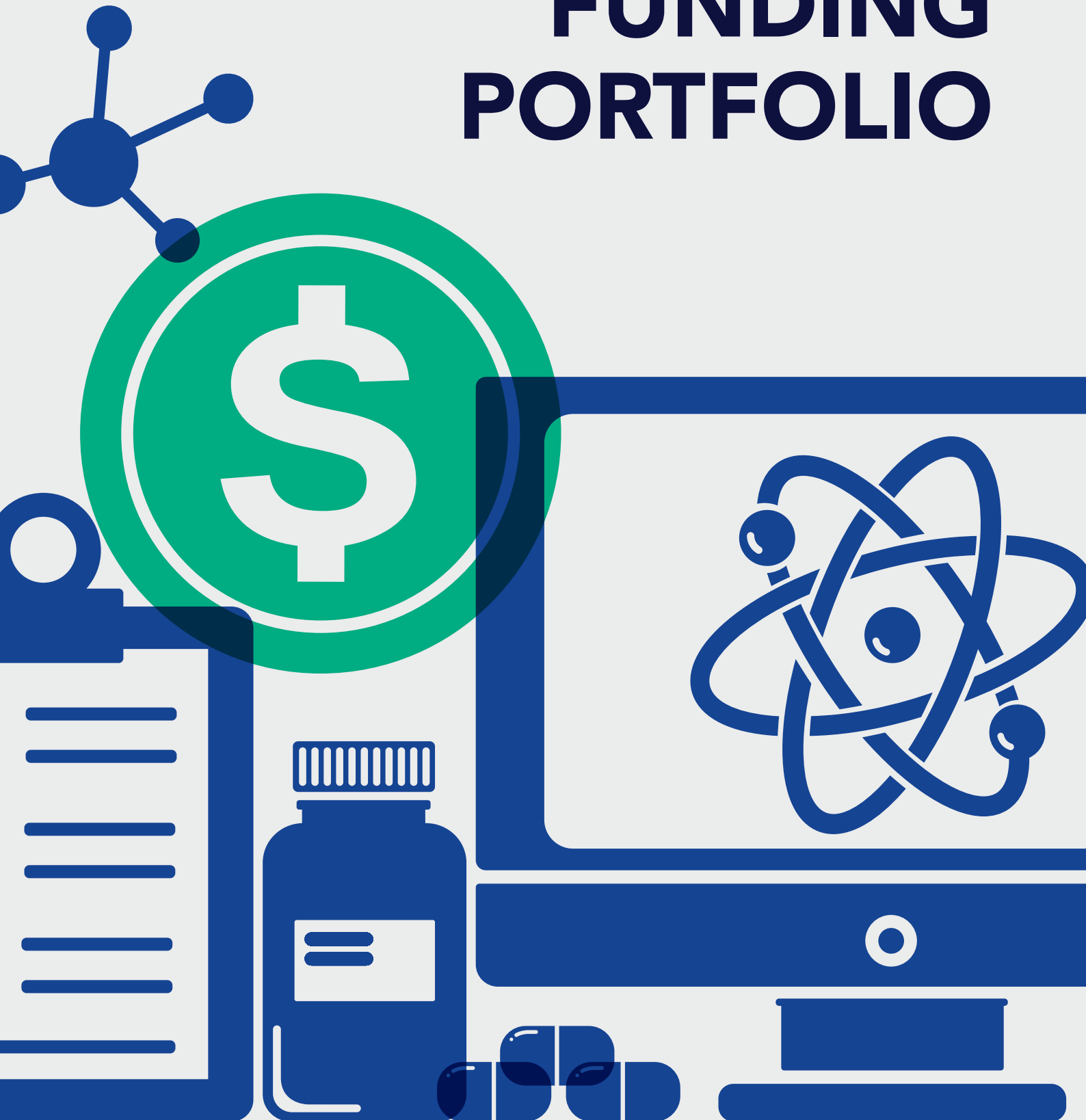*Senior Advisor*

National University Health System

Prof Wong Tien Yin

Medical Director

Singapore National Eye Centre

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 these three key areas:

Human Capital & Talent Development Programmes

▶ Singapore Translational Research (STaR) Investigator Award

▶ Clinician Scientist Award (CSA)

▶ Transition Award (TA)

▶ Clinician Innovator Development Award (CIDA)

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

▶ NMRC Research Training Fellowship

▶ MOH Healthcare Research Scholarship — Master of Clinical Investigation (MCI)

Knowledge Enablers & Infrastructure Initiatives

▶ Bioethics Advisory Council (BAC)

▶ Funding for Clinical Research Coordinators (CRCs)

▶ Health Sciences Authority Cell Therapy Facility (HSA CTF)

▶ Institutional Review Boards (IRBs)

▶ Investigational Medicine Units (IMUs)

▶ National Health Innovation Centre Singapore (NHIC)

▶ National Large Animal Research Facility (NLARF)

▶ Research Space Funding (RSF)

▶ Science, Health and Policy-relevant Ethics in Singapore (SHAPES)

▶ Singapore Clinical Research Institute (SCRI)

Research Grants

NMRC/MOH Grants

▶ 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

▶ Large Collaborative Grant (LCG)

▶ Individual Research Grant (IRG)

▶ Young Individual Research Grant (YIRG)
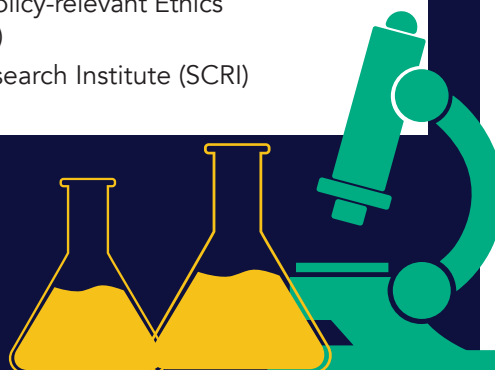
HUMAN CAPITAL & TALENT DEVELOPMENT

PROGRAMMES

NURTURING A VIBRANT COMMUNITY OF CLINICIAN SCIENTISTS

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 allows 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 Innovator Development Award (CIDA)
- 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)

HUMAN CAPITAL
AWARDS

Singapore Translational Research (STaR) Investigator Award

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

Clinician Scientist Award (CSA)

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

Transition Award (TA)

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

Clinician Innovator Development Award (CIDA)

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

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

The CS/CISSP supports clinical research by providing salary support for clinicians involved in research. In recognition of support received from clinical departments for their clinicians' time and participation in research, the funding award is channelled to respective departments, who in turn are allowed flexibility to use funds to support research activities.
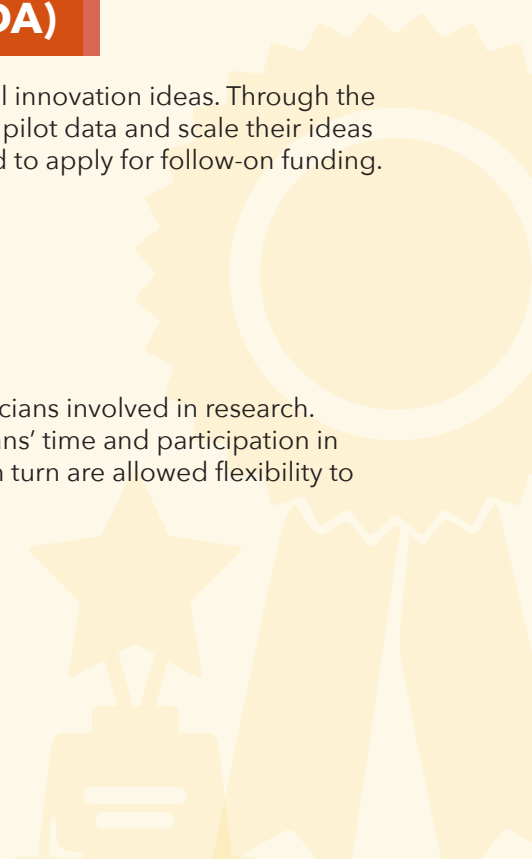
Singapore Translational Research Investigator Award Recipients

An Artificial Intelligence-Powered Approach to Precision Immunotherapy of Human Arthritis

Prof Salvatore Albani

Director
SingHealth Translational Immunology and Inflammation Centre, Singapore Health Services

Professor
Duke-NUS Medical School

Rheumatoid Arthritis (RA) is the epitome of common autoimmune diseases. With no cure for RA, effective transformational interventions are a priority due to the partial efficacy and high costs of available treatments today, on top of the chronic burden on patients and society. An incomplete understanding of the mechanisms governing immune tolerance contributes to a lack of therapeutic immune interventions capable of restoring immunological balance safely, effectively, clinically and financially. Hence, a safe and affordable therapeutic approach which relies on the true restoration of immunological balance via the induction of tolerance is yet to be fulfilled.

In previous work, we treated 96 RA patients for six months with clear safety, biological and clinical effects, and have generated mechanistic hypotheses and the tools to address them. This project aims to develop programmes of high translational value to achieve the following objectives:

(1) identify and dissect mechanisms of induction of immune tolerance in RA patients in response to immune therapy with dnaJP1, a microbiome-derived peptide from E.coli developed for immune tolerance;

(2) discern how RA perturbates the architecture of the healthy immunome, and distil mechanisms and cell subsets that are clinically and pathologically relevant;

(3) investigate if the increase in PD1 Treg is the pivot for clinically relevant immune tolerization; and

(4) explore if the interface between microbiome and immunity affects tolerization as dnaJP1 is a microbiome peptide.

This project integrates artificial intelligence in immune therapy of RA, with the potential to directly benefit patients via developing an effective, safe and financially viable cure.

Singapore Angle Closure Glaucoma Programme: From Genetics to Precision Medicine and Therapy

Glaucoma is the leading cause of irreversible blindness worldwide, with primary angle closure glaucoma (PACG) a major form of glaucoma in Singapore and Asia. For the past decade, our research programme has made substantial contributions to the understanding of the epidemiology, risk factors, genetics, imaging features, clinical phenotype and management of PACG. However, I have almost no data to inform clinical practice about which individuals are at greatest risk of developing advanced PACG and blindness. While we have made advances via genome-wide association studies and have identified common genetic variants that increase risk for PACG, there is a need to identify and evaluate more genetic factors for PACG via whole exome sequencing in order to uncover new genetic risk factors, pathways/mechanisms and thus potentially new treatments to prevent blindness.

We hope to integrate novel genetic and ocular biomarkers of PACG using a multimodal artificial intelligence approach in order to identify individuals with highest risk of advanced visual loss so as to develop and enhance personalised management strategies for PACG. We will then validate this new algorithm for the prediction of advanced PACG using prospectively ascertained clinic-based cohorts. Finally, with the identification of new genes with deleterious rare variants conferring large effect sizes from whole exome sequencing, we need to better understand the biological impact and physiological relevance of new gene(s) and their role in the PACG disease process. Such genetic findings have the potential to illuminate therapeutic targets.

This programme will capitalise on the multi-disciplinary team of clinician scientists and researchers with unique access to clinical data and DNA that we have collected over a decade from ongoing studies in Singapore. Furthermore, we have a network of international collaborators with access to global PACG data, and have demonstrated our ability to lead and utilise these datasets for important findings.

Prof Aung Tin

Executive Director
Singapore Eye Research Institute

Deputy Medical Director (Research)
Singapore National Eye Centre

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

Personalising Sleep Recommendations across the Lifespan Using Large-Scale Device Data

Prof Michael Chee Wei Liang

Director
Centre for Sleep and Cognition and Centre for Translational MR Imaging, Yong Loo Lin School of Medicine, National University of Singapore

Many Asians have poor sleep habits that impact health, well-being and productivity. This can be transformed by:

(1) developing and integrating smartphone and wearable-based technologies to unobtrusively obtain long-term measurements of sleep patterns and cognition;

(2) collecting data using the aforementioned platform to characterise sleep patterns across the lifespan, and from there uncover their associations with outcome variables relevant to cognition, mood, cardiometabolic health and ageing; and

(3) using the above knowledge to personalise age-specific sleep recommendations in a manner relevant to Asians.

Existing cohorts of adolescents, young adults and old adults will be assessed for sleep habits, physical activity and cognitive performance continuously for over at least two months using human smartphone interactions, ecological momentary assessment and consumer health wearables to yield population-level characterisation of sleep habits. Age-specific sleep duration recommendations for different outcome variables will be derived from a subset of participants having habitual >±1hr variation in sleep duration. This will require mapping the associations between sleep measures and cognitive performance, mood, motivation, physical activity and metabolic health using multiple multivariate regression and convolution neural network-based methods. The subset will also cross-validate device-generated measures of sleep and cognition against established methodologies like polysomnography and computer-based cognitive testing. The accuracy of model-predicted personalised optimal sleep duration will be tested using multi-night exposure to the predicted sleep duration and durations offset by ±1 hour. This will occur in a pseudo-laboratory setting incorporating extensive cognitive testing, polysomnography and continuous blood-glucose monitoring. Resting state metabolic rate (MR) in a subset will determine whether the temporal preponderance of connectivity states related to vigilance explains interindividual differences in response to different sleep durations.

The findings from this study will contribute to recommendations that could reduce the burden of non-communicable diseases related to lifestyles associated with shortened or ill-timed sleep.
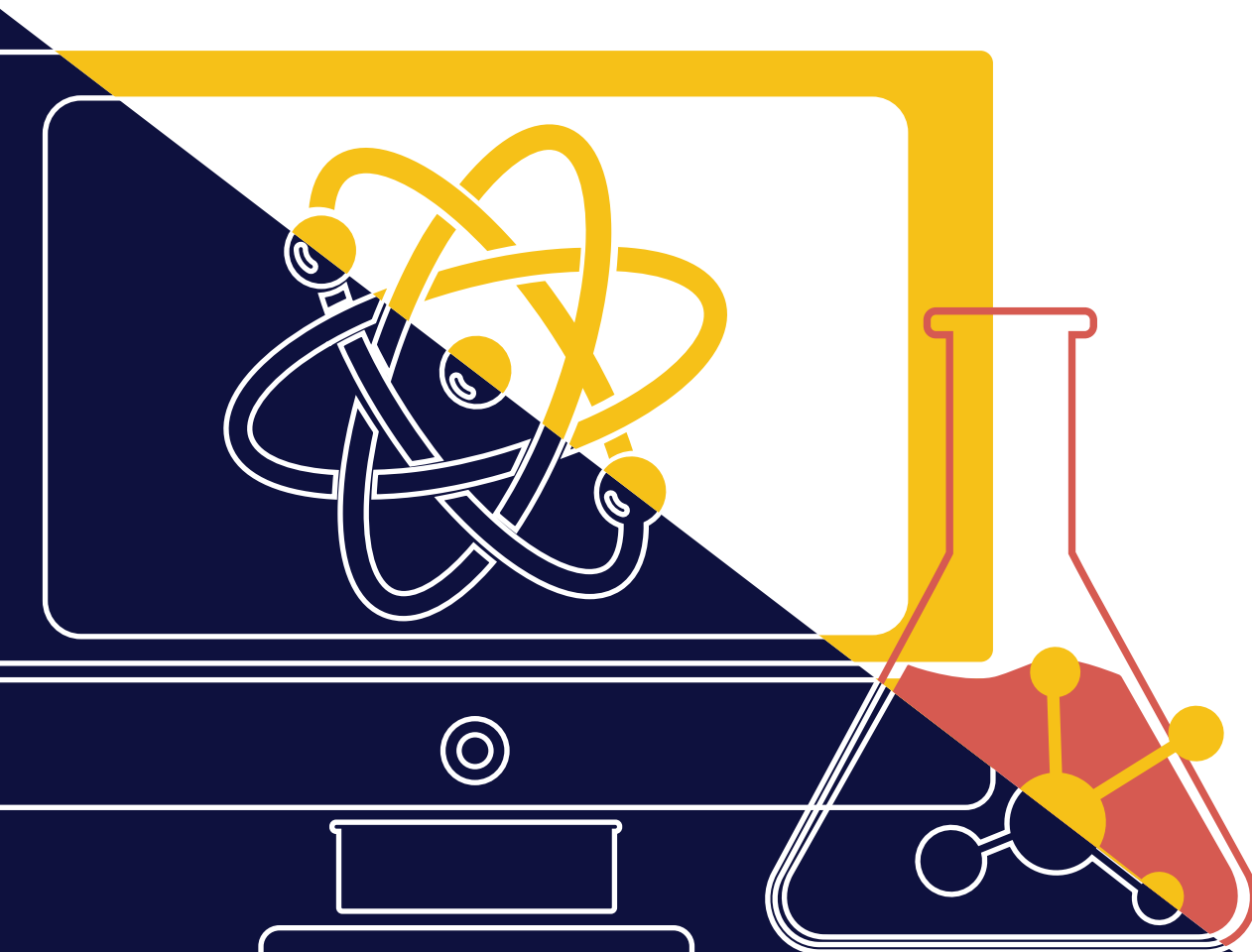
Clinician Scientist Award (Senior Investigator) Recipients

Management of Atypical Infections and Altered Immunity: Novel Diagnoses and Immune-Targeted Therapy

A/Prof Chai Yi Ann Louis

Senior Consultant
Division of Infectious Diseases, Department of Medicine, National University Hospital

Associate Professor
National University of Singapore

The central tenet in the practice of infectious disease has long been to target pathogens with antimicrobials. The 'host' and appropriateness of the host response to infection have only gained better appreciation today as the other vital arm in determining outcome.

We hypothesise that susceptibility and response to atypical infections, namely Mycobacteria and invasive fungal diseases, are determined by either immune dysregulation or latent host immune traits mediated genetically. Adjunctive therapy against identified immune targets in conjunction with conventional antimicrobials may further optimise outcomes.

In this project, we examine patients with severe/recurrent Mycobacteria infections and invasive fungal diseases (IFD) with the following aims:

(1) investigate the role of immune dysregulation predisposing patients with anti-cytokine auto-antibodies to such infections;

(2) elucidate novel or latent immune modulating genetic traits conferring susceptibility to atypical infections in our yet-to-be-characterised Asian population; and

(3) explore immunotherapeutic options targeting the identified immune defects, for treatment in conjunction with conventional antimicrobials.

In (1), we will perform immunophenotyping for patients with severe/recurrent Mycobacteria infections and IFD, and who are detected to have auto-antibodies. We will assess the functional immune response of these patients to various ligands and pathogens, and investigate the hypothesis if the underlying mechanism of this new condition may be attributed to:

(i) regulatory B cell dysfunction;

(ii) immune energy;

(iii) alternative autoantibodies through immunoprotein screening; or

(iv) immunogenetics.

For patients with no anti-cytokine autoantibodies in (2), we will look for occult immune genetic defects using state-of-art whole exome or genome sequencing coupled with functional immune assays probing candidate variants/pathways of interest and validation through cloning/transfection methodologies. In our last aim (3), we will explore the usage of immunotherapeutic agents in conjunction with conventional antimicrobials for treatment against the identified target immune dysfunction. We will also investigate the use of checkpoint inhibitors anti-PD1 and anti-CTLA4 as adjuncts in treating opportunistic invasive fungal infections.

Precision Oncology Approach to Identification and Expansion of Tumour-Targeting Cytotoxic T-lymphocytes in Head and Neck Squamous Cell Cancer

Given the limited efficacy of targeted therapy, there is tremendous interest in the role of immunotherapy in treating patients with head and neck squamous-cell carcinoma (HNSCC). Despite the presence of tumour-infiltrating T-cells (TILs), most tumours evade the immune system, suggesting that these are dysfunctional. Furthermore, drugs that inhibit immune-checkpoint receptors (ICB) which are intended to reverse this are only effective in less than 20% of patients.

Conventional therapy further depletes effective cytotoxic T-cell (CTL) populations, which is evident in trials where neo-adjuvant ICB therapy appears to be more effective than the adjuvant setting. Undoubtedly, there is a need to reconfigure treatment strategies such that ICBs are instituted when effective CTL populations are more prevalent.

Therefore, we hypothesise that untreated tumours contain the most effective source of CTLs capable of targeting more heterogeneous populations of cancer cells. We will utilise a number of unbiased and marker-based strategies to identify tumour-targeting T-cells in untreated primary/metastatic lymph nodes, and match tumour

recurrences using single-cell analysis and high-dimensional flow cytometry. Functional efficacy of specific subpopulations will be tested by expanding these in TIL-cultures, and tested in cytotoxicity assays against matched, patient-derived tumour culture. Markers for tumour-targeting CTLs will also be validated in independent cohorts of treatment-naïve and ICB-treated tumours.

Our secondary hypothesis posits that exhaustion status varies between patients (requiring individualisation) and within patients (primary versus metastatic versus recurrent tumours), hence requiring different strategies to reinvigorate CTL-based cytotoxicity. To address this, we will compare drivers of exhaustion across tumours to identify differences amenable to specific ICB therapy. Alternatively, we will set up medium-throughput screens to identify drugs that enhance CTL-based killing of matched tumour-cells to uncover actionable differences between T-cell reactivation in these states. The eventual aim is to identify the best source and CTL subpopulation with the ability to maximise tumour kill; either through immunomodulation with drugs or to effect cellular therapy with expanded, bio-banked CTL populations.

Prof Narayanan Gopalakrishna Iyer

Head and Senior Consultant
Division of Medical Sciences, National Cancer Centre Singapore

Head and Senior Consultant
Department of Head & Neck Surgery, Division of Surgery & Surgical Oncology, Singapore General Hospital and National Cancer Centre Singapore

Professor
Duke-NUS Medical School

Multi-Dimensional Frailty in Community-Dwelling Elderly – The Singapore Chinese Health Study

Prof Koh Woon Puay

(with effect from Feb 2021)

Professor
Healthy Longevity Translational Research Programme
Assistant Dean (Faculty Development)
Yong Loo Lin School of Medicine, National University of Singapore
Principal Investigator
Singapore Chinese Health Study

(before Feb 2021)

Director
Centre for Clinician-Scientist Development, Duke-NUS Medical School
Professor
Duke-NUS Medical School

Frailty is age-related decline and deterioration in physiological reserves, resulting in a state of limited capacity to maintain homeostasis. It also comes with increased vulnerability to stressors of daily living, and is an indicator of vulnerability to adverse health outcomes.

