



**DRIVING EXCELLENCE IN**

# HEALTHCARE RESEARCH

Annual Report 2015





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# MESSAGE FROM CHAIRMAN

## ADVANCING SINGAPORE'S HEALTHCARE NEEDS

We are in the midst of a transition to the next five-year phase of the Research, Innovation and Enterprise (RIE) Plan. The RIE Plan has been instrumental in helping Singapore establish its firm footing as a world-class R&D hub. Moving on from RIE2015, RIE2020 will provide Singapore the strategic direction to make greater strides in addressing national needs and global opportunities.

Under RIE2020, NMRC will reinforce its commitment to help healthcare institutions leverage these opportunities by facilitating the translation of excellent research into impactful outcomes. With the increased funding, we will be better positioned to support and coordinate translational and clinical research (TCR), and contribute towards Singapore's health and wealth outcomes.

NMRC has, through its strategic funding and resource-sharing initiatives, greatly increased its support of clinician scientists and investigators. This has led to high quality translational research in Singapore. The fruits of our labour have begun to show through the development of new therapeutics and diagnostics, especially for cancer and infectious diseases. The academic medical centres: National University Health System and SingHealth Duke-NUS Academic Medical Centre, are also flourishing.

The establishment of our National Health Innovation Centre (NHIC) has, in a very short span of time, fostered interest in commercialisation of medical discoveries and technologies from individuals across the healthcare sector and fostered numerous collaborations between institutions and industry. NHIC has been an effective vehicle to translate discoveries into real-world innovations that address unmet healthcare needs.

## SEIZING GLOBAL R&D OPPORTUNITIES

Each stride forward on the global R&D stage brings not only great challenges, but also extraordinary opportunities for Singapore. Health systems in Singapore and around the world are stressed by increasing needs and burgeoning costs. There is an increased focus on evidence-based practice and proper application of R&D knowledge to facilitate better healthcare. Emerging technologies, such as big data and precision medicine, are demonstrating utility in the care of patients.

NMRC will play an increasingly pivotal role in helping Singapore leverage these opportunities to build capabilities in health services research, advance evidence-based research, and accelerate healthcare innovations. Through its TCR programmes, NMRC will remain focused on seeding research in areas which are of strategic importance to Singapore.


As we look back at RIE2015 and chart ahead with RIE2020, I am glad to invite my predecessors and previous Executive Directors to share their personal stories and insights on the future of biomedical research. Their outstanding leadership and commitment to NMRC's vision and mission contributed immensely to what NMRC is today.

NMRC will intensify its engagement and collaboration with various stakeholders to ensure that Singapore can better capitalise on emerging R&D opportunities, while setting the stage towards achieving the new goals under RIE2020. I am confident that our investments will continue to bring health and wealth benefits to the Singaporean community.

“ With the increased funding, we will be better positioned to support and coordinate translational and clinical research, and contribute towards Singapore’s health and wealth outcomes. ”



**Professor  
Ranga Krishnan**  
Chairman



“ NMRC, together with MOH, has identified five therapeutic areas of focus for translational research ... (to be) ... emphasised in our grant funding. ”

**Ms Tricia  
Huang**  
Executive  
Director

# MESSAGE FROM EXECUTIVE DIRECTOR

## GROWING THE RESEARCH ECOSYSTEM

It has been an impactful year in NMRC's continuing drive to advance excellent, innovative medical research to improve health outcomes. NMRC was instrumental in spearheading many of the Biomedical Sciences (BMS) initiatives under Singapore's Research, Innovation and Enterprise (RIE) 2015 Plan.

Having succeeded A/Prof Tan Say Beng as Executive Director of NMRC in July 2015, I was naturally grateful to have inherited a great team that successfully implemented many of the key BMS programmes, including competitive grants, talent development awards, as well as enabling infrastructure.

We have made significant achievements under RIE2015. In the last five years, we have grown the healthcare research ecosystem through \$886.4 million in project grants, \$157.5 million in infrastructure grants, and 210 talent and manpower awards. To develop a globally competitive research talent pool, we have since supported 106 national clinician-scientists with our Human Capital Awards.

More importantly, our programmes, such as the TCR Flagship and Bedside & Bench grants, have helped bring the basic science and clinical research communities closer together. This puts us in a much stronger position to collaborate for impact under the new Research, Innovation and Enterprise (RIE2020) Plan, which commenced on 1 April 2016.