A multi-dimensional conceptual definition of frailty has been proposed, which describes frailty as a dynamic pre-disability state that includes physical frailty, psychological frailty (defined as decline in cognition, mood and motivation) and/or social frailty (defined as decline in social activities, relations and support). There is a pressing need for studies that investigate the different domains of frailty in a cohesive manner in a single population.

Therefore, the overall aim of this proposal is to take a broad, integrated and holistic approach in examining the independent and joint effects of frailty across the physical, psychological and social domains. Our first aim is to measure the co-existence of frailty across the three domains and to study the effect of this multi-dimensional frailty on the development of adverse ageing outcomes in community-dwelling elderly. Our second aim is to study the influence of midlife environment factors (including lifestyle and diet), genetic variants and midlife blood biomarkers on the development of multi-dimensional frailty at late-life.

This proposal is nested in 5,000 participants aged 65 to 100 years old from the Singapore Chinese Health Study, a well-characterised cohort with more than 20 years of follow-up and with well-established cohort databases, as well as archived biospecimens (blood and urine) collected more than 15 years ago. This proposal will advance knowledge about frailty in terms of phenotype diversity, etiologic heterogeneity and factors underpinning pathophysiologic pathways. Findings will also provide the scientific evidence and foundation for a multi-dimensional approach so that personalised and targeted interventions can be implemented for individualised care and management of frail elderly.

Studies on Low-Cost and Novel Therapies for Non-Alcoholic Steatohepatitis (NASH)

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of liver disease worldwide, occurring in approximately 40% of the adult population in Singapore. NAFLD frequently accompanies obesity and diabetes, and represents a disease spectrum that includes hepatosteatosis, steatohepatitis (NASH) and cirrhosis. While hepatosteatosis is thought to be relatively benign, NASH requires intervention in order to prevent its progression to cirrhosis. Currently, there is no available pharmacologic therapy to treat this condition.

Since my last CSA application five years ago, we have identified three very promising and low-cost potential treatments for NASH:

(1) thyroid hormone (TH) stimulates hepatic autophagy, b-oxidation of fatty acids, and mitochondrial turnover. Additionally, the intrahepatic concentration of T3, the active form of TH, was decreased in a rodent model of NASH. Our studies in diabetic patients with NAFLD showed that levothyroxine can decrease hepatosteatosis;

(2) short chain fatty acids (SCFAs) produced by gut microbiota can stimulate hepatic autophagy and oxidative phosphorylation, suggesting that they may be able to reduce hepatosteatosis and improve NASH; and

(3) vitamin B12/folate decreased serum homocysteine levels and hepatic inflammation and fibrosis.

We also observed hyperhomocysteinemia and hepatic protein homocysteinylation in a mouse model NASH. Accordingly, we hypothesise that TH, SCFAs, and Vitamin B12/folate can prevent and/or treat NASH. If so, what are the underlying molecular, cell signalling and metabolic mechanisms for their beneficial effects?

We will employ a dietary rodent model of NASH progression that we developed, as well as a primate model of obesity for these studies. Since NASH also involves macrophage and hepatic stellate cell activation that cause inflammation and fibrosis, we also will study the effects of these compounds in these cells during NASH. We anticipate that our studies will generate important new insights into the pathogenesis and treatment of NASH, and provide the foundation for future clinical studies.

Prof Paul M. Yen

Professor
Duke-NUS Medical School

Clinician Scientist Award (Investigator) Recipients

To Establish a Predictive Artificial Intelligence (AI)-Based Model Using Immune-Phenotype Correlation for Disease Stratification and Prognosis in Patients with Ocular Tuberculosis (OTB)

A/Prof Rupesh Agrawal

Senior Consultant
Department of Ophthalmology, Tan Tock Seng Hospital

Associate Professor
Lee Kong Chian School of Medicine

Ocular infections from Mycobacterium tuberculosis (Mtb) may masquerade as infective and non-infective entities with insidious and chronic clinical course. The clinical presentation of Ocular Tuberculosis (OTB) is heterogeneous, and Mtb is rarely found in ocular fluid samples. This renders the diagnosis of OTB challenging, complicating clinical decision-making and counselling about the management and prognostication of disease.

The treatment of OTB requires a combination of anti-tubercular therapy (ATT) and immunosuppression. However, the evaluation of treatment response is complex due to the paradoxical clinical response to ATT, as well as evolving trends in Mtb antibiotic resistance. Due to the lack of reliable randomised controlled trials, it remains uncertain whether current treatment methods are effective. Thus, there is a clinical need to develop well-defined evidence-based guidelines for the management of OTB.

Fundamentally, there are three hypotheses regarding the mechanism of TB-associated ocular inflammation. First, being an inflammatory response to intra-ocular Mtb infection; second, being an Mtb-driven autoimmune response; and lastly, a remote immune priming by Mtb in the periphery. Based on these, the diagnosis and treatment of OTB are aimed at the detection and elimination of latent Mtb infection using anti-inflammatory medications with adjunctive ATT.

Herewith, we aim to evaluate the immune cell signatures from biological samples in patients with established clinical phenotypes of OTB, derive clues that would point to the likely one of three possible pathways contributing to each phenotype and conclusively establish its pathologic mechanisms. The overall aim of this study will be to develop an OTB management algorithm using clinical, laboratory, imaging and immunotyping data, enabling early detection and prevention of TB-related vision loss. This study may lead to new paradigm shifts in the understanding and management of OTB.

The Role of Uteroplacental Inositol in Inhibiting Preterm Labour-Onset and Rupture of Membranes

Preterm birth (PTB) complicates 10% of livebirths, of which a third is associated with preterm pre-labour rupture of membranes (PPROM). PTB is the leading cause of perinatal mortality and morbidity, with many survivors displaying long-term sequelae. Majority of PTBs occur in women with no apparent risk factors, and there are at present no suitable PTB prevention measures for them. Recent small trials suggest that antenatal inositol supplementation may reduce PTB risk but the mechanism of effect is unknown.

This proposal seeks to establish the biological plausibility for this effect and enable targeting of treatment to specific subgroups of women. We hypothesise that the placenta is the primary focus of inositol action; a premature or accelerated decline in placental inositol content during gestation will increase the risk of PTB and PPROM through the promotion of eicosanoid production and pro-inflammatory activity within the uteroplacental environment, which induces uterine contractions and reduces the tensile strength of amnio-chorionic membranes.

This study will leverage on NiPPeR, the largest randomised controlled trial (RCT) of an inositol supplement, and the only one where placenta was collected. We aim to:

(1) associate placental inositol with eicosanoid and inflammatory factors, and assess impact of the NiPPeR intervention;

(2) determine the effects of inositol and inositol-treated-placental-conditioned-media on amnio-chorionic membrane tensile strength and myometrial contractility; and

(3) assess if longitudinal maternal plasma and urinary inositol measures represent biomarkers for improved PTB prediction, and if they can stratify women who may benefit from inositol prophylaxis.

This innovative study employs advanced technologies and data science, utilising unique biosamples from an intervention trial with extensive phenotypic data, thus providing an unprecedented opportunity to address how inositol can suppress PTB, and bring novelty to PTB prediction and prevention. The evidence gathered will provide critical scientific underpinning for the design of definitive inositol RCTs for PTB reduction with substantial impact worldwide.

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Th17 and Natural Killer Cells as Modulators of the Central Nervous System in Childhood Epilepsy

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Epilepsy is one of the commonest brain disorders. The current first-line treatment – anticonvulsants – aims to control seizures after epilepsy is established. But in one-third, the epilepsy persists. This refractory epilepsy requires complicated and expensive treatments. Ideally, treatment should target epileptogenesis, the underlying process that creates and perpetuates epilepsy and leads to refractory epilepsy. There is an urgent need to understand mechanisms in epileptogenesis in order to develop treatments to prevent the development of epilepsy and progression to refractory epilepsy.

Inflammation plays a key role in epilepsy. Our pilot work shows increased T-helper 17 (Th17) and CX3CR1+Natural Killer (NK) cell-mediated pro-inflammatory processes in refractory epilepsy. Th17 and CX3CR1+NK modulation of immune dysfunction in epilepsy is a coherent target for further research.

This project has three aims:

(1) to determine Th17 and CX3CR1+NK-mediated immune dysregulation between established refractory and non-refractory epilepsy;

(2) to investigate CX3CR1+NK-mediated immune dysregulation in the peripheral immune system and central nervous system in refractory epilepsy; and

(3) to explore Th17 and CX3CR1+NK-mediated immune dysregulation in the development of epilepsy and progression to refractory epilepsy.

We hypothesise that in (1), refractory epilepsy patients have upregulation of Th17 and downregulation of CX3CR1+NK cells in the peripheral immune system, compared to non-refractory epilepsy. In (2), our hypothesis is that Th17 upregulation and CX3CR1+NK downregulation is present in both the peripheral immune system and central nervous system in refractory childhood epilepsy. Lastly in (3), we hypothesise that in first afebrile seizure or newly diagnosed epilepsy, Th17 and CX3CR1+NK dysregulation is associated with disease progression.

The exploratory aim of this project is to explore the roles of the microbiome and genetic factors in non-refractory and refractory childhood epilepsy. Our innovative approach will provide a deeper understanding of the immune system's role in epilepsy to identify therapeutic targets to dampen and prevent induction of the innate response and the adaptive immune response, in order to develop clinical treatments to reduce the evolution to epilepsy, reduce clinical seizure severity and prevent development of refractory epilepsy.

Optimising Surgical Management and Patient-Related Outcomes of Epiretinal Membrane: Predictive Analytics and Randomised Trial

Epiretinal membrane (ERM) is a common age-related eye disease that can cause significant visual impairment with an adverse impact on quality of life.

Clinical management of ERM is currently hampered by two major challenges. First, it is difficult for clinicians to predict prognostic outcomes for ERM patients being managed conservatively or considered for surgical intervention. A major unmet medical need is therefore to develop a new method to improve prognostic assessment for patients with ERM. Second, surgeons are often faced with a dilemma when they manage patients with concomitant ERM and cataract, because it is unclear which surgical approach is the most appropriate for these patients. Combined cataract and ERM surgery is a popular choice, but this approach may result in unnecessary surgery being performed for ERM that may not contribute significantly to visual impairment.

Emerging evidence suggests that cataract surgery alone, which is a cheaper and potentially safer option with faster visual rehabilitation, may achieve similar visual outcome as compared to combined surgical approach for many of these patients. Thus, another major unmet medical need is quality evidence to determine the best surgical approach for patients with concomitant ERM and cataract.

In this project, we will conduct a large, multi-ethnic, prospective clinical cohort study of 1,000 patients with ERM. Based on comprehensive clinical and multimodal retinal imaging data, we will develop, with the use of predictive analytics and machine learning, an algorithm that provides accurate risk prediction for clinically meaningful prognostic outcomes. In addition, we will conduct a pilot randomised controlled trial to evaluate a new surgical approach that may achieve a similar visual outcome while reducing the number of unnecessary ERM surgeries for patients with concomitant ERM and cataract. Taken together, we anticipate our study to generate impactful data that will greatly optimise the surgical management and patient-related outcomes of ERM.

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Reinvigorating Cytolytic Tissue Resident Memory T Cells (cTRM T cells) for Treating Recurrent/Relapsed Nasopharyngeal Cancer

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Epstein Barr Virus (EBV)-driven nasopharyngeal cancer (NPC) is highly endemic in Southern China and Southeast Asia, including Singapore. Up to 80 new cases per 100,000 persons are reported annually in these regions. Despite a relatively good clinical outcome (five-year overall survival of 75–80%), a significant number (~20%) of NPCs develops loco-regional failure or distant relapse following definitive treatment. Therefore, newer and more effective treatment options are needed to manage NPCs with recurrences/relapses.

Our preliminary study showed that when tumour-infiltrating lymphocytic (TIL) T cells were primed with a pool of EBV peptides, they increased tumour specificity and incrementally killed EBV-positive NPC cells by nearly three-fold. We have further identified a specific clone of cytolytic CD8+CD69+CD103+ T cells, termed cytolytic tissue resident memory T cells (cTRM T cells), in approximately 50–60% of our expanded TIL T cell populations. Based on these findings, we hypothesise that our expanded EBV-primed cTRM T cells are novel, cellular therapy candidates that can be used either alone or in combination with other immunotherapies, such as the programmed cell death protein (PD1) monoclonal antibody, to increase treatment efficacy in recurrent/relapsed NPC cases.

We will test our hypothesis with the following specific aims:

(1) compare the cytotoxicity levels and functional immune activity of EBV-primed cTRM T cells versus EBV-primed peripheral blood mononuclear cell (PBMC)-derived cytolytic T cells (CTLs) against NPC in vitro;

(2) compare the treatment effect between EBV-primed cTRM T cells and EBV-primed CTLs against NPC in vivo using patient-derived xenograft (PDX) models; and

(3) determine if combination of EBV-primed cTRM T cells with the PD1 monoclonal antibody enhances the anti-NPC efficacy using humanised NPC PDX models.

Results from this study will establish the fundamental role for cTRM T cells and their potential therapeutic utility to treat NPCs with recurrences/relapses.

Modulating Endoplasmic Reticulum Stress as a Prophylactic Approach against Symptomatic Viral Infection

Zoonotic pathogens continue to emerge to threaten human health at an even quicker pace since the turn of this century but development of vaccines and drugs lags behind these outbreaks. Therefore, it is imperative that we advance our understanding of the molecular basis of host-viral interaction that defines clinical outcomes to gain insights into how such epidemics can be effectively managed.

Using the live-attenuated yellow fever 17D vaccine to induce a mild acute viral illness, we have shown in two separate studies that baseline adaptive endoplasmic reticulum (ER) stress and compensatory reduced tricarboxylic acid (TCA) cycle activity increased susceptibility to symptomatic infection: Infection in such individuals triggered maladaptive ER stress response with the production of reactive oxygen species (ROS). ROS in turn triggered downstream innate immune and pro-inflammatory responses that correlated with symptomatic infection. Metformin, a widely used anti-diabetic drug has recently been shown to act on multiple pathways in the cell, in addition to its anti-glycaemia function. One of its functions is ER stress modulation. Our preliminary data also showed that metformin reduced the expression of key intermediates in the ER stress-induced apoptotic pathway, suggesting its potential to reduce maladaptive ER stress and subsequent cell death.

The goal of this proposal is to show proof of concept that modulating ER stress alone with metformin can reduce the rate of symptomatic viral infection. We will employ a placebo-controlled experimental medicine approach to test the utility and efficacy of metformin as an ER stress modulator to reduce the likelihood of symptomatic YF17D infection, complemented with comprehensive omics-level analyses to define how metformin modulates the host response to YF17D infection and thus alter symptomatic outcomes. If successful, this study would clarify a poorly understood but clinically important aspect of host-viral interaction and show a therapeutic pathway to minimise the impact of emerging viral epidemics.

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Precision Medicine in Systemic Sclerosis Gastrointestinal Disease: Evaluating Imaging and Stool Biomarkers for Differentiating Disease Stages and Treatment Responses

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Systemic sclerosis (SSc) has one of the highest mortalities among autoimmune diseases (66% 10-year survival), with SSc-associated gastrointestinal disease (SSc-GI) being the second highest cause. Intestinal failure leading to malabsorption necessitates costly long-term parenteral nutrition. Although it is one of the earliest manifestations of disease, SSc-GI is often diagnosed late after fibrosis has occurred. Unmet needs in SSc-GI management are non-invasive biomarkers for:

(i)   early diagnosis;

(ii) differentiation of SSc-GI stages; and

(iii) treatment response.

We hypothesise that SSc-GI fibrosis is preceded by an early inflammatory stage that represents a window of opportunity for immunosuppressive treatment.

This project aims to determine if imaging biomarkers differentiate patients with early SSc from those with late SSc and evaluate imaging biomarker changes over a six- and 12-month treatment period with mycophenolate mofetil (MMF) in patients with early SSc. In both cases, stool markers will be used as secondary biomarkers supporting inflammation.

The exploratory aim of the project is to map imaging and stool biomarkers over one year in untreated patients with early SSc. We will use combined 18F-Fluorodeoxyglucose-positron emission tomography and magnetic resonance imaging T1-MOLLI mapping as a novel tool to distinguish inflammation from fibrosis as the predominant pathological process in the bowel wall. Stool biomarkers indicative of an inflammatory state will be derived using metagenomic analysis of the microbiota, metabolomics and faecal-calprotectin.

In a cross-sectional study of the first aim outlined above, we will compare biomarkers between patients with early [pre-scleroderma stage of "Very early diagnosis of SSc" or ≤3 years onset; (n=40)] and late SSc (>5 years onset; n=20). In symptomatic early SSc patients (n=25), we will determine change in biomarkers after six and 12 months of MMF as delineated in the second aim of the project. This project will greatly advance the field of SSc by enhancing evaluation of SSc-GI, using non-invasive biomarkers that enable the stratification of SSc-GI disease stages and treatment responses.

Understanding, Influencing and Empowering the Spouses of Colorectal Cancer Patients

This study has three aims:

(1) to determine the quality of life (QoL) of colorectal cancer (CRC) patients and their spouses in the first year from curative surgery and to ascertain the differences between the patients and their spouses;

(2) to explore if tailored interventions would overcome previously identified barriers to improve CRC screening rates of the spouses via a randomised controlled trial (RCT); and

(3) to find out if spouses of CRC patients are willing to be advocates for CRC screening to their loved ones.

We hypothesise that the QoL of spouses is also impaired and will recover to pre-operative level within 12 months from the index operation, tailored interventions will improve screening rates amongst the spouses of CRC patients, spouses can be mobilised as advocates for CRC amongst their loved ones, and that those who are currently undergoing screening are more likely to be successful advocates for screening.

We will recruit patients with CRC who are scheduled for elective surgery and their spouses to participate in the study. Validated QoL instruments will be applied to the couple during the first year of the cancer journey. At the same time, an RCT comparing a targeted intervention programme in which issues related to a lack of education and inconvenience are addressed, against the current standard of care. The primary outcome will be the number of spouses who underwent Faecal Immunochemical Test (FIT). Lastly, we will explore if these spouses could be empowered to become advocates for CRC screening amongst their family and friends with the necessary resources.

This study will seek to understand the impact of CRC on patients' spouses, and determine if tailored interventions could get these spouses to undergo screening. It also explores if empowering the spouses of patients with CRC could mobilise them as advocates for CRC screening in the community.
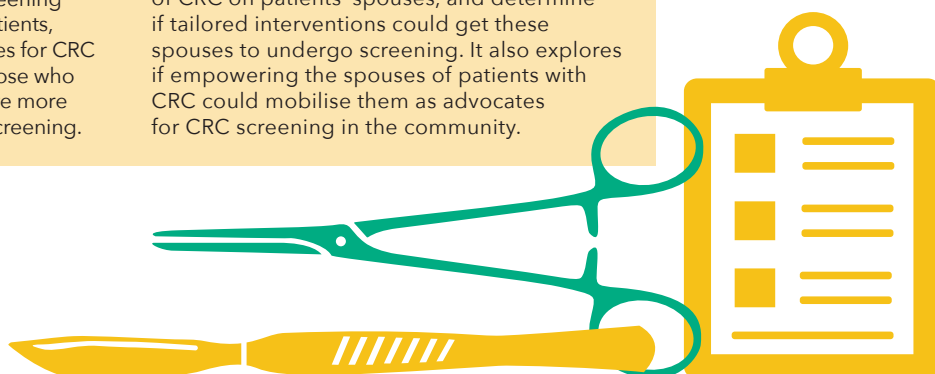
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Deciphering the Tumour Microenvironment of Primary TKI-Resistant EGFR-Mutant NSCLC

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Extending the observations on genomic determinants of primary resistance to EGFR TKI, this proposal aims to further characterise immune microenvironment of both naive and TKI-resistant EGFR-mutant NSCLC specifically to facilitate the design of rational combinations of immune modulators. Emerging clinical data suggest a need for angiogenic approaches in combination with platinum-based chemotherapy and checkpoint blockade.

Our preliminary RNA-Seq data of EGFR TKI-resistant samples suggests subsets of "inflamed" EGFR M+ tumours that are associated with shorter time to progression on TKI. In silico dissection of immune subsets further delineates myeloid-derived suppressor cells (MDSCs) to a predominant cell population.

In this proposal, we aim to apply state-of-the-art immuno-monitoring (cyTOF or symphony flow cytometry) on primary resistant tumours, and extend the transcriptomic and genomic datasets through designing a clinical protocol to systemically interrogate biospecimens of EGFR-mutant NSCLC undergoing immunotherapy and combinations thereof. There are ongoing discussions with industry partners (Pfizer, AstraZeneca and MSD) to design a proof-of-concept phase I/Ib trial specifically to address this major unmet need for lung cancer in Asia.
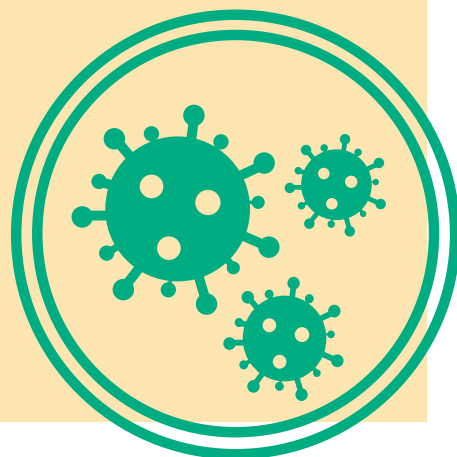
Transforming Patient Care through Development of Non-Invasive, In-Vivo Bedside Skin Imaging Tools for Diagnosis, Classification and Delineation of Skin Cancer

Currently, diagnosis of skin cancer is done through skin biopsy, which involves an invasive surgical procedure, a waiting time of two weeks and results in unsightly scars. When diagnosed, current treatment involves complete surgical excision with wide margins to ensure clearance. Wide excision usually requires extensive surgery which inevitably results in poor cosmetic effects.

Therefore, the aim of this translational research proposal is to transform patient care through the development of novel non-invasive, in-vivo skin imaging tools that can be used in clinics to instantly and automatically diagnose and stratify Non-Melanoma Skin Cancers (NMSC); doing away with the need for traditional biopsies, while improving surgical management by precisely mapping the tumour before surgery to allow for individualised surgery.

This will be achieved with the following specific aims:

(1) automated detection, diagnosis and stratification of NMSC through artificial intelligence. We will develop image analysis algorithms to automatically detect, diagnose and stratify NMSC lesions in acquired in-vivo confocal images;

(2) developing in-vivo 3D imaging of NMSC. Currently, we have good preliminary results on in-vivo 3D mapping of pigmented Basal Cell Carcinoma (BCC) through photo-acoustics imaging (PAI) systems. In this specific aim, we will further develop our PAI system by addressing shortcomings identified in our preliminary studies through an iterative clinical-pathological-imaging correlation process to achieve a sensitivity and specificity of 95%; and

(3) validation of systems developed in Specific Aims (1) and (2). We will validate the automated detection, stratification and diagnosis algorithm as well as the 3D mapping system for BCC through a prospective clinical study.

We are confident that with an integrated team approach of clinicians, biophotonics and imaging experts from Singapore Bioimaging Consortium (SBIC) and image processing expertise from Nanyang Technological University (NTU) and Technical University of Munich (TUM), we will be able to automate diagnosis of NMSC and map out that skin cancer in-vivo.

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Transition Award Recipients

The Immunostimulatory Effects of Gentamicin: Translating Aminoglycoside Antibiotics into Antiviral Therapeutics for Pandemic Response

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Viral epidemics continually threaten global health. In the last five years alone, we have witnessed outbreaks of Ebola, Zika and yellow fever viruses. These infections universally have no effective treatments, and development of new therapeutics cannot keep pace with the emergence of such outbreaks.

A potential solution is thus to exploit licenced drugs that exhibit potentially useful off-target antiviral properties. Such drugs could be used as a first-line pharmacological response during viral outbreaks. One such class of drugs are aminoglycoside antibiotics. Aminoglycosides are antibacterial drugs with well-established safety and pharmacokinetic profiles. In mouse models of mucosal infection, topical aminoglycosides exerted antiviral effects against respiratory and genital tract infections by stimulating toll-like receptors to induce interferon-simulated gene (ISG) expression: ISGs effect antiviral responses in cells.

In this proposed study, my goal is to show proof of concept that parenterally administered gentamicin, an aminoglycoside, can generate a systemic-level antiviral state. Such an approach has the added advantage of preventing secondary Gram-negative bacterial sepsis that often complicates the clinical outcome of viral infections. Critically, parenteral aminoglycosides do not enter the gastrointestinal tract to disrupt the gut microbiome and hence pose minimal risk for antibiotic resistant bacterial selection.

The specific aims of my study are thus to:

(1) define ex vivo the effects of gentamicin on the innate immune transcriptional response in different subsets of peripheral blood mononuclear cells;

(2) define the optimal dose of intramuscular (IM) gentamicin required to elicit an innate immune transcriptional response in whole blood of healthy adults; and

(3) determine the efficacy of prophylactic intramuscular gentamicin in reducing live attenuated yellow fever virus (YF17D) infection in a placebo-controlled trial.

If successful, this study would not only demonstrate the impact of gentamicin on systemic-level antiviral response, it would also pave the way to translate a pharmacological approach as an emergency response to viral outbreaks.

Protein Supplementation in Critically Ill Children: A Pilot Randomised Controlled Trial

Protein malnutrition is prevalent among critically ill children and associated with poor clinical outcomes. Current guidelines for provision of protein in daily management of critically ill children in paediatric intensive care units (PICUs) are based on limited and not high-quality evidence. The current protein supplementation approach, a "one-size-fits-all" nutrition prescription, may not be appropriate for every critically ill child. Given the heterogeneity of the patients admitted to the PICU, a targeted approach based on individuals' needs represents a potential advancement in PICU care.

Our central hypothesis is that protein supplementation in PICU care leads to improved clinical outcomes in subgroups of patients only. We propose a dual-centre pilot randomised controlled trial in Singapore with two major aims:

(1) to obtain key information for planning and conducting a large-scale multicentre study in Asia; and

(2) to evaluate the benefit of protein supplementation to critically ill children with body mass index (BMI) z-scores on PICU ≤ -2.

The main clinical outcome of interest is total number of days of hospital stay (from PICU admission to hospital discharge). Two protein supplementation regimes (≥ 1.5g/kg/day versus standard care) will be randomly allocated to PICU patients with BMI z-scores ≤ -2. We will determine the effect of protein supplementation on total length of hospital stay and other clinical outcomes, and assess the impact of protein supplementation on acquired functional impairment of PICU survivors six months after hospital discharge. In addition, we will explore whether muscle ultrasound is a biomarker for protein balance in paediatric critical illness. Upon completion of this study, we will have strong preliminary data to plan, refine our study approach and execute a future large multicentre study across Asia. These data will ultimately guide protein provision and nutritional management of patients in PICU setting.

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Understanding and Targeting the Interleukin-1 Receptor-Associated Kinase 1 (IRAK1) Pathway in Solid Tumours

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Patients with refractory solid tumours have poor prognosis and often lack effective treatment options. The interleukin-1 receptor-associated kinases (IRAKs) mediate toll-like receptor (TLR) and interleukin-1 receptor (IL-1R) signalling, influencing downstream processes including inflammation and apoptosis. Our previous studies have indicated that chromosome 1q21.3 copy number amplification is observed in patients with recurrent and advanced stage solid tumours and can be detected from cell-free DNA (cfDNA) using blood samples. Using breast cancer as a study model, we have shown that chromosome 1q21.3 copy number amplification leads to over-expression of IRAK1, causing increased tumour growth. Inhibition of IRAK1 through knockdown and use of a IRAK1 inhibitor pacritinib decreased tumour growth.

We propose a clinical study using pacritinib to treat patients with refractory solid tumours harbouring chromosome 1q21.3 copy number amplification. We have included several translational components to investigate potential biomarkers for identification and monitoring of response, and also to study how pacritinib affects immune modulation.

We hypothesise that IRAK1 is effective in disease control in patients with refractory solid tumours harbouring 1q21.3 amplification. Plasma cfDNA monitoring of 1q21.3 may be a potential biomarker for patient selection and response. Treatment with IRAK1 causes immune modulation that affect the tumour microenvironment and interact with tumorigenesis.

We will adopt a two-phase study with single agent pacritinib conducted in patients with solid refractory tumours harbouring 1q21.3 amplification. Patients will be treated with oral pacritinib twice daily and observed for therapeutic efficacy in terms of improvement in progression-free survival (primary endpoint) and response rate (secondary endpoint). Serial blood sampling will be carried out to identify and monitor changes in both 1q21.3 copy numbers and immune markers, and correlated to treatment outcome. Paired biopsies will be carried out for further interrogation of changes in tumour microenvironment, and findings will be investigated in pre-clinical models.

Development and Validation of a Myopia-Specific Item Bank Administered Using Computerised Adaptive Testing: The MyoCAT Study

Myopia imposes a massive public health burden, with almost 85% of young adults having this disease. People with myopia not only suffer from impaired vision, but also experience side effects from corrective therapies and are at increased risk of developing sight-threatening complications such as pathologic myopia (PM). Therefore, understanding the impact of un- or under-corrected myopia, PM and the effectiveness of myopia corrective therapies from the patient's perspective is becoming increasingly important, with many governing authorities mandating the use of patient-reported outcomes data to guide and improve clinical management, support medical decision-making, and inform policy decisions in healthcare measures and resource allocation.

While several questionnaires exist to measure myopia-related quality of life (QoL), there are serious psychometric shortcomings with these instruments due to issues related to conceptualisation, generalisability, validity and responsiveness. Moreover, current myopia-specific questionnaires are paper-pencil-based, and are therefore static, inflexible and burdensome to administer and answer. Evidently, a culturally valid instrument that allows a rapid, accurate and comprehensive assessment of the impact of myopia and its associated complications and corrective therapies from the patient's perspective in Asia is urgently required.

Fortunately, these problems can be overcome by using item banking (IB) and computerised adaptive testing (CAT). An IB is a large pool of questions calibrated for difficulty based on participant response and the use of modern psychometric techniques. IBs are operationalised by CAT, which is 'smart' technology that adapts the items asked based on participants' responses to previous items, enabling a precise and reliable assessment while minimising measurement error and reducing test length.

The main objective of this project is to develop, validate and evaluate the clinical applicability of a novel IB and CAT system for myopia (MyoCAT) that is able to comprehensively assess the QoL impact of un/under-correction, PM and the different corrective therapies in a multi-ethnic Singaporean population.

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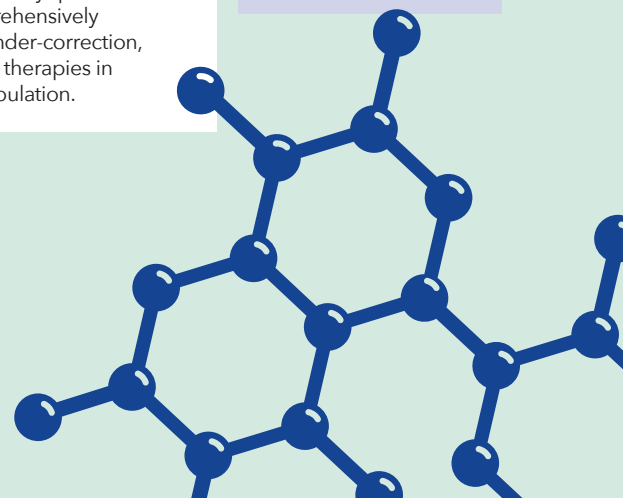
Using Novel Imaging Biomarkers to Predict Vascular Endothelial Growth Factor Inhibitor Retreatment Load for Neovascular Age-Related Macular Degeneration

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Current treatment for neovascular age-related macular degeneration (nAMD) requires frequent injections of vascular endothelial growth factor (VEGF) inhibitors. Retreatment strategies are dependent on disease activity assessed at every visit which is defined as a combination of clinical signs and fluid detected in the different compartments of the retina by optical coherence tomography (OCT). This strategy results in large variability of retreatment (4–12 injections per year) and it is currently unknown which patients may have higher or lower retreatment requirements.

This study aims to use disease features on OCT in the early treatment phase (baseline to month 3) to predict which patients require low or high retreatment. A "severity score" will be derived by the associations of OCT features detected at baseline and changes of these features at month 3 (assessed by trained graders and with a novel machine learning (ML) algorithm) with patients with optimal outcomes that have either required high retreatment (≥ 6 treatments/year) or low retreatment (<6 treatments/year) over 12 and 36 months. This will be a retrospective analysis using data from a comprehensive AMD registry. This score will be validated using a prospective cohort study with patients divided into high and low retreatment groups based on the severity score and treated with standard of care. The primary outcome will be to compare the number of injections required over one year between groups.

Early stratification of patients can help to identify those that may require closer monitoring and may potentially benefit the most from a switch in drugs. A comprehensive dataset from the validation study can be used to further inform retreatment interval at each visit allowing for even more individualised treatment. Overall, these results may change current clinical practice by providing more precision in retreatment decisions, individualising management for each patient from visit to visit.

Novel Palliative Care Model for Advanced Cancer Patients: A Randomised Controlled Trial Study

Cancer is the leading cause of death in Singapore, accounting for 30% of deaths in 2017. Advanced cancer patients have a poor quality of life (QoL) and high utilisation of acute healthcare services. When provided alongside standard oncology care, early access to palliative care improves the QoL of patients with advanced cancers and their caregivers, and reduces acute healthcare utilisation and costs by these patients. Yet, in Singapore and elsewhere around the world, palliative care is delivered only to a minority of advanced cancer patients shortly before death, with a median time of only 30 days between the first consult to death.

We propose to conduct a randomised controlled trial of the 'Supportive and Palliative care Review Kit in Locations Everywhere' (SPARKLE) intervention, an outpatient-based model of early palliative care. The SPARKLE intervention comprises regular symptom monitoring using questionnaires, early identification and prompts treatment of problems identified. Proactive screening for problems facilitates earlier palliative care interventions for advanced cancer patients, whenever the need arises.

The SPARKLE intervention extends palliative care to a larger number of advanced cancer patients and delivers palliative care before terminal phase of life, whenever patients have physical, psychological or social needs. We hypothesise that the SPARKLE care model results in:

(1) improved QoL of both advanced cancer patients and their caregivers; and

(2) reduced acute healthcare utilisation and costs by these patients.

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Profiling of Circulating Exosomes in Ischemic Stroke for a Nanoplasmonic Stroke Diagnostic Device

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This project specifically aims to identify suitable exosome-based markers of ischemic stroke to lead to a platform for rapid diagnosis of ischemic stroke. Its secondary aims are to develop serum markers predictive of clot characteristics that will impact the endovascular thrombectomy technique (i.e. fibrin versus red blood cell (RBC) rich clots, and to profile serum markers to determine the underlying etiology of ischemic stroke, which will have impact on long-term treatment decisions.

We hypothesise that exosome surface markers and its contents (miRNA and proteins) contain markers which are specific for ischemic stroke. This can be used in a novel technology – the amplified plasmonic exosome (APEX) technology, to create a blood-based platform for the rapid diagnosis of acute ischemic stroke.

This project will include acute stroke patients who are amenable for thrombectomy. The clot extracted, blood drawn from around the clot (peri-clot) and blood from a peripheral vein which is typically discarded, will be stored for analysis. This will allow us to isolate exosomes and subsequently determine specific markers which are raised in increasing concentration in the peripheral blood, peri-clot blood and blood clot. Using the APEX technology created by the team, we will leverage in situ enzymatic conversion of localised optical deposits and double-layered plasmonic nanostructures to enable sensitive, multiplexed population analysis. We will be able to detect exosome-bound markers directly from blood with superior sensitivity (approximately 200 exosomes) to profile and identify specific diagnostic and prognostic markers for ischemic stroke and its underlying cause.

With a lack of non-radiological stroke biomarkers, this study will be able to discover a blood-based marker for ischemic stroke diagnosis. It will also help to pre-determine the clot characteristics, which is important for acute treatment decisions. In addition, it will identify the source of the blood clot causing the stroke, having major implications for long-term pharmacological treatment.

Investigating the Effect of Adiposity on Skin Barrier Function in a General Population Cohort

Obesity is a major public health problem, and known to be associated with a range of chronic diseases including chronic inflammatory skin diseases such as atopic dermatitis (AD).

We hypothesise that adiposity promotes skin epidermal barrier dysfunction through activation of inflammatory cytokine pathways, leading to loss of anti-microbial peptides and barrier lipids in the stratum corneum, and that these molecular processes are linked to the development of abnormal skin microbial colonisation and worsening of AD. However, our understanding of the relationships between adiposity and skin barrier dysfunction has significant limitations. While adiposity is associated with cytokine disturbances in blood, whether adiposity directly influences inflammation in skin is not known. Furthermore, no study has evaluated the microbial disturbances in obese individuals, or whether this is linked to underlying disturbances in the molecular and physiological profile of the skin.

Therefore, we aim to address these knowledge gaps by carrying out experiments among study participants in an ongoing general population cohort to address specific aims. We will determine whether skin concentrations of selected inflammatory cytokines, anti-microbial peptides and lipid metabolites relevant to epidermal biology and skin barrier dysfunction are different between lean and obese participants. We will also characterise the skin microbiome profile of study participants and investigate how microbial composition relates to disturbances of inflammatory cytokines, anti-microbial peptides, and metabolic variation in skin, observed in obese individuals.

In addition, we will quantify serum proteomic profile of study participants and determine whether systemic inflammatory signatures relate to cytokine and microbial composition of the skin, and to skin barrier function in lean and obese individuals. Finally, we will assess the potential causal relationship between obesity, and the identified molecular, microbial and functional disturbances in skin biology, through quantification of these biomarkers in obese participants before and after weight loss.

Dr Yew Yik Weng

Consultant
Department of Dermatology, National Skin Centre

Assistant Professor
Lee Kong Chian School of Medicine
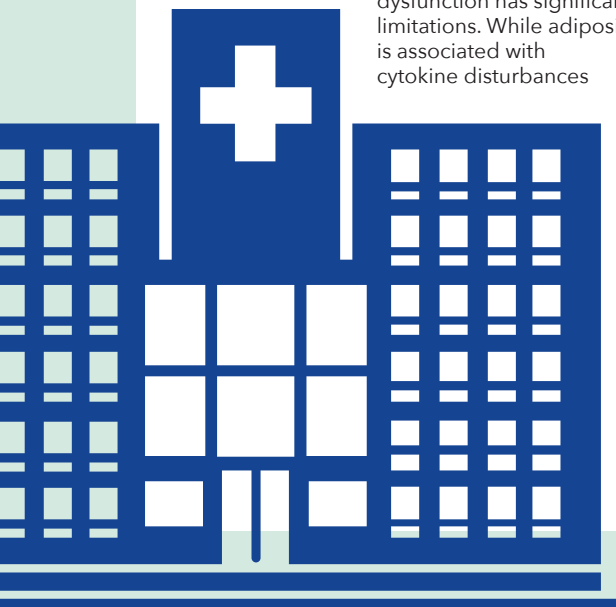
Clinician Innovator Development Award Recipients

Algorithm for Diagnosis of Peripheral Blood Films via Deep Learning and Computer Vision

Dr Fan Bingwen Eugene

Consultant
Department of Haematology, Tan Tock Seng Hospital

Visiting Consultant
Department of Laboratory Medicine, Khoo Teck Puat Hospital

This proposed research is an investigation into using an artificial intelligence-powered software to automate both peripheral blood film blood cell identification and the interpretation and diagnosis of blood films in the laboratory setting. Peripheral blood films are currently reviewed physically by laboratory technologists and haematologists using light microscopy, and films with unusual and/or abnormal characteristics, or unclear diagnosis are further escalated to a senior haematologist. The software will facilitate standard screening and reporting of peripheral blood film duties by a laboratory technologist or haematologist and reduce the total bench time required per staff.

This collaboration will involve laboratories from the National Healthcare Group, software programming from a startup, Gallenco, and industry support/integration with Sysmex Corporation. This project has the potential to improve peripheral blood film reporting workflows globally and is likely to have a high commercial value if it passes clinical/bench-top testing and regulatory review.
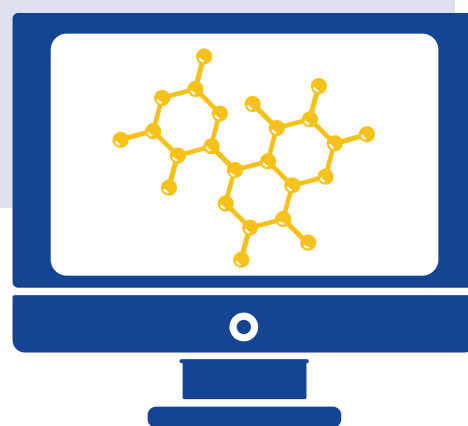
Safety of the Ingestible Magnetically Inflated Balloon Capsule (IMI-BC) for the Treatment of Obesity

One of the non-invasive treatments for obesity is the intragastric balloons (IGBs). The IGBs occupy a part of the stomach, making the patient feel fuller faster and limit what they can eat. However, current IGBs require invasive procedures for insertion/removal.

The aim of this study is to demonstrate the safety of a novel self-inflating capsule that we developed which can be ingested orally and inflated with a handheld magnet in animal and human trials. The capsule's location will be tracked using an external sensor. We hypothesise that the capsule can be safely ingested and excreted without complications.

In the animal study, five live pigs will swallow the capsule and an external sensor will track the capsule's position until it is excreted. In the human trial, five healthy volunteers will swallow the capsule in an outpatient clinic. After capsule activation, diet will resume. An external sensor will perform daily tracking of the capsule's position in an outpatient clinic, until it is excreted.

Our capsule is superior to other IGBs. Its compact size allows for easy ingestibility, with no invasive procedures required for insertion/inflation. This provides a convenient, cheaper and comfortable treatment option for patients.

Dr Kaan Hung Leng

Associate Consultant
Department of General Surgery, National University Hospital
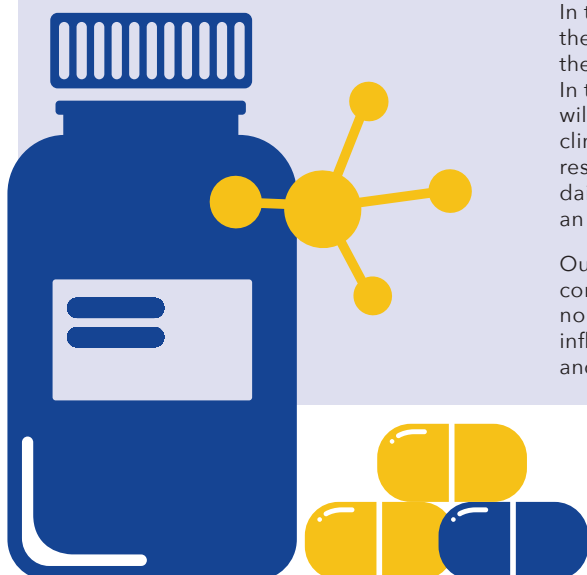
WeeCare – Bringing Personalised Care to Patients with Lower Urinary Tract Symptoms (LUTS) into Community

Dr Ng Tze Kiat

Senior Consultant
Department of Urology, Singapore General Hospital

The Urology Department at Singapore General Hospital sees 25,000 patients with lower urinary tract symptoms (LUTS) annually, representing around 50% of the clinic visits. This number is set to grow with an ageing population.