## SHAPING THE FUTURE OF HEALTH

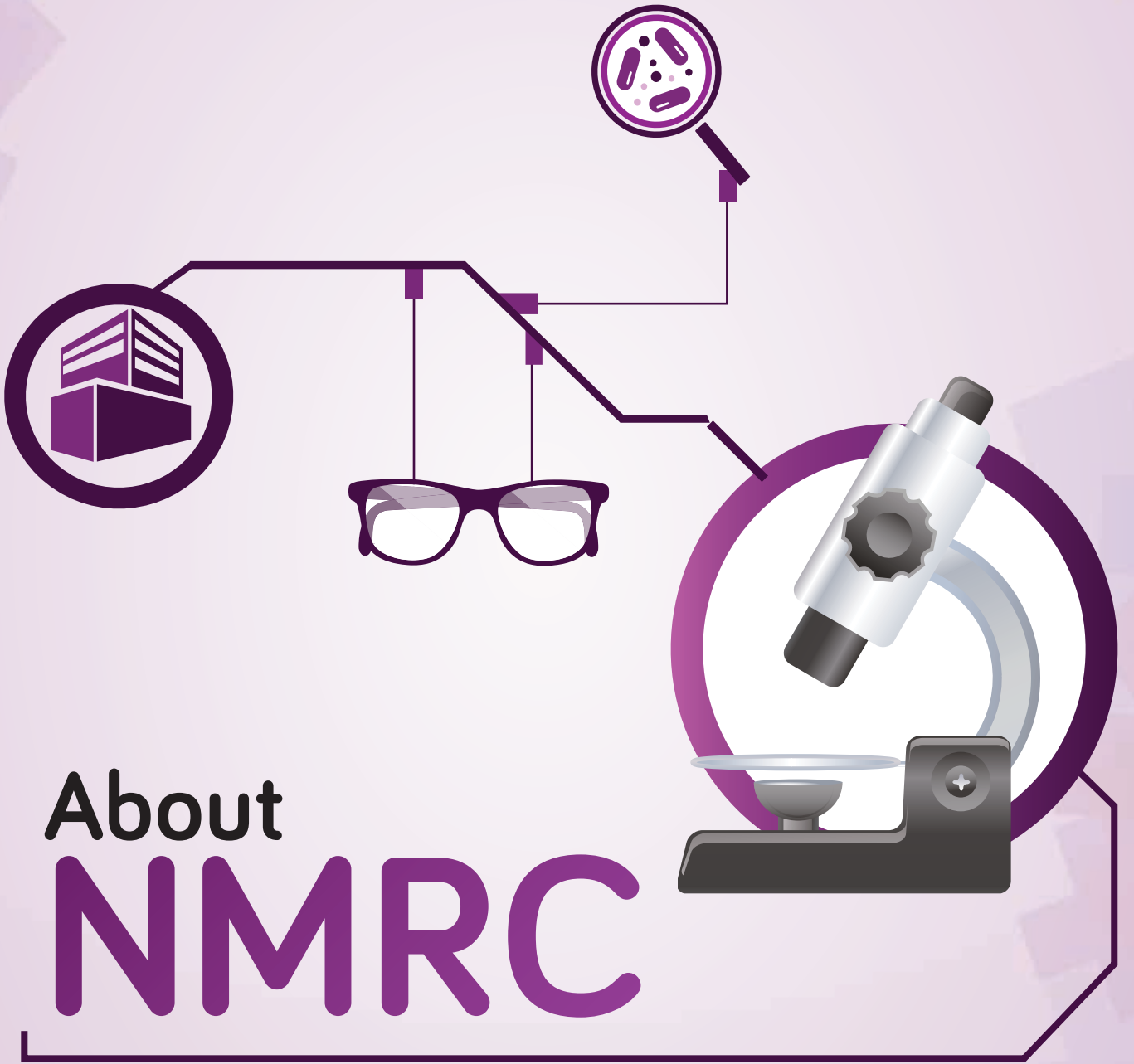
The emphasis on 'health' in RIE2020 is clear, with the renaming of BMS to Health and Biomedical Sciences (HBMS), and the allocation of \$4 billion to HBMS – the biggest share of RIE2020's \$19 billion budget. It provides us and our partner agencies, including A\*STAR, EDB and NRF, as well as the entire biomedical and clinical research community, greater impetus to translate groundbreaking research into solutions that address Singapore's health challenges.

In the next five years, we will also be expanding the role of the National Health Innovation Centre (NHIC) beyond the commercialisation of medical research in healthcare clusters. NHIC will be able to facilitate the translation of medical research funded by NMRC into new knowledge, products and solutions that can transform clinical practice and benefit patients.

NMRC, together with MOH, has identified five therapeutic areas of focus for translational research: cancers, cardiovascular diseases, diabetes, infectious diseases, and neurological and sense disorders. These will be emphasised in our grant funding.

Lastly, we strongly encourage the medical research community to participate in research on Health Services and Health Systems, and Population Health. Both research programmes aim to improve the accessibility, quality and cost of Singapore's health services.

It is a privilege for us to work with and serve the HBMS communities in Singapore. Our work would not have been possible without strong support from the leadership and colleagues in MOH, the NMRC Board, the healthcare community, and our partner agencies and stakeholders. Together, we will make RIE2020 a success.



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.

Under the Research, Innovation and Enterprise 2015 (RIE2015) Plan was on the greater integration of activities across the entire Biomedical Sciences (BMS) community, including the private and private sector performers, hospitals and government agencies. NMRC continued to spearhead these investments to realise long-term health and wealth outcomes.