The clinical evaluation of patients with LUTS and, in particular, males with benign prostate enlargement (BPE) involves history taking, clinical examination and investigations including uroflometry (measuring peak urine flow rate, among other parameters), both at the time of initial diagnosis and subsequent follow-up visits.

LUTS form the bulk of referrals from primary care physicians to tertiary urology centres.

Due to a lack of affordable and available equipment (i.e. clinic setting uroflometry machines), these referrals are usually made with reference to patients' subjective complaints of voiding and storage symptoms, without any objective clinical parameters.

We aim to develop a portable device which can empower the primary care physician in assessing and monitoring patients with BPE, a chronic condition prevalent in the ageing population of Singapore. The primary care physician will then be able to use this device with ease to follow up on patients with BPE on their subsequent visits.
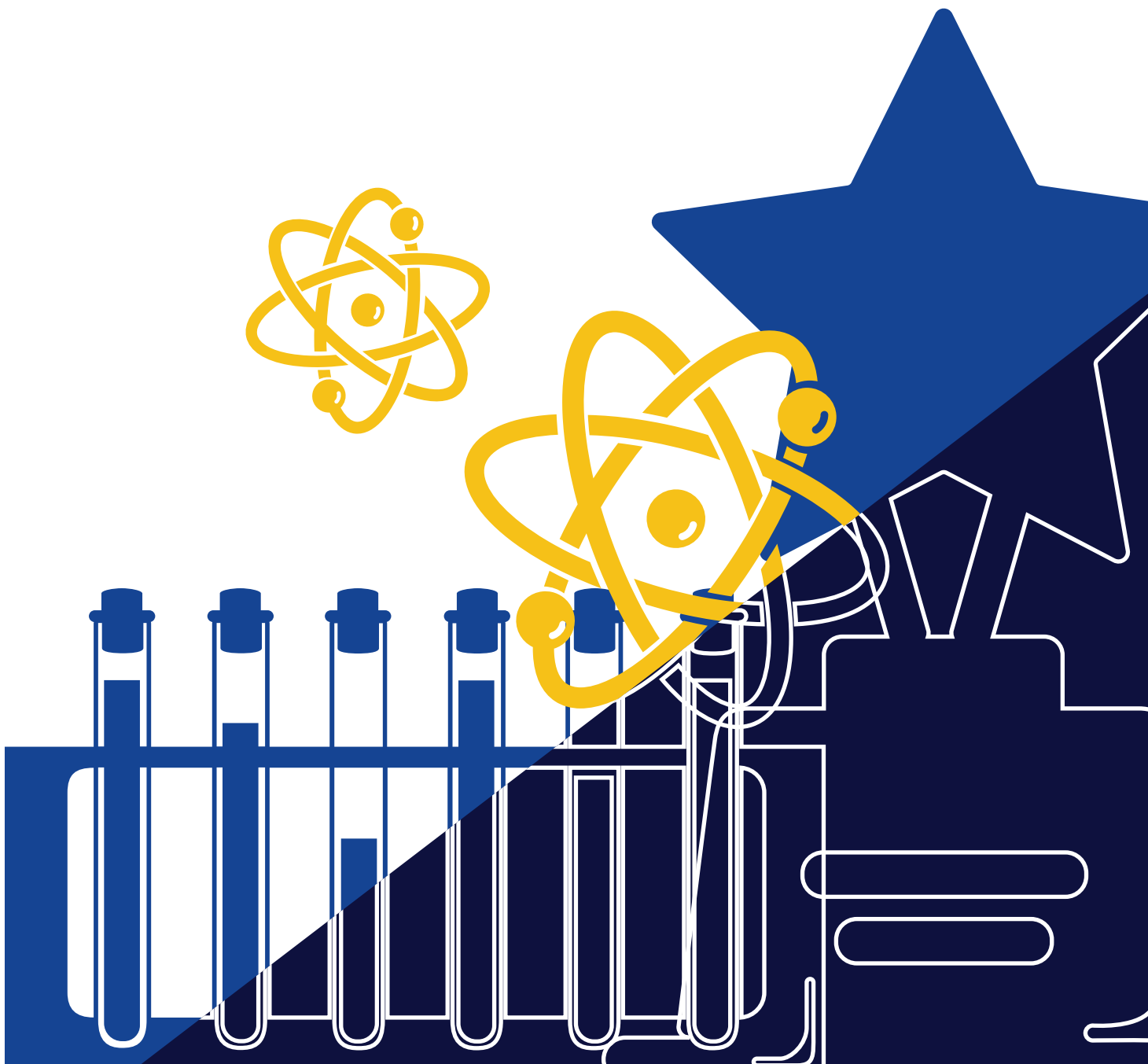
TALENT DEVELOPMENT PROGRAMMES

NMRC Research Training Fellowship

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

Practicing medical doctors, dental surgeons, health science professionals and biostatisticians are all eligible to apply.

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

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

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

National Outstanding Clinician Scientist (CS) Resident Award

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

TALENT DEVELOPMENT AWARD RECIPIENTS

NMRC RESEARCH TRAINING FELLOWSHIP

23 recipients were awarded the NMRC Research Training Fellowship.

Name	Institution and Type of Training	Project
Dr Chan Kok Hong Dedrick	**NUH** *Full-time overseas PhD*	Identification and Characterisation of Dedifferentiating Colorectal Cancer Transcriptomic Targets Using Single Cell RNAseq
Dr Soon Yu Yang	**NUH** *Full-time overseas PhD*	Non-Adherence to Cancer Treatments and the Survival Gains Observed in Pivotal Phase 3 Trials and Expected in Routine Practice
Dr Chong Jun Hua	**NHCS** *Full-time local PhD*	Improving Acute Myocardial Infarction Outcomes by Reducing Myocardial Infarct Size and Preventing Adverse Cardiac Remodelling through the Use of Pharmacological and Telemedicine Strategies
Dr Lo Zhiwen	**TTSH** *Full-time local PhD*	Evaluating and Decreasing the Socio-Economical Burden of Wound Care in Singapore through Health Systems Innovations and Health Literacy

Name	Institution and Type of Training	Project
Dr Michaela Seng Su-fern	**KKH** *Full-time local PhD*	Developing the Application of T Regulatory Cells and CD62L-Depleted T Cells in Adoptive Cell Therapy
Dr Amanda Chee Yun Chan	**NUH** *Part-time local PhD*	The Search for Pathophysiology of Small Fiber Neuropathy, with a Focus on Immunological and Genetic Mechanisms and Interactions
Dr Goh Lay Hoon	**NUH** *Part-time local PhD*	Role of Primary Care Networks in Diabetes Care Delivery in Singapore
Dr Hairil Rizal Bin Abdullah	**SGH** *Part-time local PhD*	Utilising Machine Learning and Natural Language Processing Methods on Real-World Electronic Medical Record Data for Automated Surgical Complications Prediction and Detection
Dr Kaan Hung Leng	**NUH** *Part-time local PhD*	Optimising the Robotic Endoscope for Clinical Application
Dr Ko Kwan Ki	**SGH** *Part-time local PhD*	Surveillance of Hospital Environmental Microbiome for Healthcare-Associated Infection (HAI) Outbreaks
Dr Koong Ying Leng Agnes	**SHP** *Part-time local PhD*	Integrated Community Care Team to Better Meet the Needs of Complex Patients in Primary Care
Dr Lee Hsien Ren Shawn	**NUH** *Full-time overseas attachment and part-time local PhD*	Immunosequencing and Deep Profiling of T Cells in Children with Acute Lymphoblastic Leukemia (IMPACT)
Dr Low Kiat Mun, Serena	**AdMC** *Part-time local PhD*	Understanding the Paradigm of Elderly and Middle-Age Onset of Diabetes
Dr Bryce Tan	**NUS** *Part-time local PhD*	Lysosomal Calcium Channels in Neurodegeneration and Cancer Therapeutics
Dr Tan Cheng Sim Anna	**SERI** *Part-time local PhD*	Digital Technology Solutions to Improve the Vision-Specific Quality of Life and Social Engagement in the Visually Impaired Older Population – A Pilot Study
Dr Tan Hong Chang	**SGH** *Part-time local PhD*	Obesity-Related Glycine Deficiency: Investigating a Longstanding Metabolic Paradox Using Bench and Bedside Approaches
Ms Janhavi Ajit Vaingankar	**IMH** *Part-time local PhD*	Youth Positive Mental Health: Getting the Full Picture
Dr Yang Peiling	**NUH** *Part-time local PhD*	Overcoming Resistance to Radioactive Iodine (RAI) Therapy in RAI-Refractory Advanced Thyroid Carcinoma
Dr Jiang Lei	**SGH** *Full-time overseas Master's*	Spinal Cord-Computer Interfaces (SCCI): Restoring Volitional Motor Activity in a Murine Spinal Cord Injury Model
Dr Hamid Rahmatullah Bin Abd Razak	**SKH** *Full-time overseas attachment*	Evaluating the Effects of Autologous Protein Solution Using a Mechanical Model of Primary Osteoarthritis in Rats
Dr Huang Qingyao Daniel	**NUH** *Full-time overseas attachment*	A Novel RNA-Based Approach to NAFLD Hepatocellular Carcinoma Oncogenesis
Dr Mark Dhinesh Muthiah	**NUH** *Full-time overseas attachment*	Defining the Gene-Environment Interactions between the Normal PNPLA3 or I148M Variant and Diet in Producing Liver and Adipose Tissue Pathology in DIAMOND Mice Humanised with PNPLA3
Dr Natalie Ngoi Yan Li	**NUH** *Full-time overseas attachment*	PARP Inhibitors Modulate Immune Responses Independent of BRCAness in Ovarian Cancer Therapy

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

42 recipients were awarded the MOH Healthcare Research Scholarship – MCI.

Name	Institution and Department	Project
Dr Chan Hui Jia Gloria	**NUHS** *Department Haematology-Oncology*	Ex-Vivo Sensitivity Testing Using QPOP to Identify Drug Combinations Efficacy against Colorectal Cancer
Dr Chen Kaina	**CGH** *Department of Gastroenterology*	Study of Clinical Profiles of Non-Obese NAFLD Patients in Local Population and Identify Risk Factors for Non-Obese NAFLD
Dr Cho Jiacai	**NUHS** *Department of Medicine*	Safety and Efficacy of Tapering of Immunosuppression after Achieving Lupus Low Disease Activity State: A Randomised Controlled Trial
Dr Fan Lijia	**NUHS** *Department of Paediatrics*	Impact of Whey Protein on Stool Microbiome in Critically Ill Children – A Dual-Centre Randomised Control Study
Dr Feng Jiajun	**SGH (MOHH)** *Department of Plastic, Reconstructive & Aesthetic Surgery*	Surviving Burns: Xonnexin 43 Downregulation Prevents Burn Progression
Dr Goh Chun Peng	**NTFGH** *Department of Neurosurgery*	Rapid Diagnosis and Monitoring of Catheter-Related Urinary Tract Infection via a Novel Technique
Dr Huang Zijuan	**NHCS** *Department of Cardiology*	Prediction of Obstructive Coronary Disease Seen on Non-Invasive Testing Enabling a New Algorithm for Optimal Test Selection
Dr Koh Shimin Jasmine	**NNI (TTSH)** *Department of Neurology*	Investigating Biomarkers for a New Prognostication Algorithm towards Prevention of Acute Cardiovascular Autonomic Neuropathy in T2DM
Dr Koh Siyue Mariko	**SGH** *Department of Respiratory and Critical Care Medicine*	Comparing Benralizumab Treatment Initiated during Severe Asthma Attack to Placebo: A Randomised, Double Blind Placebo Controlled Trial
Dr Lim Yinghao	**NUHCS** *Department of Cardiology*	Evaluating the Utility of a Piezoelectric Smart Sensor in Interpretation of Heart Sounds
Dr Lim Yuan Ling Amanda	**NUHS** *Department of Medicine*	The Effect of Early Versus Mid-Day Feeding Window in 16:8 Time-Restricted Feeding on Metabolic Parameters in Overweight T2DM Patients
Dr Loh Wann Jia	**CGH** *Department of Endocrinology*	Establishing the Prognostic Value of Lipoprotein(a) Levels and Its Genetic Variants in Patients with Atherosclerotic Cardiovascular Diseases
Ms Azizah Binte Mohamed Afif	**SGH** *Department of Diagnostic Radiology*	Using Two-Dimensional Shear-Wave Elastography as a Predictive Diagnostic Tool for Assessing Allograft Fibrosis in Renal Transplant Recipients Correlating to Biopsy
Mr Neoh Eng Chuan	**TTSH** *Department of Physiotherapy*	Community-Based Rehabilitation Model after Total Knee Replacement: A Pilot Study
Dr Nishal Kishinchand Primalani	**NUHS** *Department of Neurosurgery*	Intraoperative Neurophysiologic Monitoring as a Potential Predictor for Neurological Outcome in Metastatic Spine Tumour Surgery
Dr Sia Ching Hui	**NUHCS** *Department of Cardiology*	Association of Left Ventricular Thrombosis with Increased Risk of Cognitive Decline
Dr Sim Hui Wen	**NUHCS** *Department of Cardiology*	"Internet-of-Things" Smart-Film to Improve Adherence to Apixaban in Atrial Fibrillation
Dr Tan Kah Hwee Jarrod	**NUHS** *Department of Surgery*	Use of Rectus Sheath Block for Laparoscopic Cholecystectomy to Improve Post-Operative Outcomes
Dr Tan Yee Jueen Vanessa	**SGH** *Department of Otolaryngology*	Prestin as an Early Biomarker to Predict Hearing Loss in Nasopharyngeal Cancer Patients Undergoing Chemoradiation
Dr Tan Yong Qiang Benjamin	**NUHS** *Department of Medicine*	CLOT – Biological Analyses and Composition
Dr Tay Rong Jie Matthew	**TTSH** *Department of Rehabilitation Medicine*	Muscle Ultrasound as a Predictor of Functional Status in Spinal Cord Injury Patients
Dr Wong Yu Jun	**CGH** *Department of Gastroenterology*	Rifaximin as Primary Prophylaxis for Spontaneous Bacterial Peritonitis in Decompensated Chronic Liver Disease with Small Bowel Bacterial Overgrowth: A Randomised Trial
Dr Yip Cherng Hann Benjamin	**NTFGH** *Department of Gastroenterology & Hepatology*	Video Game Use and Endoscopy Proficiency amongst Gastroenterology Trainees

Name	Institution and Department	Project
Dr Chan Gek Cher	**NUHS** *Department of Medicine*	Study on the Role of Galectin-3 in Diabetic Nephropathy
Dr Chan Wan Ying	**NCCS** *Department of Oncologic Imaging*	Diagnostic Performance of Contrast Enhanced Spectral Mammography (CESM) and in Combination with 2D Full-Field Digital Mammography (FFDM) and 3D Tomosynthesis Mammography in Recalls from Breast Cancer Screening
Dr Chia Yew Woon	**TTSH** *Cardiac Intensive Care Unit*	Cerebral Oximetry Monitoring in Post-Cardiac Arrest Management
Dr Choo Rou-En Joan	**NUHS** *Department of Haematology-Oncology*	Study of Effects of Combination of Selinexor and Nivolumab and Ipilimumab on Tumour Activity
Dr Kok Yee Onn	**SGH** *Department of Plastic, Reconstructive & Aesthetic Surgery*	Piscesderm as an Alternative to Biobrane for Healing of Superficial Partial Thickness Burns
Dr Law Jia Hao	**NUHS** *Department of Surgery*	Incidence of POGAS and Its Related Complications of Esophagitis and Barrett's Esophagus in Asian Population
Dr Law Yi Xi Terence	**NUHS** *Department of Neurology*	Risk Factors for Postoperative Urinary Retention after Laparoscopic Inguinal Hernia
Dr Lee Xinwei Matilda	**NUHS** *Department of Haematology-Oncology*	Study of Talazoparib and Selinexor on Clinical Efficacy in Triple Negative Breast Cancer (TNBC)
Dr Li Weiling Lydia	**CGH** *Department of Anaesthesia and Surgical Intensive Care*	A Prospective Randomised Controlled Trial of Analgesic Efficacy of Erector Spinae Plane Block versus Tumescent Anaesthesia in Radical Mastectomy
Dr Liow Ming Han Lincoln	**SGH** *Department of Orthopaedic Surgery*	Cost-Effectiveness of Robot-Assisted Total Knee Arthroplasty: A Markov Decision Analysis
Dr Ng Zhi Min	**KKH** *Department of Paediatrics, Neurology Service*	Effectiveness of the Mollii Suit in Improving Personalised Therapeutic Goals and Function in Children with Cerebral Palsy
Dr Tan Siang Joo Eugene	**NUHCS** *Department of Cardiology*	Effects of Routine Exercise Treadmill Stress Test (TMX) Post-CRT Implantation on Improving CRT-Response and Outcomes
Dr Tan Xiang Xuan Eunice	**NUHS** *Division of Gastroenterology & Hepatology, Department of Medicine*	Effects of Intermittent Fasting on NASH Regression and Changes in Gut Dysbiosis
Dr Tan Yu Guang	**SGH** *Department of Urology*	Evaluation of the Prevalence of Genetic Mutation in mPCa Patients
Dr Tan Zehao	**SGH** *Department of Vascular and Interventional Radiology*	Pre- and Post-Procedure IA-CT Perfusion for More Accurate Assessment of Tumour Perfusion for TACE and TARE
Dr Tay Hui Boon	**SKH** *Department of General Medicine*	Cross-Sectional Study of Patients Referred to Renal Clinic on Their Understanding of CKD
Dr Tay Yu-Kwang Donovan	**SKH** *Department of General Medicine*	Characterising the Non-Classical Effects of Primary Hyperparathyroidism on Body Composition, Bone Quality and Physical Function in Relation to Irisin and PTH
Dr Xu Xinni	**NUHS** *Department of Otolaryngology*	The Relationship between Olfactory Function and Neurocognitive Decline in the Elderly – A Community-Based Prospective Cohort Study
Dr Zhuang Qingyuan	**NCCS** *Department of Supportive and Palliative Care*	Study on Palliative Home Care to Reduce Healthcare Utilisation

NATIONAL OUTSTANDING CLINICIAN SCIENTIST (CS) RESIDENT AWARD

There are two recipients for the National Outstanding CS Resident Award.

Name	Cluster and Clinical Specialty
Dr Ho Fu Wah Andrew	**SHS**, *Emergency Medicine*
Dr Wang Ziting	**NUHS**, *Urology*

CLINICIAN SCIENTISTS IN THE SPOTLIGHT

Personalising Sleep Recommendations across the Lifespan Using Large-Scale Device Data

Optimising performance has been a lifelong passion of Professor Michael Chee, third-time successive recipient of the prestigious STaR Investigator Award. Starting de novo, sans formal training in cognitive neuroscience, he made a name in the functional brain imaging of bilinguals before using his first STaR award to probe the neuro-behavioural effects of a single night of sleep deprivation. This resulted in several pioneering functional imaging findings concerning working memory, risky decision-making, effort discounting and visual attention.

With philanthropic support and a second award, Prof Chee shifted to focus on investigations with more direct societal impact, exemplified by the five-part "Need for Sleep" studies which probed the effects of successive nights of sleep restriction on adolescents. His team tested different combinations of nocturnal sleep and mid-afternoon naps, and documented their effects on sleep architecture, vigilance and memory, particularly encoding and long-term retrieval. They also engaged local schools to evaluate the benefits of starting school later and structured sleep education. Fundamental knowledge about sleep was advanced through uncovering the role of the hippocampus in supporting gains in nap-related memory encoding, and via characterising of dynamic functional connectivity states associated with fluctuating arousal.

Prof Chee's current work seeks to clarify what constitutes 'adequate sleep' across the lifespan for East Asians, at both age-group and individual levels. This ambitious goal is motivated by a conviction that our penchant for 'diligence' has gone over-the-top, becoming counter-productive and damaging the health and well-being of millions. Defining norms that people can realistically live by entails the collection and analysis of data by multiple parties. Prof Chee's team will contribute niche expertise

Prof Michael Chee Wei Liang

STAR INVESTIGATOR AWARD

Director
*Centre for Sleep and Cognition and Centre for Translational MR Imaging,
Yong Loo Lin School of Medicine,
National University of Singapore*

in sleep science, appraisal of wearable data, and unobtrusive measurement of cognition and behaviour in local cohorts like GUSTO (adolescents), HiSG (young adults) and SG 70 (old adults). These efforts leverage on collaborations with companies involved in wearable sleep and physiological tracking, together with behaviour reflected in smartphone usage patterns, as well as teams with expertise in metabolic health. Complementing the large-scale studies are targeted ones, for example, examining how sleep patterns affect maturational brain cortical thinning, and electroencephalogram (EEG) slow-wave sleep decline in adolescents.

Advancing science, with the public good in mind, involves careful listening, clear communication, and wily resourcefulness coupled with lifelong learning. Above all, it requires a resilient and persistent desire to improve health and well-being sustainably.

"I've been blessed with opportunities and the ability to acquire knowledge, skills, social networks and experiences that allow me to make a difference," reflects Prof Chee. "When I started out, the focus was technical mastery. Over time, it became clear that greater and more enduring satisfaction arises from enabling others and in leading collaboration for a greater cause. Unlocking human potential through understanding and improving sleep is a great vehicle to realise this dream and I hope others enjoy and benefit from the ride too."

Innovating to Enhance Immunotherapy in Patients

Driving the core of Professor Narayanan Gopalakrishna Iyer's research are the two fundamental tenets of innovation and reinvention. Having been deeply involved in the field of Head and Neck Cancers (HNCs), Prof Iyer is constantly searching for new ways to adapt existing drugs for patients, and developing novel therapeutics and drugs to meet the challenges of the fast-changing landscape of immunotherapies.

The shifting prevalence of HNCs – once thought to be a disease of the poor and Asians, to now bearing a global impact – and the dearth of well-researched studies in this field continue to keep Prof Iyer grounded in his research endeavours. Together with the surge in new treatment modalities in the landscape of HNCs in the last five years, he is also continually innovating and rethinking how to harness the repertoire of varying treatments for patient care, which he sees as an exciting yet daunting prospect.

Prof Iyer's current work focuses on better matching patient profiles with existing drugs, and reinventing new ways to treat patients who do not respond to existing drugs and treatments, so as to make immunotherapy available to a larger pool of patients. Additionally, he is also investigating the diagnostics of thyroid cancer, a commonly over-diagnosed condition, with a scientific team in Hangzhou, China. Their aim is to profile 1,000 patients to explore new diagnostic tools and make distinctions between thyroid cancer and benign thyroid disease.

As Head and Senior Consultant at the Division of Medical Sciences and Department of Head and Neck Surgery, Division of Surgery and Surgical Oncology at the Singapore General Hospital (SGH) and National Cancer Centre Singapore (NCCS), as well as Professor at Duke-NUS Medical School, Prof Iyer juggles multiple roles and responsibilities. He is also passionate about nurturing the next generation of clinician scientists, and devotes substantial time to informal and formal mentorships. But what keeps him grounded in these demands?

Prof Iyer attributes his dedication to seeking out novel therapeutics and reinvention to his patients. "When I see patients failing treatments, recurrences and deaths, it makes me more determined to find a way to reverse the process." Research, he believes, sets him on a viable path to achieve this.

Having received the CSA (Investigator) and SingHealth Distinguished Researcher Award previously, Prof Iyer is grateful for the extended protected time of five years with the current CSA (Senior Investigator) and the funding provided by NMRC to conduct his extensive work in HNCs. He is also honoured to receive local recognition, citing the cultural shift in Singapore hospitals and institutes to recognise the works of clinician scientists.

His advice to aspiring clinician scientists is to complete the full training period, in both clinical research and PhD, as he believes that the immersion period of the PhD and clinicals is crucial to "deep dive" into the field. "You cannot just throw in the towel and apply it to the rest of your career. There are no shortcuts in life."

Prof Narayanan Gopalakrishna Iyer

CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR)

Head and Senior Consultant
Division of Medical Sciences, National Cancer Centre Singapore

Head and Senior Consultant
Department of Head and Neck Surgery, Division of Surgery and Surgical Oncology, Singapore General Hospital and National Cancer Centre Singapore

Professor
Duke-NUS Medical School

Advancing Research in Systemic Sclerosis

Though rising in occurrence, outstanding female clinician scientists in the field are few and far between. However, to the recipient of three NMRC talent development and human capital NMRC awards, i.e. the MCI, TA and CSA, Dr Andrea Low is no stranger to being in the spotlight for her outstanding research contributions in the field of systemic sclerosis (SSc).

As Head and Senior Consultant at the Department of Rheumatology and Immunology at SGH, and Assistant Professor at Duke-NUS Medical School, Dr Low has always been focused on exploring the multi-systemic disease of SSc which is characterised by immune dysregulation, vasculopathy, and fibrosis. Although relatively rare, it has one of the highest mortalities among autoimmune diseases. Fascinated by this disease of premature senescence of the immunome, with a process of uncontrolled excessive production of collagen leading to fibrosis, Dr Low continues to conduct quality research in hopes of translating the science to improve patient outcomes in SSc and other fibrosing diseases.

Dr Low is well known in the field of SSc, being a leading clinician scientist at the national, regional and international levels. In 2008, she spearheaded a nation-wide collaborative SSc research workgroup dedicated to advancing clinical care and research in SSc comprising rheumatologists from five institutions. At SGH, she leads a comprehensive SSc programme that includes both dedicated SSc and multidisciplinary combined clinics which facilitate research and clinical care across four themes: (i) understanding disease burden and its impact on quality of life; (ii) improving early diagnosis and prognostication; (iii) leading clinical translational research; and (iv) therapeutics. The department was also recognised as a Centre of Excellence by the Asia Pacific League of Associations for Rheumatology in research, education and clinical care in 2017, and subsequently renewed in 2020. Internationally, Dr Low coordinates and leads research efforts in the Asia-Pacific region.

Crediting her TA in 2012 for launching her career path as a clinician scientist, Dr Low remains grateful for the valuable experience under the TA to run investigator-initiated clinical trials, manage a scientific team and build a clinical trials network. Her current CSA project on using novel non-invasive imaging methods and stool biomarkers of the gut microbiome to manage SSc gastrointestinal disease also comes as a result of the TA, which focuses on a clinical trial of probiotics in SSc gastrointestinal disease and understanding microbiome changes with treatment.

Deeply honoured and elated to be a recipient of the prestigious CSA (Investigator), Dr Low is thrilled to embark on her next slate of research to integrate the various "-omics" of immunomics, systems genomics and radiomics in stratifying the heterogeneous disease of SSc. She is also working on bringing an early discovery protein for SSc therapeutics into the Phase I trial, which has already had its patent of the protein filed for in several countries. With two FDA-approved drugs for SSc-related lung fibrosis in the last few years, Dr Low is looking forward to better apply precision medicine and targeted therapies "to the bedside", and finds that there have never been more "exciting times working in the field of SSc!"

Dr Andrea Low Hsiu Ling

CLINICIAN SCIENTIST AWARD (INVESTIGATOR)

Head and Senior Consultant
Department of Rheumatology and Immunology, Singapore General Hospital

Assistant Professor
Duke-NUS Medical School

Pushing the Boundaries of Neurology in the Treatment of Stroke

With a specialisation in neurology and training in neurointervention, Dr Leonard Yeo has always been intrigued by the rapidly evolving field of stroke, which to him, is undergoing a "revolution" in recent years. The young vascular neurologist, whose interests reside in acute stroke, intracranial atherosclerotic diseases and developing endovascular devices for ischemic stroke, is fascinated by how the treatment landscape and trajectory of ischemic stroke has evolved in the last five years.

Once considered a terminal event, patients who experienced ischemic stroke now possess an over 50% chance to return to functional independence, with further improvements on the way as the first successful neuroprotective agents for stroke seemingly in sight. Spurred on by this, Dr Yeo has continually sought novel treatment modalities for stroke.

After examining the collateral circulation in acute stroke under the New Investigator Grant (NIG) in collaboration with the National University of Singapore's (NUS) School of Computing, Dr Yeo has been equipped with imaging work experience which allowed him to understand the limitations of imaging, and levers and boundaries of machine learning. He brings this exposure and his specialised neurological training and interests on board a multidisciplinary team that is focused on developing new methods to treat intracranial stenosis, a condition where artery vessels within the brain narrow, leading to potential brain damage and death. As there is currently no definitive treatment modality for intracranial atherosclerotic stenosis, Dr Yeo and his team are seeking to push the leading edge of science in this field.

Through this journey of determining optimal pharmacological knowledge and treatment know-how across the different phases of stroke, Dr Yeo has developed a passion in the clinical neurological research field. As he witnesses how translational research changes the way medicine is practised, he has come to value clinical research as a critical form of scientific grounding in his medical practice.

Dr Leonard Yeo

TRANSITION AWARD

Senior Consultant
Department of Medicine, National University Hospital

Assistant Professor
National University of Singapore

With the support of the NMRC, Dr Yeo was able to undergo overseas training for a PhD which was instrumental in his career and developmental trajectory. He assisted in the development of endovascular devices, as well as the planning of large multicentric trials. What was most important to Dr Yeo however, was witnessing how "big names" faced the same problems and struggles, and that they were interested in collaborations with "common people (like us)" if there were complementary datasets, useful skill sets or good ideas.

Aside from his clinical and research commitments, Dr Yeo is a dedicated volunteer at HealthServe clinics that serve the underprivileged in Singapore, as he believes in enabling access to affordable healthcare for all. He is also an avid gamer, a hobby which helps him in connecting with his two sons.

To aspiring and budding clinician scientists, Dr Yeo encourages them to not be afraid to "cold call" scientists or engineers in the field, whenever they encounter ideas or pain points. Many times, their receptivity and distinct viewpoints may result in "surprising solutions and spin-offs".

Innovating in Pursuit of Enhanced Patient Care

Through the lens of light microscopy, Dr Fan was drawn to the beauty of blood cell morphology while rotating as a junior doctor in the Department of Haematology at Tan Tock Seng Hospital, where he was taught to appreciate and make diagnosis of diseases reflected in the blood cells mounted on glass slides. To Dr Fan, even in this age of molecular diagnosis, the blood film remains an essential screening and diagnostic tool for many medical conditions. To him, what makes laboratory work most fulfilling is the role of the haematologist in piecing together key laboratory investigations with the clinical presentation of the patient. This allows an accurate diagnosis to be formulated, enabling delivery of appropriate care for patients.

In the spirit of systems innovation, Dr Fan is constantly exploring new methods to improve clinical workflows and outcomes. His project on blood films came about because he saw an unmet need in reducing errors from human fatigue, in the arduous and labour-intensive process of using traditional light microscopy in classifying blood cells and the reporting of blood films. By harnessing digital technology and adapting it for conventional laboratory processes, his current project focuses on tapping into the potential of artificial intelligence and computer vision in translating digital images of blood cells into automated image recognition algorithms, for both accurate blood cell classification and diagnosis.

Dr Fan has interests in Thrombosis and Haemostasis, and is currently investigating COVID-19-related complications on coagulation pathways. He was awarded the Young Investigator Award at the International Society of Laboratory Haematology's XXXIV International Symposium on Technical Innovations in Laboratory Haematology 2021 for his team's work on activated Natural Killer cell subsets in COVID-19 patients. Beyond his speciality, Dr Fan is working on an ultrasound-guided lumbar puncture device with Trendlines Medical Singapore, which aims to establish real-time needle guidance for safer and more efficient procedures and delivery of intrathecal chemotherapy.

Dr Fan is deeply humbled and honoured to be a recipient of the CIDA, it being his first award from NMRC. Above all, he is heartened that the effort of the team and the merits of this project have been recognised. He is most grateful to Emeritus A/Prof Kuperan Ponnudurai for his mentorship,

as well as for the protected time provided by the CIDA. Dr Fan keeps it real when it comes to advising aspiring clinician innovators like himself: Chase your dreams and live interestingly. Life is too short not to develop that idea you thought was not workable. You never know just how many lives you may impact.

Dr Fan Bingwen Eugene

CLINICIAN INNOVATOR DEVELOPMENT AWARD

Consultant
Department of Haematology, Tan Tock Seng Hospital

Visiting Consultant
Department of Laboratory Medicine, Khoo Teck Puat Hospital

RESEARCH GRANTS

Funding Translational and Clinical Research

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

These grants are broadly categorised under:

NMRC/MOH Grants

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

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

Open Fund Grants

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

▸ Open Fund-Large Collaborative Grant (OF-LCG)
▸ Open Fund-Individual Research Grant (OF-IRG)
▸ Open Fund-Young Individual Research Grant (OF-YIRG)
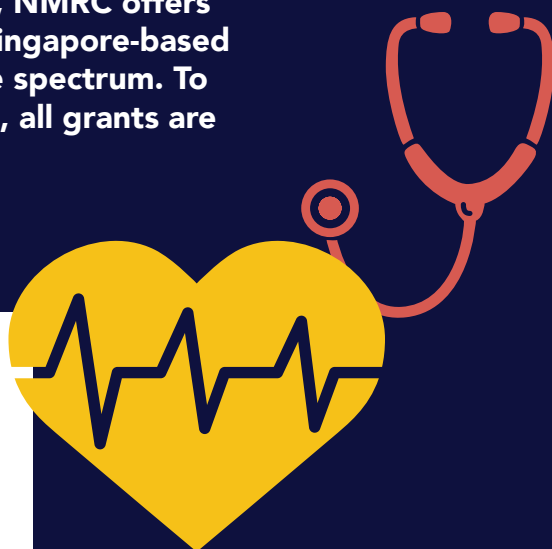
NMRC/MOH GRANTS

Centre Grant (CG)

The 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: cancers, cardiovascular diseases, diabetes mellitus and related metabolic/endocrine disorders, infectious diseases, and neurological and sense disorders; as well as address translational medicine and implementation science research, health systems research, primary care research or population health research.

Clinical Trial Grant (CTG)

The RIE2020 CTG includes two schemes:

The **Industry Collaborative Trials (ICT) scheme** supports ICTs which involve both the clinician and company contributing intellectual inputs and funds to conduct the trial and develop novel or pre-existing drugs, medical devices or 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 funding quantum of up to 30% of the TPC (inclusive of 20% indirect research costs) over a period of five years. CTG-ICT is a rolling grant call.

Period	Proposals Reviewed	Proposals Awarded	Total Sum Awarded ($ millions)
FY2020	6	6	16.01

Note: There was no proposal submitted in FY2019.

The **Investigator-Initiated Trials (IIT) scheme** supports IITs of both early and late phases which are initiated and driven by clinicians interested to conduct clinical trials on novel or pre-existing drugs, medical devices or interventions for new indications. While there are no minimum company contributions, applications with industry contributions will have higher priority. From the May 2018 grant call onwards, CTG-IIT is funded by the National Research Foundation Singapore (NRF) Central Gap. Funding for each project is capped at $1.5 million (without overheads/indirect costs). Please refer to the NRF Central Gap Fund guidelines for more details.

Funding duration is up to three years. Projects with a duration of more than three years will be evaluated on a case-by-case basis.

Grant Call	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
May 2018	15	4	26.7%	5.05
Nov 2018	13	1	7.7%	1.50
Nov 2019	7	2	28.6%	2.95
Total	**35**	**7**	**20.0%**	**9.50**

Clinician Scientist-Individual Research Grant (CS-IRG)

The CS-IRG is provided to clinician scientists to enable them to carry out medical research on a specifically defined topic 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 a year.

Period	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
May 2019	51	8	15.7%	13.34
Nov 2019	50	10	20.0%	13.34
Total	**101**	**18**	**17.8%**	**26.68**

CS-IRG-New Investigator Grant (CS-IRG-NIG)

The CS-IRG-NIG is a subcategory 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	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
May 2019	19	6	31.6%	1.43
Nov 2019	17	5	29.4%	1.18
Total	**36**	**11**	**30.6%**	**2.61**

Health Services Research Grant (HSRG)

The HSRG is a MOH research grant that promotes the conduct of HSR and enables the translation of HSR findings into policy and practice. HSRG grant calls are made twice a year.

Grant Call	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
Apr 2019	45	5	11.1%	5.86

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

The HSR-NIG is a subcategory of the HSRG. Launched with the aim of supporting new HSR researchers, the quantum support for this new subcategory is $100,000 over a period of two years. HSR-NIG grant calls are made twice a year, along with HSRG grant calls.

Grant Call	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
Apr 2019	20	3	15.0%	0.35

OPEN FUND GRANTS

Open Fund-Large Collaborative Grant (OF-LCG)

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

Key elements include:

• Collaborative efforts among clinical research communities, interdisciplinary and investigative partnerships across institutions, to leverage the full spectrum of scientific research capabilities in Singapore;
• Advancements to the study of therapeutic areas that position Singapore at the forefront of biomedical science; and
• Discovery and application of biomedical science-based ideas with clear impact/bearing to the advancement of health, including the translation of clinical findings into practices and policies.

To better realise Singapore's HBMS goals, the OF-LCG is open to proposals of the highest quality based on the five therapeutic areas identified as national priorities: cancers, cardiovascular diseases, diabetes mellitus and related metabolic/endocrine disorders, infectious diseases, and neurological and sense disorders. From the May 2018 grant calls, proposals in areas/research technologies that can be developed and applied in more than one disease area, are able to advance Singapore's human health and wellness and create economic value are considered as well.

Two-tiered funding was also introduced from the May 2018 grant call, providing funding (inclusive of 20% indirect costs) of up to $10 million and $25 million. For the May 2019 grant call, the therapeutic areas and set themes are detailed in the table below.

Emphasised Therapeutic Area(s)	Set Theme(s)
Cardiovascular Diseases	Macrovascular diseases: Myocardial infarction and chronic coronary heart disease, stroke, aortic and peripheral arterial disease
Diabetes Mellitus and Related Metabolic/ Endocrine Disorders	Primary prevention of diseases
Infectious Diseases	Infectious diseases including Emerging Infectious Diseases (EIDs) (e.g. Respiratory Tract Infection (RTI), antimicrobial resistance and healthcare-associated infection, dengue and vector control)
Neurological and Sense Disorders	Age-related neurological and eye disorders (e.g. vascular dementia, glaucoma)

The review process comprises two stages – a Letter of Intent (LOI) and Full Proposal (FP) for shortlisted LOI applications. The success rate and details of the awarded programmes for the May 2019 call are tabulated in the table below:

Funding Tier	Letters of Intent Received	Full Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
Tier-1	16	5	4	17.9%	64.33
Tier-2	12	5	1		

Awarded Programmes

Programme Title (Funding Tier)	Therapeutic Area(s) Emphasised and Set Theme(s)	Leadership Team (Institution)
Prevention of and Biomarkers for Vascular Cognitive Impairment **(Tier-1)**	Neurological and Sense Disorders – Vascular dementia	**Corresponding PI:** A/Prof Christopher Chen (NUS) **Theme PIs:** Prof Christiani Jeyakumar Henry (SICS), Prof Ecosse Lamoureux (Duke-NUS), Dr Effie Chew (NUHS), Prof John Chambers (NTU), A/Prof Josip Car (NTU), A/Prof Nagaendran Kandiah (NNI), A/Prof Helen Zhou Juan (NUS), Prof Arthur Mark Richards (NUS), Dr Chester Lee Drum (NUS), Prof Liu Jianjun (GIS), Prof Wong Tien Yin (SERI), Dr Mitchell Lai (NUS), Prof David Matchar (Duke-NUS), Dr Cynthia Chen (NUS), Dr John Pastor Ansah (Duke-NUS)
Metabolic Health in Asian Women and Their Children **(Tier-1)**	Diabetes Mellitus and Related Metabolic/Endocrine Disorders – Primary prevention of diabetes	**Corresponding PI:** Prof Chong Yap Seng (NUS) **Theme PIs:** A/Prof Jerry Chan (KKH), Dr Neerja Karnani (SICS), Prof Johan Eriksson (NUS), Prof Wong Lim Soon (NUS), Prof Marcus Ong (SGH), A/Prof Fabian Yap (KKH), Prof Lee Yung Seng (NUS), A/Prof Derrick Chan (KKH), Prof Tan Kok Hian (KKH), Prof Eric Finkelstein (Duke-NUS)
Implementing Precision Medicine in Clinical Practice: The Approach for Glioblastoma, a Neurological Disease with Unique Spatiotemporal Complexity **(Tier-1)**	Neurological and Sense Disorders – Primary adult malignant brain tumours (prevalent in ageing patients)	**Corresponding PI:** A/Prof Christopher Ang (NNI) **Theme PIs:** A/Prof Carol Tang (NNI), Prof Patrick Tan (Duke-NUS), Dr Shao Huilin (NUS), A/Prof Lin Xuling (NNI)
Achieving Functional Cure of Chronic Hepatitis B **(Tier-1)**	Infectious Diseases – Hepatitis B virus	**Corresponding PI:** Prof Lim Seng Gee (NUS) **Theme PIs:** Prof John Edward Connolly (IMCB), Prof Hong Wanjin (IMCB)
Integrated Innovations in Infectious Diseases (I3D) **(Tier-2)**	Infectious Diseases – Emerging infections; Respiratory pathogens; Therapeutic and diagnostic response to emerging infectious diseases	**Corresponding PI:** Prof Paul Tambyah (NUS) **Theme PIs:** Prof Gavin Smith (Duke-NUS), A/Prof Yeo Tsin Wen (YLLSoM), Prof Wang Linfa (Duke-NUS), A/Prof Raymond Lin (NUS), A/Prof Jenny Low (SGH), Prof Lisa Ng (SIgN), Dr Ann-Marie Chacko (Duke-NUS), Prof Ooi Eng Eong (Duke-NUS)

Open Fund-Individual Research Grant (OF-IRG)

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

Grant Call	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
Nov 2018	101	13	12.9%	17.74
May 2019	105	13	12.4%	18.29
Nov 2019	104	19	18.3%	26.20
Total	**310**	**45**	**14.5%**	**62.23**

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

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

Grant Call	Proposals Reviewed	Proposals Awarded	Success Rate	Total Sum Awarded ($ millions)
Nov 2018	68	19	27.9%	5.64
May 2019	60	20	33.3%	5.98
Nov 2019	69	22	31.9%	6.45
Total	**197**	**61**	**31.0%**	**18.07**

NATIONAL HEALTH INNOVATION CENTRE
SINGAPORE (NHIC)

The NHIC provides Singapore's public healthcare/clinical research sector with translational funding and strategic guidance to accelerate healthcare innovation. Established in 2014, NHIC seeks to enhance healthcare delivery and patient care through innovation research, by providing the necessary resources to support the translation of innovative technologies and services. This includes linking up and facilitating collaboration among researchers, clinicians and the industry to help accelerate the process, with the aim to help Singapore better tackle future healthcare challenges.
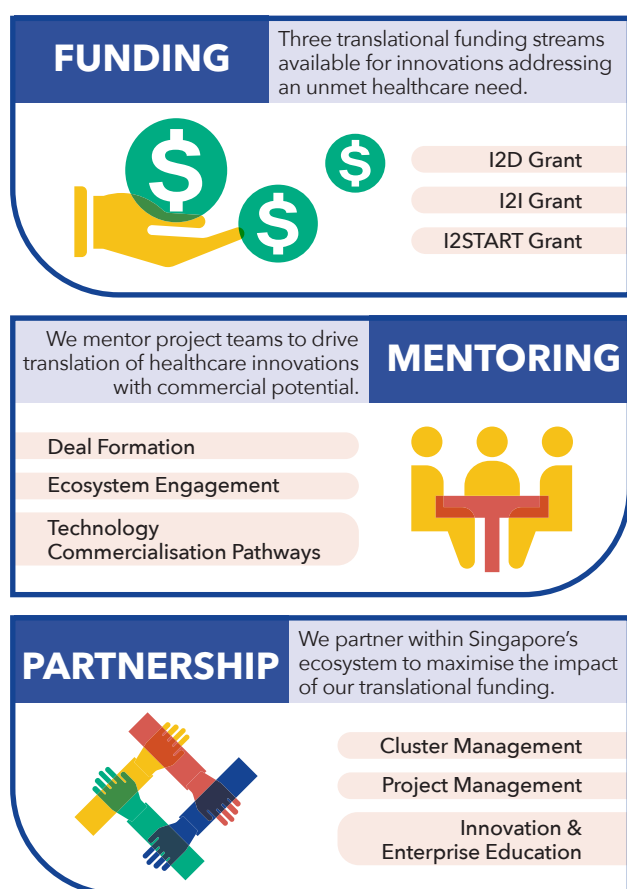
Our Vision

Singapore as a leading hub for health innovation & enterprise in Asia

Our Mission

Drive impactful health and economic outcomes for Singapore by catalysing innovation and enterprise endeavours in the healthcare research community through public and industry partnerships

Our Value Proposition

FUNDING

Three translational funding streams available for innovations addressing an unmet healthcare need.

- I2D Grant
- I2I Grant
- I2START Grant

MENTORING

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

- Deal Formation
- Ecosystem Engagement
- Technology Commercialisation Pathways

PARTNERSHIP

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

- Cluster Management
- Project Management
- Innovation & Enterprise Education

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

1 INNOVATION TO PROTECT (I2P)

This scheme funds patenting expenses to protect innovations with significant healthcare impact and commercial potential. The I2P funding supports first and secondary filing, such as the Patent Cooperation Treaty (PCT), National Phase Entry (NPE), prosecution, grant and maintenance.

2 INNOVATION TO DEVELOP (I2D)

The scheme supports the development of clinically significant and commercially viable healthcare innovations.

3 INNOVATION TO INDUSTRY (I2I)

This scheme is for successfully completed I2D projects or equivalent as deemed suitable by NHIC, where the project requires further co-development with an industry partner who demonstrates licensing interest.

4 INNOVATION TO STARTUP (I2START)

This programme is a streamlined funding pathway, which brings together three grant schemes (SMART Innovation Grant, NHIC I2D and Enterprise Singapore Startup SG Tech), to support medical technology innovation to form a startup company.

In addition to funding, NHIC also provides guidance to maximise projects' commercial potential. Researchers and clinicians are supported by NHIC team members who adopt an active role in overseeing the project from early-stage discussions, to application of funding and post-award management. This improves teams' progress and commercialisation efforts, helping to achieve the desired healthcare impact.

Notable Highlights of FY2019

In FY2019, NHIC funded the following grant applications:

50 I2P patent applications

6 I2D projects

3 I2START projects

1 I2I project

12 joint medtech projects (co-funded with Singapore Health Services (SingHealth), National University Health System (NUHS) and National Healthcare Group (NHG) for early-stage development)

In addition, NHIC facilitated the following outcomes:

3 spin-off companies

5 licences generated from gap project funding

7 licences generated from core patent funding

This resulted in more than **$1.7 million** in licensing revenue for the healthcare clusters.

Innovation to Protect (I2P)

I2P Grant	Applications Received	Grants Awarded	Success Rate	Amount Committed
First Filing	23	23	100.0%	$215,000.00
Secondary Filing	30	27	90.0%	$545,000.00

Innovation to Develop (I2D)

I2D Grant	Proposals Received	Grants Awarded	Success Rate	Amount Committed
April 2019	8	2	25.0%	$499,999.60
August 2019	5	1	20.0%	$246,000.00
December 2019	8	3	37.5%	$750,000.00

Notable Highlights of FY2020

In FY2020, NHIC funded the following grant applications:

59 I2P patent applications

3 I2D projects

1 I2I project

11 joint medtech projects (co-funded with SingHealth, NUHS and NHG for early-stage development)

In addition, NHIC facilitated the following outcomes:

2 spin-off companies

3 licences generated from gap project funding

6 licences generated from core patent funding

This resulted in more than **$116,000** in licensing revenue for the healthcare clusters.

Innovation to Protect (I2P)

I2P Grant	Applications Received	Grants Awarded	Success Rate	Amount Committed
First Filing	31	31	100.0%	$355,000.00
Secondary Filing	30*	28	93.3%	$447,500.00

Two I2P applications are pending evaluation and approval.

Innovation to Develop (I2D)

I2D Grant	Proposals Received	Grants Awarded	Success Rate	Amount Committed
April 2020	10	1	10.0%	$250,000.00
December 2020	10	2	20.0%	$500,000.00

Note: The grant call in August 2020 was cancelled due to the COVID-19 pandemic.

KNOWLEDGE ENABLERS AND INFRASTRUCTURE INITIATIVES
Consortium for Research and Innovation Singapore (CRIS)

CRIS
Consortium for Clinical Research and Innovation Singapore

In 2020, CRIS was set up as part of national efforts to strengthen synergies and promulgate strategies for clinical research and translational programmes under the stewardship of the MOH.

CRIS aims to make a positive difference to patients and researchers in Singapore by ensuring that clinical research platforms and programmes lie at the cutting edge of capability development and innovation. This is achieved through facilitated collaborations, and enduring partnerships with research and biomedical entities, and the relevant parties in the clinical and research communities.

Under CRIS, the following five business units were brought together under a common management and governance structure: Advanced Cell Therapy and Research Institute, Singapore (ACTRIS), Precision Health Research, Singapore (PRECISE), National Health Innovation Centre Singapore (NHIC), Singapore Clinical Research Institute (SCRI) and the Singapore Translational Cancer Consortium (STCC).

Advanced Cell Therapy and Research Institute Singapore (ACTRIS)

ACTRIS was established to meet the increasing clinical demand of using cellular therapeutics to treat various life-threatening diseases.

Its vision is to be the national and regional Centre of Excellence for facilitating discovery, process development and manufacturing of cellular-based therapeutics across the broad spectrum of immunotherapy and regenerative medicine, encompassing both investigational and approval products for the local market.

ACTRIS aims to achieve accreditation from national and international regulators to ensure quality compliance of resource-efficient cellular therapy manufacturing. It will also promote and foster the entire value chain of the cellular therapy ecosystem by enabling translational research and development, manufacturing, clinical service provision and commercialisation, thereby serving the healthcare, academic and industrial sectors. In addition, ACTRIS will provide value-added services such as workforce training, regulatory facilitation and ancillary material standardisation pertaining to the delivery of cellular therapy to patients.

Precision Health Research, Singapore (PRECISE)

PRECISE
Precision Health Research Singapore

PRECISE is the central entity established to drive the whole-of-government effort to implement Phase II of Singapore's 10-year National Precision Medicine (NPM) strategy.

Through partnerships with SG100K, as well as partners in the hospital clusters and biomedical technology sector, NPM Phase II aims to transform healthcare in Singapore and improve patient outcomes by furthering insights into the Asian genome and deriving data-driven healthcare solutions. NPM Phase II will also add value to our economy by attracting and anchoring overseas companies in Singapore, and enhance the breadth and depth of the Precision Medicine-related industry, while yielding new opportunities for home-grown companies.

Precision Medicine is one of the key goals of Singapore's RIE2025 vision for health and biomedical sciences, where it offers an effective means of translating research into more efficient healthcare delivery systems and better health for Singaporeans.

National Health Innovation Centre Singapore (NHIC)

NHIC aims to provide the publicly funded clinical research sector of Singapore with translational funding and strategic guidance.

By accelerating the development of innovative technologies and services to improve healthcare delivery and patient care, NHIC's funding and guidance support the translation of innovations by validating, de-risking or developing them towards market-ready products. This impacts the clinical landscape and promotes the collaboration of researchers, clinicians and industry to better position Singapore in tackling the healthcare challenges of tomorrow.

Singapore Clinical Research Institute (SCRI)

SCRI is the national academic research organisation dedicated to enhancing the standards of clinical research and coordinating clinical trials.

With a mission to spearhead and develop core capabilities, infrastructure and scientific leadership for clinical research in Singapore, SCRI also works with NMRC to assist the MOH in implementing clinical trial policy and strategic initiatives to support and develop local clinical research competencies.

In striving towards its vision, SCRI collaborates with clinicians to enhance Singapore's clinical research and strengthen its expertise in executing multi-site, multinational studies and the development of regional clinical research networks.

Singapore Translational Cancer Consortium (STCC)

STCC is a nationally coordinated initiative to synergise cancer research capabilities in Singapore. STCC brings together unmatched basic, clinical and translational talent in Singapore to create globally significant peaks of excellence in selected Asian cancers. It provides an enabling research and innovation-driven environment to foster translational research with meaningful outcomes for society.

By capitalising on the strengths of industry and academia, and through collaborative relationships among local cancer research groups, STCC helps to develop initiatives that are aligned with Singapore's goals in value-based healthcare innovations and economic value creation through its one-stop-shop concept.

EVENTS

NATIONAL MEDICAL EXCELLENCE AWARDS (NMEA)

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

In both 2019 and 2020, NMEA recognised five individuals and one team respectively, for their outstanding contributions to clinical practice and quality, research, 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 2019

Prof Aymeric Lim Yu Tang

Senior Consultant
Department of Hand and Reconstructive Microsurgery Centre, National University Hospital

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

Physician-in-Chief and Group Chief Human Resource Officer
National University Health System

A hand and reconstructive microsurgeon with nearly 30 years of experience, Professor Aymeric Lim is internationally recognised as an expert in neuromuscular anatomy and surgery. He is also well respected among his peers for his dynamic leadership and passion for nurturing the next generation of healthcare leaders. As one of the pioneer nerve surgeons in Singapore, Prof Lim's clinical expertise includes flaps, peripheral nerve reconstruction and tendon transfers, techniques which have successfully restored hand functionality to forearm and hand trauma patients. He is highly regarded for his skills in restoring the nerve functions of brachial plexus patients, as well as restoring the quality of life for stroke, brain injury and tetraplegic patients.

Prof Lim is dedicated to the advancement of clinical care and continues to raise the bar in his area of expertise for the benefit of his patients. He is credited with developing novel split muscle transfers, restoring hand function in complex trauma patients who otherwise would not have enough donor muscles for transfer. Even more signficant is his discovery of a design in upper limb innervation that allows surgeons to pinpoint the location and number of nerve branches available in each muscle and plan for freestyle nerve transfers. This has led to the development of a treatment for patients with stroke and brain injury, relieving them from uncontrollable, painful spasms and random movements that limit their social interactions. In addition, Prof Lim pushed the limits with reverse flow flaps, applying surgical techniques for the hand to the foot, and widened the scope of the specialty by getting microsurgeons to be involved in liver transplants.

During his two-term tenure as Chairman, Medical Board at the National University Hospital (NUH) from 2008 to 2016, Prof Lim demonstrated exceptional leadership and fortitude, spearheading the implementation of several critical initiatives to enhance safety and clinical outcomes for patients. One of these was the introduction of 100% procedural audits, which was subsequently adopted by the Ministry of Health (MOH) and rolled out to all public healthcare institutions.

Under Prof Lim's leadership, NUH adopted the Republic of Singapore Air Force's safety strategy with the intent of achieving zero preventable errors and building a just workplace culture, where departments are accountable for the safety of patients and staff in their units. From 2012 to 2015, the MRSA Bacteremia rates showed a consistent decrease and exceeded the national target set by the MOH. The core value of excellence he instilled during his term has become embedded and runs strongly in the hospital's day-to-day activities. Prof Lim also established the thoracic outlet syndrome service at the hospital, providing relief for patients who had previously sought multiple unsuccessful treatments elsewhere.

Beyond his clinical and teaching responsibilities, Prof Lim is heavily involved in policy planning and administration duties. As Physician-in-Chief and Group Chief Human Resource Officer with the National University Health System, he manages the planning and development of the integrated, seamless and comprehensive clinical care programme across the cluster. Prof Lim also oversees leadership and organisational development, policy perspectives, health system design and innovation within the public healthcare system in his capacity as Dean of the Healthcare Leadership College, MOH Holdings.

Over the course of his illustrious career, Prof Lim has served in various leadership roles at both institutional and national levels. He was Chairman of the MOH Specialist Training Committee from 2009 to 2010, and President of the Singapore Society for Hand Surgery from 2007 to 2009.

In 2018, Prof Lim was conferred the Public Administration Medal (Silver) at the National Day Awards for his contributions to the nation's healthcare sector. On the international front, he was also nominated to the prestigious French National Academy of Surgery and French Society for Hand Surgery in recognition of his expertise and surgical skills.

For his outstanding achievements in the advancement of hand and reconstructive microsurgery, peripheral nerve surgery, and his contributions to shaping the safety culture of healthcare services in Singapore and beyond, Prof Lim is awarded the National Outstanding Clinician Award 2019.

> *For his outstanding achievements in the advancement of hand and reconstructive microsurgery, peripheral nerve surgery, and his contributions to shaping the safety culture of healthcare services in Singapore and beyond.*

National Outstanding Clinician Award 2019

Dedicating his life to raising the standards of cardiothoracic surgery in Singapore, Associate Professor Chua Yeow Leng has been a strong advocate for the role of surgery in atrial fibrillation and valve diseases.

Since 1996, A/Prof Chua has championed the use of mitral valve repair surgery in Singapore and is the recognised leader and expert in this subspecialty, thereby contributing greatly to the reputation of the National Heart Centre Singapore (NHCS) for heart valve repairs in the region. Being one of the key opinion leaders in the surgical radiofrequency ablation technique for the treatment of atrial fibrillation, he is regularly invited as an expert speaker at many scientific meetings in Asia and the region. Beyond providing care to local patients, A/Prof Chua also assists with overseas surgical cases and offers specialised guidance for these surgeries.

When A/Prof Chua was the Head of Department of Cardiothoracic Surgery in NHCS from 1995 to 2007, new initiatives and services, such as the life-saving Mechanical Heart Assist Device Programme for patients with end-stage heart disease but unable to find a suitable heart for transplantation, as well as the Extra-Corporeal Membrane Oxygenator (ECMO) that greatly reduced mortality and morbidity rates, were introduced, which established the reputation of NHCS as the leading national and regional referral centre for heart-related problems.

A/Prof Chua was appointed the Group Director for the International Collaboration Office for SingHealth in March 2014, where he led teams of healthcare professionals in outreach and humanitarian mission efforts worldwide, such as in China, Papua New Guinea and Vietnam. He has actively participated in and led numerous mission projects partnering with organisations, such as Temasek Foundation and SingHealth Duke-NUS Global Health Institute, to help develop cardiac and other types of surgeries in the Asia-Pacific region.

A/Prof Chua is a firm believer in imparting his knowledge and skills to younger generations of doctors, as well as nursing staff and overseas fellows. He believes that each individual has their unique strengths and is committed to grooming and developing these doctors to their fullest potential in all aspects – from clinical care, research, and to personal development. His commitment has led to generations of cardiothoracic surgeons being trained in NHCS, with succession planning for leadership in this challenging specialty.

As an advocate for cardiovascular research, A/Prof Chua believes in advancing clinical capabilities through research work, and is highly involved in clinical trials and driving research in his department. He has obtained two A*STAR Biomedical Research Council grants of more than $900,000, of which he is the Co-Investigator.

For his exemplary contributions to the role of surgery for atrial fibrillation and valve disease, and the advancement of cardiothoracic surgery standards in Singapore, A/Prof Chua is awarded the National Outstanding Clinician Award 2019.

A/Prof Chua Yeow Leng

Senior Consultant
Department of Cardiothoracic Surgery, National Heart Centre Singapore

Group Director
International Collaboration Office, SingHealth

> *For his exemplary contributions to the role of surgery for atrial fibrillation and valve disease, and the advancement of cardiothoracic surgery standards in Singapore.*

National Outstanding Clinician Scientist Award 2019

Adj Prof Goh Boon Cher

Deputy Director (Research) & Senior Consultant
Department of Haematology-Oncology, National University Cancer Institute, Singapore

Adjunct Professor
Department of Pharmacology and Medicine, Yong Loo Lin School of Medicine, National University of Singapore

Group Chief Physician Leadership and Organisational Development Officer
National University Health System

Director
Investigational Medicine Unit, National University Health System

Deputy Director
Cancer Science Institute of Singapore, National University of Singapore

Adjunct Professor Goh Boon Cher is an internationally renowned and experienced cancer pharmacologist, as well as Phase I clinical trial expert highly regarded in the field of drug development. He regularly provides consultancy to early drug pipeline research teams from the pharmaceutical industry and is a key opinion leader in the development of these drugs.

Following a successful research fellowship in Clinical Pharmacology and Phase I clinical trials at the University of Chicago, Adj Prof Goh saw the value of establishing a clinical trial unit at the National University Hospital (NUH). Upon his return to Singapore in 1999, he started a clinical trial unit in the Department of Haematology-Oncology at the National University Cancer Institute, Singapore (NCIS). Through his dedication and efforts, the facility has established itself as a world-class clinical trial unit that offers state-of-the-art molecular profiling to select the most suitable patients for clinical trials. This infrastructure has enabled the National University Health System to cultivate many productive collaborations with international pharmaceutical companies and numerous therapeutic trials. Some of the trials led by Adj Prof Goh are the first in the world, for instance, the first-in-man development of Singapore's first cancer drug, SB939, a histone deacetylase inhibitor.

Adj Prof Goh is well recognised as an expert in head and neck cancer, particularly for nasopharyngeal carcinoma (NPC), one of the most prevalent head and neck cancers in Singapore. He is currently leading efforts at NCIS to translate laboratory discoveries to clinical trials in nasopharyngeal cancer, a type of cancer which is endemic and difficult to treat, and in urgent need of new treatment options.

Adj Prof Goh has been studying anti-VEGF therapy and immunotherapy in NPC, and has presented some of this work and published a study which investigates nivolumab. These have led to promising leads in evolving the way that NPC is being treated, with the potential to revolutionise the care of this disease. He has also pioneered the application of anti-angiogenic drugs in modifying the NPC tumour micro-environment, enhancing drug permeability and the trafficking of immune cells into the core of the tumour. This work was the result of a completed four-arm clinical trial that has since been presented twice at the Annual Meeting of the American Society of Clinical Oncology (ASCO). The presentation will be transcribed into a manuscript this year, and will serve to guide future research in this promising area of study.

In the field of molecular diagnostics, Adj Prof Goh has spearheaded work in the development of a panel of proteins from plasma particles called exosomes that is being evaluated for early diagnosis of lung cancer. This work is currently filed for patent as intellectual property.

As a prominent clinician scientist, Adj Prof Goh has also been dedicated to the mentoring and nurturing of the next generation of basic and clinician scientists through the years – both in formal structures initiated by the Ministry of Health, as well as within his own personal capacity to provide invaluable research opportunities, supervision and career guidance to many currently successful researchers.

With his wealth of research achievements, Adj Prof Goh has published 190 peer-reviewed articles to date and is a regular keynote speaker at national and international conferences and workshops. He is also frequently invited to contribute on the editorial boards of prestigious journals of oncology and clinical pharmacology. He is currently serving on the editorial board of Annals of Oncology, the official journal of the European Society of Medical Oncology. He has also written a book chapter on "Pharmacogenomics" in "De Vita, Hellman and Rosenber (editors) Principles and Practice of Oncology 7th Edition, 2005", a highly regarded reference publication in the field of oncology.

For his outstanding and pioneering contributions in cancer pharmacology and drug development, bringing hope to cancer patients through promising experimental treatments, Adj Prof Goh is awarded the National Outstanding Clinician Scientist Award 2019.

> *For his outstanding and pioneering contributions in cancer pharmacology and drug development, bringing hope to cancer patients through promising experimental treatments.*

National Outstanding Clinician Mentor Award 2019

In his illustrious career of more than three decades, Professor London Lucien Ooi Peng Jin has worn many hats. Currently Senior Consultant at both the Department of Hepato-pancreato-biliary and Transplant Surgery at Singapore General Hospital (SGH), and the Division of Surgical Oncology at the National Cancer Centre Singapore, Prof Ooi has excelled in varied roles. He is a surgeon, researcher, administrator and teacher, and importantly, a mentor to successive generations of surgeons and clinicians, many of whom bear witness to his generous and inspiring leadership.

He has been imparting knowledge and skills, as well as strong values of generosity and collegiality to young clinicians and other healthcare professionals throughout his career. During his term as the Chairman of SGH's Division of Surgery between 2006 and 2015, Prof Ooi was actively involved in the mentorship of potential leaders for the 16 clinical departments in his division. Most of his leadership mentees went on to head departments and divisions – who have, in turn, gone on to mentor others.

During that time, he was also instrumental in bringing together the several surgical departments and services to function as a family. Prof Ooi's strong and inspiring leadership allowed him to successfully galvanise the surgeons, nurses, technicians and administrative staff to give their best to improve patient care and train the next generation of surgeons in the best tradition.

Prof Ooi saw the growing importance of technology and the use of high-tech imaging, robotics-assisted devices to enhance operating procedures, as well as the possibilities of technology in teaching; adopting an important role in designing and building the skills simulation laboratories at the Academia. He engaged industry players to provide top-of-the-line, state-of-the-art instruments and operating theatre systems to enable training of the next generation of clinicians and healthcare professionals.

Prof Ooi was also instrumental in establishing entities like SingHealth Transplant, which incorporated nine transplant programmes and served as a platform for developing and mentoring clinicians in leadership roles in transplantation, and the SingHealth Tissue Repository, which provided a powerful resource for clinician researchers.

More recently, as Chairman of Surgery Academic Clinical Programme, he established new roles and appointments in academic medicine to allow clinicians to embrace academic leadership in research and training. He continues to mentor clinician leaders in higher leadership appointments.

Prof Ooi holds several appointments that allow him to shape the evolution of surgical training and assessments for generations of general surgeons in Singapore. These include Chairman of the Joint Committee on Specialist Training General Surgery Exit Examinations Committee (since 2016), Chief Examiner of the American Board of Surgeons Singapore Board MCQ Examinations (since 2014), Chief Examiner of the Joint Specialties Fellowship Conjoint Exit Examination in General Surgery with the College of Surgeons of Hong Kong and the Royal College of Surgeons of Edinburgh (since 2007).

Prof Ooi continues to be highly sought after by trainees for pre-examination tutoring with his characteristic collegial manner, patience and kindness, never failing to oblige them when they need his guidance. A true academic surgeon, he excels in clinical expertise, research, teaching and administration, and combines all in order to be a mentor extraordinaire in these areas.

For his inspiring leadership in grooming successive generations of surgeons who became leaders in their own right, and passing on strong mentoring values of generosity, collegiality and patience, Prof London Ooi is awarded the National Outstanding Clinician Mentor Award 2019.

Prof London Lucien Ooi Peng Jin

Senior Consultant
Department of Hepato-pancreato-biliary and Transplant Surgery, Singapore General Hospital

Professor
Surgery Academic Clinical Programme, SingHealth Duke-NUS Academic Clinical Programme

Associate Dean (Recruitment, Admissions, Financial Aid) and Professor
Duke-NUS Medical School

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

> *For his inspiring leadership in grooming successive generations of surgeons who became leaders in their own right, and passing on strong mentoring values of generosity, collegiality and patience.*

National Outstanding Clinician Educator Award 2019

A/Prof Tan Boon Yeow

Chief Executive Officer and Senior Consultant Physician
St Luke's Hospital

Associate Programme Director
National University Health System Family Medicine Residency Programme

A passionate and indefatigable clinician educator and administrator, Associate Professor Tan Boon Yeow is a trained Family Physician and currently Chief Executive Officer and Senior Consultant at St Luke's Hospital. A/Prof Tan has been heavily involved in undergraduate and postgraduate residency and fellowship educational work since 2003. He is an inspirational role model who has trained many doctors, clinician leaders and clinicians in the public, private and people (non-profit) sectors, nurturing future generations of clinicians in Singapore.

When Singapore introduced the Accreditation Council for Graduate Medical Education – International (ACGMEI) residency programme in 2010, A/Prof Tan seized the opportunity and helped establish the first Family Medicine Residency Programme in National University Health System (NUHS). He took over as Programme Director from 2012 to 2019 and led the programme to successful accreditation. As NUHS did not own any public primary care assets then, he innovatively collaborated with private and voluntary sectors to establish the programme, paving the way for fruitful public-private-people sector cooperation for the national good.

A/Prof Tan was instrumental in developing a robust training curriculum with core faculty, and motivating residents in actively creating a conducive learning environment to achieve core competencies and values in Family Medicine. To ensure high educational standards of residents and continual training for faculty development, he presents on most Friday night training sessions and personally conducts most of the home visit teaching sessions with residents on Saturday afternoons.

A/Prof Tan is also a visionary leader. A rigorous Fellowship programme for the College of Family Physicians Singapore (CFPS) was established when he was the Censor in Chief of CFPS. Working together with the other college and academy leaders, he was also instrumental in helping to establish the Chapter of Family Medicine in the Academy of Medicine. One of the main aims of the Chapter is to promote the recognition and development of Family Medicine as a specialty in Singapore. He was inaugural Chairperson of the Chapter of Family Medicine (2015 – 2016) and currently Vice Chairperson (since 2016).

As one of the longest-serving Censor in Chief of CFPS, A/Prof Tan managed to significantly increase the number of doctors trained in the various programmes that CFPS oversees, such as the Graduate Diploma in Family Medicine (GDFM), the College Programme for the Masters of Medicine course and the Fellowship Programme. The high standing of Family Medicine and the popularity of the discipline today has its roots in these well-run and well-subscribed programmes.

Furthermore, A/Prof Tan contributed to the establishment of the Family Medicine and Continuing Care Department of Singapore General Hospital as a Visiting Consultant, where he conducted weekly grand rounds and teaching from 2007 to 2013.

A/Prof Tan continues to teach and train medical students in his role as adjunct A/Prof in Family Medicine Academic Clinical Programme, Duke-NUS Medical School, as well as Yong Loo Lin School of Medicine, National University of Singapore. He also continues to support the NUHS Family Medicine Residency Programme as Associate Programme Director and Site Director for St Luke's Hospital.

In recognition of his passion and contribution in clinician education, A/Prof Tan has received teaching awards such as the NUHS Postgraduate Teaching Excellence Award in 2013, NUHS Teaching Excellence Award 2015, Singapore Chief Residency Programme Mentoring Excellence Award 2016 and Trailblazer Programme Director Award 2019. His latest award recognised his outstanding leadership and driving postgraduate education in NUHS Residency.

For his extraordinary dedication and visionary contributions to education in Family Medicine, A/Prof Tan is awarded the National Outstanding Clinician Educator Award 2019.

> *For his extraordinary dedication and visionary contributions to education in Family Medicine.*

National Clinical Excellence Team Award 2019

SINGAPORE INTEGRATED DIABETIC RETINOPATHY PROGRAMME (SIDRP)

For their outstanding contributions and achievements in establishing a national diabetic retinopathy screening programme for the benefit of patients with diabetes in Singapore.

Asst Prof Gavin Tan Siew Wei

Senior Consultant
Surgical Retina Department, Singapore National Eye Centre

Clinical Director
SNEC Ocular Reading Centre, Singapore National Eye Centre

Assistant Professor
Duke-NUS Medical School

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

Clinical A/Prof Wong Hon Tym

Medical Director
National Healthcare Group Eye Institute

Senior Consultant
National Healthcare Group Eye Institute

Clinical Director
Centre for Healthcare Innovation Institute

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

A/Prof Colin Tan Siang Hui

Senior Consultant
National Healthcare Group Eye Institute

Head
Fundus Image Reading Centre, National Healthcare Group Eye Institute

Clinician Scientist
National Healthcare Group Eye Institute

Associate Professor
Department of Ophthalmology, Duke-NUS Medical School

Assistant Professor of Ophthalmology
Lee Kong Chian School of Medicine, Nanyang Technological University

Ms Haslina Binte Hamzah

Senior Manager
SNEC Ocular Reading Centre, Singapore National Eye Centre

Diabetic retinopathy (DR) is a significant complication of diabetes and a leading cause of vision impairment in Singapore. About 10% or 400,000 of Singaporeans aged between 18 and 69 years have diabetes mellitus. Of these, approximately 30% (120,000) have DR and 10% (40,000) have vision-threatening DR. Vision loss from DR is preventable if diagnosed early and treated appropriately.

The team, led by Assistant Professor Gavin Tan and Clinical Associate Professor Wong Hon Tym, with members from the National Healthcare Group Eye Institute and Singapore National Eye Centre, established a new Singapore Integrated Diabetic Retinopathy Programme (SIDRP), which is a comprehensive screening model based on "real-time" assessment of DR from photographs. This is a major improvement from the old DRP model as the assessment can now be done centrally by a team of trained and accredited non-physician readers, supported by a robust tele-ophthalmology IT infrastructure. Patients' photographs are graded within one business day and if necessary, they will be referred to tertiary eye care, based on a standardised protocol.

SIDRP started in 2010 and is one of the first successful joint cluster programmes between National Healthcare Group and SingHealth. With SIDRP, the programme has initiated improvements when compared to the traditional model, such as:

1. Faster – Shorter turnaround time for reports

99.8% of the reports are generated within one business day, with about 50% reported within an hour, in comparison to two to four weeks previously. The short turnaround time allows for early detection of eye diseases and prevents delay in diagnosis and treatment.

2. Better – Higher accuracy, standardised protocol with recommended timeframe

With online training and audit monitoring features available, readers are trained, tested and consistently monitored to ensure strict compliance to the new harmonised grading protocol to detect eye diseases. Patients with Mild DR are monitored closely in the primary care centres instead of referral to tertiary care.

3. Cheaper – Cost-savings by upskilling non-physician readers to perform image assessment

SIDRP has upskilled the allied health workforce by equipping them with new skill sets of assessing and reporting DRP images. Results have shown that the present value of future cost savings associated with the SIDRP model is estimated to be $29.4 million over a lifetime horizon.

To date, SIDRP has screened more than 267,000 patients in the polyclinics, and expanded its scope to the endocrinology clinics and community by including community healthcare centres, optometry practices and primary care networks. The SIDRP system is a major paradigm shift in the management of DR with direct benefit to patients, improved productivity and cost savings to the healthcare system.

For their outstanding contributions and achievements in establishing a national diabetic retinopathy screening programme for the benefit of patients with diabetes in Singapore, the SIDRP team is awarded the National Clinical Excellence Team Award 2019.

National Outstanding Clinician Award 2020

A/Prof Sum Chee Fang

Senior Consultant
Division of Endocrinology, Khoo Teck Puat Hospital

Senior Consultant
Diabetes Centre, Admiralty Medical Centre

Associate Professor Sum Chee Fang is known to many as an outstanding clinician and leader with "a heart for his patients and all whom he had worked with and mentored". He has excelled in varied roles over the past three decades as a doctor, physician and endocrinologist with deep clinical skills and expertise in all areas of internal medicine and endocrinology. He is also a well-respected teacher and mentor to generations of doctors and nurses.

A/Prof Sum is a pioneer in setting up the Diabetes Centre in Alexandra Hospital in 2001. The centre adopted a comprehensive interdisciplinary approach to diabetes care and management of patients with complex diabetes problems. He recognised early on the critical importance of upskilling nurses by training them in the area of diabetes care. His foresight led to a collaboration with like-minded professionals in Singapore and the Nanyang Polytechnic team to establish the Specialist Diploma in Nursing (Diabetes Management and Education) in 2000.

A/Prof Sum's passion to create a culture of interdisciplinary learning helped the team keep up with evolving healthcare demands and patient needs. When the Diabetes Centre moved to Khoo Teck Puat Hospital (KTPH) in 2010 – in line with the transition from Alexandra Hospital to KTPH – A/Prof Sum established the Centre with a strong emphasis on patient engagement and education, built on a foundation of academic research.

A/Prof Sum also initiated the Advanced Practice Nurse (APN) Programme at the Diabetes Centre. Recognising the crucial role APNs play in patient care, he personally trained a number of Diabetes Educators in the clinical aspects of patient care in diabetes, which inspired most of them to take up further studies. He was also one of the first clinicians to upskill and train the APNs and worked out a Collaborative Prescribing Agreement for the Centre, which allowed its APNs to prescribe diabetes medications for patients under clinician supervision.

A/Prof Sum also chaired the National Healthcare Group (NHG) Diabetes Disease Management Committee from 2001 to 2008, and the Ministry of Health Diabetes Strategy Advisory Committee in 2008. In addition, he set up the NHG Diabetes Registry that has provided valuable data for research projects across multiple healthcare institutions. This registry continues to serve as one of the most important resources for monitoring and improving diabetes management within NHG.

Beyond the hospital, A/Prof Sum generously extended his knowledge and time to improve the standards of diabetes management care at Woodlands Polyclinic since 2016. On top of advising the care team, A/Prof Sum led them in analysing patient data and identified areas that could be improved upon to enhance patient care experience.

A/Prof Sum remains a leader in diabetes and endocrinology care. He has been instrumental in developing and enhancing diabetes care in the public sector through his various contributions in hospital management, national committees and in the training of staff. A passionate educator and researcher, A/Prof Sum has more than 100 publications in peer-reviewed journals.

His dedicated service and contributions over his 36-year career have been recognised with his award of the National Healthcare Group Outstanding Citizenship Award in 2006, and the Ministry of Health Distinguished Senior Clinician Award in 2016.

For his exemplary contributions and unwavering commitment to developing and advancing diabetes and endocrinology care, A/Prof Sum is awarded the National Outstanding Clinician Award 2020.

> *For his exemplary contributions and unwavering commitment to developing and advancing diabetes and endocrinology care.*

National Outstanding Clinician Scientist Award 2020

As one of Singapore's leading medical researchers, Professor Yong Eu Leong has pushed the frontiers of knowledge for menopausal osteoporosis and human fertility for over 30 years.

A significant contributor to the understanding and treatment of male and female infertility, Prof Yong's research has shed light on how androgen receptor mutations and polymorphisms cause sexual reversal in XY individuals and low sperm counts in men. With the help of the Molecular Diagnosis Centre at the National University Hospital (NUH), his findings have been translated into novel genetic testing services for patients in Singapore and around the world.

In 2014, Prof Yong started the Integrated Women's Health Programme (IWHP), a unique study that focused on the key health concerns of mid-life Singaporean women which scientifically characterised the size and scope of women-specific health issues, such as menopause, osteoporosis, anxiety, depression, pre-diabetes, pre-hypertension, urinary incontinence, poor sleep and hip fractures, for the first time. Equipped with this knowledge of women's health needs, Prof Yong went on to lead more randomised control trials to study innovative interventions adapted to the Singapore context, such as a smartphone app to restore optimum weight in women with gestational diabetes, and novel drugs targeting bone signalling proteins from the Traditional Chinese Medicinal plant, Epimedium, for post-menopausal osteoporosis.

A prolific researcher, Prof Yong has authored more than 150 peer-reviewed publications to date. In 1999, he received a Ministerial Citation from the then-National Science and Technology Board, for his contributions to research on the genetics of human fertility. In 2004, he received the Biomedical Research Council (BMRC) – National Medical Research Council (NMRC) Clinician Scientist Investigator Award, given to outstanding clinician scientists to carry out internationally competitive translational and clinical research. In 2011, Prof Yong received the NMRC Clinician Scientist Award (CSA) under the Senior Investigator category, and successfully renewed his award for another five years in 2017. For his current CSA research, he and his team aim to improve the clinical management of osteoporosis by identifying new protein target sites for osteoporotic drug development.

From 2001 to 2003, Prof Yong served as Vice-Chairman (Research) Medical Board, National University Hospital, where he spearheaded many initiatives to train new clinician scientists and develop Singapore's research infrastructure. He was the founding Director (Research) at the NUH Office of Biomedical Research, predecessor of the current NUH Research Office, as well as a founding member of the NUH Investigation Medicine Unit, an inpatient facility to improve the quality of clinical research.

Prof Yong's research excellence is matched by his dedication to the education of young doctors and clinical care of patients. As Professor and past-Head of the Department of Obstetrics and Gynaecology at both NUH and NUS, Prof Yong lends his academic prowess and expansive clinical experience to the training of future generations of clinician scientists and medical practitioners. During his 11-year tenure as the Head of Department of Obstetrics and Gynaecology (2008 to 2019), the department trained a new generation of confident and highly skilled specialists dedicated to caring for women and their foetuses. Under his leadership, the department also made remarkable strides in improving the quality of care and value-driven outcomes for patients, in procedures such as lower segment Caesarean section and hysterectomies. During this period, the number of women who chose to deliver their babies in NUH doubled, a development that testifies to Prof Yong's leadership, emphasis on teamwork, and innovations to address the concerns of Singaporean women.

For his outstanding research in women's health and human fertility, and his exemplary leadership in innovations to improve medical care, Prof Yong is awarded the National Outstanding Clinician Scientist Award 2020.

Prof Yong Eu Leong

Senior Consultant
Department of Obstetrics and Gynaecology, National University Hospital

Professor
Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore

> *For his outstanding research in women's health and human fertility, and his exemplary leadership in innovations to improve medical care.*

National Outstanding Clinician Mentor Award 2020

A/Prof Keson Tan

Senior Consultant
National University Centre for Oral Health, Singapore

Associate Professor
Faculty of Dentistry, National University of Singapore

Since beginning his career in 1988 as a Senior Tutor in the Faculty of Dentistry at National University of Singapore (NUS), Associate Professor Keson Tan has been passionate about the teaching and mentoring of dental students as well as expanding the field of knowledge in Prosthodontics.

A/Prof Tan has served as Programme Director of the Graduate Prosthodontic MDS Residency Training Programme since 2001. This programme is a three-year full-time residency course leading to the degree of MDS (Prosthodontics), and is the recognised Basic Specialist Training for the specialty of Prosthodontics. Programme residents have won several international research awards, and seven ex-residents have been inspired to join academia in Singapore, Malaysia and the US. The programme owes its success to A/Prof Tan's close mentorship of residents and his strong programme philosophy of uncompromising clinical standards coupled with thought independence in treatment plan development and multidisciplinary joint consultations in the management of highly complex cases. A/Prof Tan maintains close contact with graduates from this programme, supporting them after graduation as they develop their careers as specialists.

In 2001, A/Prof Tan was appointed Dean of the Faculty of Dentistry and served until 2009. In 2007, he oversaw the enhancement of the Adjunct Staff Scheme to include private dental practitioners in the Undergraduate and Postgraduate faculty. Among the adjunct faculty were many alumni who were inspired by A/Prof Tan's belief in mentorship, and his efforts to better support future dental professionals in their education.

A/Prof Tan also contributed to the Undergraduate Bachelor of Dental Surgery (BDS) course that encompasses preclinical and clinical teaching modules through all four years of the course. For example, he introduced the Integrated Course in Occlusion in 1993, a preclinical module that is foundational for the clinical phases of the BDS course.

A/Prof Tan has been instrumental in shaping the future of dental education in Singapore. The concept of a national dental centre that synergistically incorporates the domains of education, research and clinical service was mooted during his tenure as Dean. Even after he stepped down, he continued to offer his expertise and insights in layout, process interface and advanced pedagogical designs. These eventually materialised in the modern 11-storey National University Centre for Oral Health, Singapore (NUCOHS), which officially opened in July 2019.

Beyond the University, A/Prof Tan also contributed to the Prosthodontics specialty and dental fraternity in Singapore. He is a supportive and active contributor to the Prosthodontic Society of Singapore. He has also served in various capacities in the Academy of Medicine Chapter of Dental Surgeons, the Dental Specialty Board for Prosthodontics and the Singapore Dental Council. In 2008, the Ministry of Health appointed him to the Dental Specialists Accreditation Board. In all these appointments, A/Prof Tan consistently guided and provided holistic guidance to younger clinicians.

A/Prof Tan is also active in research. He has published over 55 publications, and has won the 2009 William R Laney Award for the best article published in the International Journal of Oral and Maxillofacial Implants. Today, he continues to actively mentor and inspire young academics in their research journey and lifelong learning.

As a visionary and mentor, A/Prof Tan has taken the lead in shaping and nurturing dentistry students, residents and staff, including a large pool of well-qualified adjunct staff, in order to build a strong dental fraternity. In the process, he has helped raise the global stature of the school.

For his vision, passion, and dedication in grooming future generations of dentists, A/Prof Tan is awarded the National Outstanding Clinician Mentor Award 2020.

For his vision, passion, and dedication in grooming future generations of dentists.

National Outstanding Clinician Educator Award 2020

A passionate advocate for education and learning, Associate Professor Nicholas Chew has been at the forefront of undergraduate and postgraduate education since joining the National Healthcare Group (NHG) in 2001. He has displayed outstanding leadership in advancing graduate medical education, both in NHG and in Singapore.

A/Prof Chew has spearheaded various initiatives for faculty and leadership development at the cluster level and is a respected mentor among his peers. He played a pivotal role in establishing the NHG Residency Programme in 2009. A key member of the startup team, he helped design, implement and enhance the Programme's system, policies, and procedures to effectively guide residents, as well as create a conducive training environment for them. He was also instrumental in the development of a new training model for Postgraduate Year 1 (PGY1) medical students with the Accreditation Council for Graduate Medical Education-International (ACGME-I) in 2010.

A/Prof Chew was Designated Institutional Official (DIO) of the NHG Residency Programme between 2011 and 2018. Under his leadership, the Programme received national and international recognition for its quality and rigorous standards of training.

In 2015, A/Prof Chew was appointed NHG Group Chief Education Officer, overseeing the development and implementation of NHG Group Education strategies to reinforce NHG's population health mission. Striving to build a strong pipeline of future healthcare professionals, he has championed initiatives to advance leadership competencies and capabilities among staff, including improving inter-professional faculty development, and fostering a culture of Collective Leadership in the organisation.

A/Prof Chew inspires with his spirit of innovation. He helmed the launch of the NHG Training and Education Database (TEDBase) across NHG institutions in 2015, in order to improve the efficiency and accuracy of faculty information. He also led the implementation of the LEAP (Learning Evaluation & Assessment Platform) mobile application, which streamlines administrative processes and allows residents to monitor their own training progress.

At the national level, A/Prof Chew has collaborated extensively with international experts and the Ministry of Health (MOH) to introduce innovative development programmes for residency faculty members and the inter-professional community in Singapore. He continues to be actively involved in faculty and leadership development through workshops and conferences, both locally and internationally.

A/Prof Chew served as a member of the Joint Committee on Specialist Training from 2011 to 2015, Specialist Accreditation Board from 2011 to 2018, and Training and Assessment Sub-Committee for PGY1s. He contributed to the implementation of the National PGY1 Training and Assessment Framework and led a workgroup to restructure the PGY1 Training Assessments. He presently serves on the Psychiatry Residency Advisory Committee.

As Chairman Medical Board of Woodlands Health Campus (WHC), A/Prof Chew oversees the development of care strategies, clinical services, policies and governance. He advises on the planning and employment of medical staff, including training and development, as part of the institution's efforts to build a robust pool of competent clinicians to meet the needs of patients as WHC progressively opens from 2023.

For his inspiring dedication and exemplary contributions in advancing graduate medical education, A/Prof Chew is awarded the National Outstanding Clinician Educator Award 2020.

A/Prof Nicholas Chew Wuen Ming

Group Chief Education Officer
National Healthcare Group

Chairman Medical Board
Woodlands Health Campus

Senior Consultant
Department of Psychological Medicine, Tan Tock Seng Hospital

For his inspiring dedication and exemplary contributions in advancing graduate medical education.

National Outstanding Clinical Quality Champion Award 2020

**Dr Chow
Mun Hong**

**Senior Consultant
Director, Quality
Management
Chief Risk Officer**
*SingHealth
Polyclinics*

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

**Vice-Chair,
Strategy and
Innovation**
*SingHealth
Duke-NUS
Family Medicine
Academic Clinical
Programme*

Dr Chow Mun Hong has dedicated his professional career to improving patients' lives. In his 30-year medical career, he has nurtured generations of healthcare professionals in SingHealth Polyclinics (SHP), and instilled systemic improvements to ensure that improving patient care continues to be a key focus at SHP.

Dr Chow founded the SHP Quality Management Department in 2006 and built an integrated Quality Framework for work areas including clinical governance, quality assurance, patient safety, patient experience, enterprise risk management, improvement, and culture and capacity building.

He set up a system of multidisciplinary expert groups in various aspects of quality and safety, workgroups in various clinical fields, and Improvement Collaboratives that connected SHP-level Clinical Leaders and clinic-based improvement teams. This enabled every member of SHP to thrive in an integrated interdisciplinary system which emphasises institutional learning and knowledge management, governance and improvement.

Having great passion for transforming care delivery systems, Dr Chow spearheaded the design of the Clinical Information System that provided point-of-care decision support, generation of reports to support improvement, as well as registry-based views of patients to enable proactive patient monitoring. These functions were foundational to SHP's ability to consistently provide quality chronic disease management by multidisciplinary teams at high volumes. SHP's development of Telecare has also enabled them to transform from a reactive to proactive mode of care delivery, delivering care to patients even when they are not physically present at the clinics.

At the Singapore Healthcare Improvement Network (SHINe), Dr Chow co-chaired the National Curriculum Workgroup for Patient Safety and Quality Improvement (PSQI) that developed a common set of learning objectives for various topics on PSQI, and is currently the Co-Executive Lead for a Large-Scale Initiative on Transitions of Care that works on improving the safety and effectiveness of care transitions at various healthcare institutions across Singapore.

Dr Chow has been training Family Physicians and other healthcare professionals in Quality and Safety since 1999, and is committed to developing future generations of physicians. Each member of the SHP family participates in a Quality and Safety training framework developed by Dr Chow that guides them in skills development as they progress in their career. Many senior clinicians at SHP today remember the lessons they have learned and apply them now as leaders.

Concurrent to his role at SHP, Dr Chow served at SingHealth Headquarters as Director, Clinical Governance and Quality Management, and thereafter as Director, Innovation and Quality Management. He expanded the Quality and Safety training for all SingHealth Residents and other staff, and introduced Design Thinking as a complement to existing initiatives for improvement.

For his inspiring leadership, exemplary efforts in advancing system-wide quality and safety for patients, and commitment to developing healthcare professionals to ensure continuity across generations, Dr Chow is awarded the National Outstanding Clinical Quality Champion Award 2020.

For his inspiring leadership, exemplary efforts in advancing system-wide quality and safety for patients, and commitment to developing healthcare professionals to ensure continuity across generations.

National Clinical Excellence Team Award 2020

KK HUMAN MILK BANK PROGRAMME

> *For their outstanding contributions and achievements in establishing a national Donor Human Milk Bank programme for the benefit of premature and critically ill babies in Singapore.*

Clinical Asst Prof Chua Mei Chien

Head and Senior Consultant
Special Care Nursery and Department of Neonatology, KK Women's and Children's Hospital

Director, KK Human Milk Bank
KK Women's and Children's Hospital

Clinical Assistant Professor
Duke-NUS Medical School

Adjunct Assistant Professor
Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

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

Dr Agarwal Pooja Jayagobi

Consultant
Department of Neonatology, KK Women's and Children's Hospital

Clinical Assistant Professor
Duke-NUS Medical School

Clinical Teacher
Yong Loo Lin School of Medicine, Singapore

Adjunct Assistant Professor
Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

Ms Wong Anng Anng

Senior Milk Bank Coordinator, KK Human Milk Bank
KK Women's and Children's Hospital

The KK Human Milk Bank (KKHMB) was launched in August 2017, with an aim to provide a ready supply of safe pasteurised donor human milk (PDHM) for premature and critically ill babies with insufficient supply of their mothers' own milk. Breast milk is scientifically proven to be the best nutrition for all infants, especially for those born premature. The World Health Organisation and the American Academy of Paediatrics recommend the use of donor human milk as the first choice for preterm infant feeding after a mother's own milk.

KK Women's and Children's Hospital (KKH), Singapore's largest academic medical centre specialising in women's and children's health, is equipped with a 40-bed neonatal intensive care unit that serves the largest birth cohort in Singapore and manages neonates with the most complex medical and surgical conditions. Recognising that the exclusive use of human milk in very low birth weight (VLBW) infants averaged only 11.5% over the past 12 years, and the important role of human milk in reducing necrotising enterocolitis (NEC)[7], the team planned to set up the first and only donor human milk bank in Singapore.

Due to the lack of local and regional expertise in donor human milk banking, the team went on a study trip to the Perron Rotary Express Milk Bank in Western Australia to attain the necessary knowledge and skills required. With support from Temasek Foundation, careful planning of the supply chain process, as well as the infrastructure set-up based on international best practices, KKHMB was thus established.

As of 30 September 2020, KKHMB has recruited 691 donors and benefited more than 1,844 recipients. The exclusive use of human milk in the vulnerable neonatal population in KKH has increased dramatically from the baseline of less than 20%, to 97%. More importantly, the incidence of NEC has reduced drastically from 5.8% in VLBWs to no cases in 2018. This has helped to significantly reduce total medical bill sizes, as well as the length of hospital stay of these patients.

Since its launch, the KKHMB has garnered strong public support with many mothers coming forward to donate their excess breast milk. Mothers of recipients report a better sense of well-being knowing that PDHM offers better outcomes for their babies. With the milk bank working closely with the lactation service in the hospital, mothers of recipients also feel better supported in their endeavour to breastfeed, with many managing to increase their own milk supply.

Beyond Singapore, KKHMB has received regional interest to understand more about the effective establishment of such a programme. With the success of KKHMB, an additional grant from Temasek Foundation was secured in July 2019, enabling the milk bank to grow its capacity to provide PDHM to patients up to 12 months of age with a broader range of medical conditions, and even after hospital discharge.

For their outstanding contributions and achievements in establishing a national Donor Human Milk Bank programme for the benefit of premature and critically ill babies in Singapore, the KK Human Milk Bank team is awarded the National Clinical Excellence Team Award 2020.

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7. Necrotising enterocolitis is a lethal gut condition where instestines become damaged due to tissue death, leading to potential severe illness and even death of babies. It is primarily seen in premature infants, and is potentially life-threatening, with survivors suffering from possible long-term health issues associated with poor growth and cerebral palsy.

NMRC AWARDS CEREMONY AND RESEARCH SYMPOSIUM 2019

In 2019, the NMRC Awards Ceremony and Research Symposium were held concurrently as a 1.5-day event that attracted more than 400 clinician scientists, researchers, industry partners and other key players in the biomedical research field. The event, held at One Farrer Hotel on 3 and 4 April 2019, recognised outstanding clinicians and researchers for their achievements and contributions to the field, and provided a useful platform for interaction amongst individuals from healthcare institutions, academia and industry.

In addition, the event marked the Silver Jubilee of NMRC as the Council was formed under the MOH in 1994. Themed "Research for a Better Future", NMRC hoped that the event would provide the opportunity to foster stronger collaborations towards research excellence, and improved healthcare and economic outcomes for a better future.

Awards Ceremony

The NMRC Awards Ceremony served to recognise awardees under the NMRC Human Capital and Talent Development Programmes, as well as the remarkable efforts and contributions of past and current NMRC Chairmen as part of the Council's 25th Anniversary celebration. Awardees who received the STaR Investigator Award, CSA, TA, MOH Healthcare Research Scholarship – MCI and NMRC Research Training Fellowship were honoured, with then Minister for Health Mr Gan Kim Yong as the Guest of Honour for the Ceremony.

NMRC was also privileged to invite four eminent overseas experts, Professor Ashok Venkitaraman, Director of Medical Research Council Cancer Unit at the University of Cambridge, Professor Nir Barzilai from the Albert Einstein College of Medicine, Professor Ray Chaudhuri, Clinical Director of National Parkinson Foundation Centre of Excellence, King's College London, and Dr David K. Henderson, Deputy Director for Clinical Care at the National Institutes of Health Clinical Centre. They shared their experience and insights in the area of cancers, ageing/diabetes mellitus and related metabolic/endocrine disorders, neurological disorders and infectious diseases respectively.

Research Symposium

A platform to promote and inculcate the spirit of translational clinical research in Singapore's biomedical and healthcare research landscape, the Research Symposium featured outstanding clinician scientists and showcased the various research projects funded by NMRC grant programmes. Discussions on the various aspects of biomedical research were also facilitated, with participants having a chance to visit exhibition booths put up by the NHIC, SCRI, Diagnostics Development Hub, Singapore Biodesign, Experimental Drug Development Centre and College of Clinician Scientists during the event.

On Day One, concurrent sessions took off after the Awards Ceremony with parallel sessions on Cancers and Cardiovascular Diseases, followed by a combined session on Clinical Research and Industry. The day concluded with a wine and cheese reception, providing a comfortable platform for industry, clinical and research community participants to network, exchange knowledge and explore collaboration opportunities after the forum discussions.

On Day Two, the symposium continued with parallel sessions on diabetes mellitus and related metabolic/endocrine disorders, neurological and sense disorders, infectious diseases and health services research. The parallel sessions covered over the 1.5 days of the Symposium addressed key strategic research areas in which NMRC anticipates to further strengthen translational biomedical research, featuring a total of 32 local and overseas experts in the sessions.

HEALTH AND BIOMEDICAL SCIENCES INTERNATIONAL ADVISORY COUNCIL (HBMS IAC) MEETING 2020

From 17 to 19 August 2020, Singapore's HBMS IAC held its annual meeting via a video conference call, which comprised an opening plenary, four deep dives into high-priority topics and a closing plenary.

Chaired by Sir Richard Sykes, the meeting focused on seeking the IAC's advice and suggestions on the RIE2025 Plan for the new HHP domain, in particular the proposed HHP RIE2025 goals to Transform and Protect Health, Maximise Economic Value and Advance Human Potential, and the corresponding strategies and key thrusts for these.

The IAC commended the proposed HHP RIE2025 strategic framework and supported the addition of Human Potential to its scope, noting that many of the elements needed to accomplish HHP's RIE2025 vision were already present in Singapore, including the robust base of HBMS Research & Development (R&D) capabilities, strong governance and the promising growth in biotech and medtech startups and companies.

With regard to Transform and Protect Health, the IAC endorsed the goal of making data a key differentiator and strongly affirmed the importance of data as a major driver of the HHP RIE2025 strategic framework. The IAC was supportive of the diversification of talent schemes to support other types of clinician scientists (CSs) in the areas of Health Technology and Population Health/Health Services Research. They also highlighted the need to bring in talent from other disciplines (e.g. data science, artificial intelligence and bioengineering) to transform health and to expand the scope of the schemes supporting CSs to actively encompass other healthcare professions such as nurses and pharmacists.

On the impact of COVID-19 on HHP RIE2025 strategies, the IAC supported the proposed establishment of a national R&D programme for epidemic preparedness and response, and highlighted the importance of maintaining sustained and long-term funding to prepare Singapore for the next epidemic, as well as the value of building local last-mile capabilities during peace time that could be quickly activated or repurposed for pandemics.

Moving ahead into RIE2025, NMRC looks forward to working with its partners in the research community to build on the good progress in RIE2020. We will continue to develop and maintain mechanisms to further enable the translation of research outputs into real-world applications and value capture, so as to position us well to transform and protect the health of Singaporeans.

CHARTING AHEAD WITH RIE2025

The Next Five Years of Advancing Singapore's RIE Objectives

Overview of the RIE2025 Framework

RIE remains a cornerstone of Singapore's development into a knowledge-based, innovation-driven economy and society. It is a key enabler in creating new avenues of growth and raising Singapore's economic competitiveness. It also generates scientific breakthroughs that meet our societal needs, and improves the lives of Singaporeans.

For RIE2025, Singapore will emphasise three strategic focus areas to build on the progress achieved in the past RIE plans and create greater value from our RIE investments:

i. Expand the RIE mission to tackle a broader spectrum of national needs;
ii. Enrich our scientific base; and
iii. Scale up platforms to drive technology translation and strengthen the innovation capabilities of our enterprises.

Singapore's RIE2025 efforts will be organised along four strategic domains, and supported by three cross-cutting horizontals:

Manufacturing, Trade and Connectivity (MTC)
Leveraging R&D to reinforce Singapore's position as a global business and innovation hub for advanced manufacturing and connectivity

Human Health and Potential (HHP)
Better transform and protect health, advance human potential and create economic value for Singapore

Urban Solutions and Sustainability (USS)
Renew and build a liveable, resilient, sustainable and economically vibrant city for tomorrow

Smart Nation and Digital Economy (SNDE)
Develop technology leadership to drive our Smart Nation ambition, and anchor Singapore's position as a trusted digital innovation hub

Academic Research
Build a robust base of research capabilities and peaks of international excellence

Manpower
Nurture a strong research and innovation talent pipeline

Innovation and Enterprise
Accelerate enterprise innovation

RIE2025 Budget

The Singapore government will sustain investments in research, innovation and enterprise at about 1% of Singapore's GDP from 2021 to 2025 for RIE2025, about $25 billion, to reflect the government's sustained and long-term commitment to R&D through economic cycles.

White Space
$3.75B set aside for agility; support new programmes to respond to future needs and emerging opportunities

15%

Mission-Oriented Research
$6.5B to support the expanded missions of RIE domains

26%

Talent Development
$2.2B for postgraduate programmes, I&E talent development

9%

$25 BILLION

21%

$5.2B to establish new I&E platforms, strengthen enterprise innovation capabilities, and develop entrepreneurial talent

Dedicated Innovation & Enterprise Activities

29%

$7.3B to strengthen our core capabilities in universities and A*STAR Research Institutes

Core Capabilities in Universities and A*STAR Research Institutes

Envisioning the Future in Human Health and Potential (HHP)

The HHP domain has its origins in the Singapore BMS initiative, which was launched in 2000 to develop the life sciences as a pillar of Singapore's economy. Its initial focus was on establishing strong biomedical research capabilities, critical human capital and research infrastructure. Subsequently, there was a greater focus on translational and clinical research to derive both health and economic outcomes.

Under the RIE2020 plan, the BMS efforts were driven under the HBMS domain. Its key strategies included focusing on five disease areas with higher prevalence in Singapore and Asia (including various cancers and cardiovascular diseases); establishing new pathways to support the translation of research discoveries into improved health outcomes and economic value; and developing a vibrant Innovation and Enterprise (I&E) ecosystem for pharmbio and medtech.

HHP Vision

In RIE2025, the HHP domain will build on our existing HBMS capabilities and incorporate a new emphasis on furthering human potential. Our vision is to make Singapore a leading hub that transforms and protects health, advances human potential and creates economic value through excellence in research and its application for Singapore, Asia and the world.

HHP Strategy at a Glance

1. Transforming and Protecting Health

With our rapidly ageing population and rising chronic disease burden, a fundamental shift towards health promotion and disease prevention is critical, and individuals need to be empowered to better manage their own health and chronic conditions.

We will seek to support a more data-driven and patient-centric health system to deliver value-based care, by developing the innovative use of technology and digital solutions at scale. Additionally, we will expand our National Precision Medicine (NPM) research programme, and develop the infrastructure and capabilities to use data in a trusted, confidential and secure way for better health outcomes.

2. Maximising Economic Value

Smaller-scale biotech companies, supported by global venture capital, are the new engines of innovation. Multinational pharmaceutical corporations have adopted new models to build their therapeutic pipelines. In the same vein, we aim to grow a vibrant mix of startups and scale-ups in Singapore, with a strong clinical translational ecosystem that provides multiple effective pathways to rapidly bring innovations to market.

We will also further strengthen our major I&E platforms and enablers, enhance public and private sector I&E financing, and harness bio-accelerators to strengthen the local ecosystem for users such as startups, clinicians, researchers and companies.
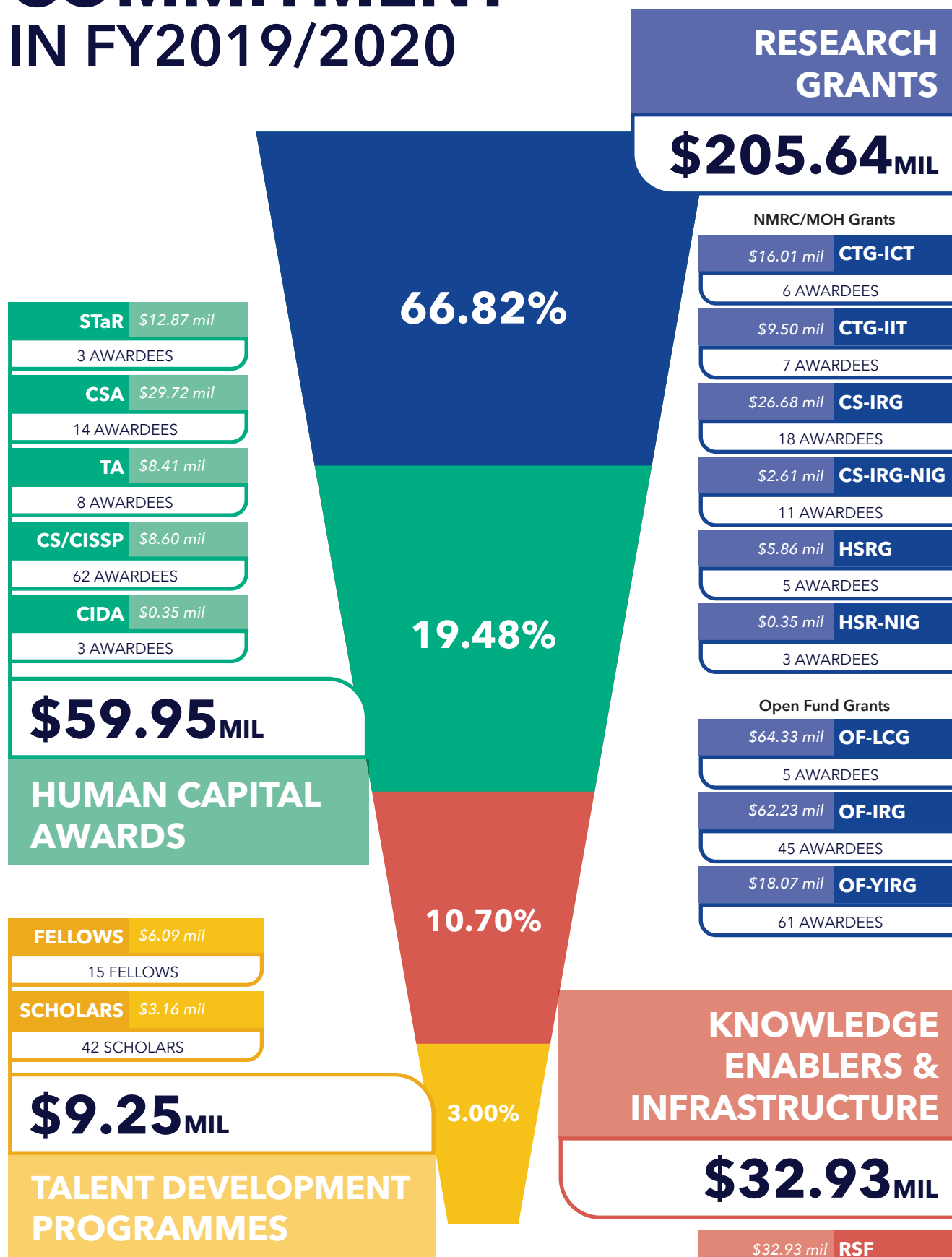
3. Advancing Human Potential

Advancing human potential is absolutely critical for Singapore, as human capital is our principal and most valuable resource. We will drive R&D and translation activities to support improvements in health, productivity and learning capacity across an individual's life course.

We will build on our existing research strengths in prenatal and early childhood development, to identify, pilot and evaluate evidence-based interventions that may improve long-term health and learning capacity, with effective interventions progressively scaled. In addition, we will build on the Science of Learning initiative and neurocognitive science research to support programmes that improve learning outcomes for children and promote re-skilling in adult workers. We will also expand basic and translational research in healthy longevity to benefit older Singaporeans, and build on existing research capabilities in disease prevention, cognitive health, regenerative medicine, nutrition and rehabilitation.

For more information, please refer to the RIE2025 Handbook at https://www.nrf.gov.sg/rie2025-plan.

OVERVIEW OF FUND COMMITMENT
IN FY2019/2020

RESEARCH GRANTS

$205.64MIL

66.82%

NMRC/MOH Grants

$16.01 mil	**CTG-ICT**
6 AWARDEES	
$9.50 mil	**CTG-IIT**
7 AWARDEES	
$26.68 mil	**CS-IRG**
18 AWARDEES	
$2.61 mil	**CS-IRG-NIG**
11 AWARDEES	
$5.86 mil	**HSRG**
5 AWARDEES	
$0.35 mil	**HSR-NIG**
3 AWARDEES	

Open Fund Grants

$64.33 mil	**OF-LCG**
5 AWARDEES	
$62.23 mil	**OF-IRG**
45 AWARDEES	
$18.07 mil	**OF-YIRG**
61 AWARDEES	

19.48%

STaR	$12.87 mil
3 AWARDEES	
CSA	$29.72 mil
14 AWARDEES	
TA	$8.41 mil
8 AWARDEES	
CS/CISSP	$8.60 mil
62 AWARDEES	
CIDA	$0.35 mil
3 AWARDEES	

$59.95MIL

HUMAN CAPITAL AWARDS

10.70%

FELLOWS	$6.09 mil
15 FELLOWS	
SCHOLARS	$3.16 mil
42 SCHOLARS	

$9.25MIL

TALENT DEVELOPMENT PROGRAMMES

3.00%

KNOWLEDGE ENABLERS & INFRASTRUCTURE

$32.93MIL

$32.93 mil	**RSF**

Figures presented reflect funding committed in the FY and grant calls completed by the time of print. For the other KE&E initiatives, funding for the tranche has been committed at the time of award.