As 2015 drew to a close, Singapore will see continued support to research, with an increase in investment from \$16 billion for the RIE2015 Plan to \$19 billion in the

RIE2020 Plan. Funding will be prioritised in four strategic technology domains where Singapore has competitive advantages and/or important national needs, including Health and Biomedical Sciences (HBMS). NMRC is one of the beneficiaries of this boost in funding, reinforcing the Council's mandate as the champion for translational and clinical research in Singapore

NMRC spearheads MOH's vision for healthcare research to deliver better health and wealth outcomes for Singaporeans. Five therapeutic areas of focus have been identified by MOH which NMRC will complement the top-down directed strategic research by funding research proposals received by the various competitive grants and awards administered. In 2013, the National Health Innovation Centre (NHIC) was established to coordinate across the industry cluster to support a vibrant ecosystem comprising local enterprises, start-ups and multinational corporations.

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

# NMRC BOARD

## BOARD MEMBERS

The NMRC Board advises the Council on the formulation of strategies and priorities to promote excellence in translational and clinical research in Singapore with the objective of improving human health. By overseeing the implementation of the research programmes approved by MOH and the BMS Exco, the Board ensures that the Council is being effectively managed to meet its mission and key performance targets. The Board also ensures that governance frameworks are in place, such that NMRC's budget is appropriately managed and optimally utilised.

In FY16, the NMRC Board consists of 18 members.



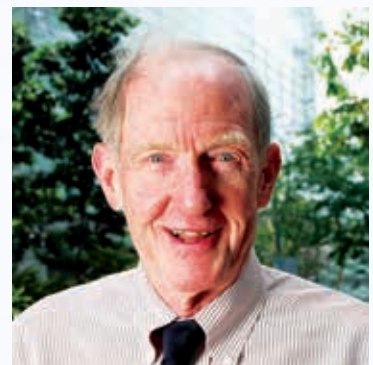
**Prof Ranga Krishnan**

*Chairman,  
National Medical Research Council*



**Ms Tricia Huang**

*Executive Director,  
National Medical Research Council*



**Prof Edward Holmes**

*Advisor,  
National Research Foundation*



**Prof Ivy Ng**

*Group Chief Executive Officer,  
SingHealth*



**A/Prof Benjamin Ong**

*Director of Medical Services,  
Ministry of Health*



**Dr Anand Tharmaratnam**

*President (Asia Pacific),  
QuintilesIMS*



**Prof John Wong**

*Chief Executive,  
National University Health System*



**Prof James Best**

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



**Dr Cheong Wei Yang**

*Deputy Chief Executive Officer,  
National Research Foundation*



**Prof Chong Siow Ann**

*Vice Chairman of Medical Board  
(Research),  
Institute of Mental Health*



**A/Prof Chong Yap Seng**

*Executive Director,  
Singapore Institute for Clinical  
Sciences*



**Prof Thomas Coffman**

*Dean,  
Duke-NUS Medical School*



**Prof Ian D. Graham**

*Professor,  
School of Epidemiology,  
Public Health and Preventive  
Medicine, School of Nursing,  
University of Ottawa*



**Prof Lim Tock Han**

*Deputy Group CEO (Education &  
Research),  
National Healthcare Group  
Singapore*



**Prof Peter Piot**

*Director & Handa Professor of  
Global Health,  
London School of Hygiene &  
Tropical Medicine*



**Dr Benjamin Seet**

*Executive Director,  
Biomedical Research Council,  
A\*STAR*



**Prof Wong Tien Yin**

*Medical Director,  
Singapore National Eye Centre*



**A/Prof Yeoh Khay Guan**

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

# LOOKING BACK

## A MOMENTOUS JOURNEY OF GROWING SINGAPORE'S RESEARCH INITIATIVES

NMRC is in the midst of a transition between RIE2015 and RIE2020. With RIE2015 drawing to a close, an opportune time has come for us to reflect upon the achievements and impact that NMRC has made in support of clinical research and the larger HBMS landscape.

We have invited our executive leaders past and present to share their reflections on their illustrious journey with NMRC, as well as their hopes and vision for the future of research.

### **PROF LIM YEAN LENG** **CHAIRMAN OF NMRC (2000 - 2003)**

I could vividly remember how my tenure as Chairman of NMRC began in 2000 at the cusp of Singapore's foray into biomedical research. Three Ministries, namely Education, Health, and Trade and Industry, had combined resources to spearhead and steer its development.

A Life Sciences Executive Committee, comprising the world's leading scientists from the USA, Europe and Australia, was established. I represented NMRC in this Committee to bring Singapore's biomedical research to the world stage.

One of my first key challenges as Chairman was to introduce the tracking of outcomes for awarded grants. My vision was to bring NMRC from an administrator of research applications and grant awards to an advocate that drives the translation of excellent biomedical research into health and wealth outcomes for Singapore. With the support of the Council and scientific sub-committee, we established a robust database of international standards to monitor all awarded research grants and their outcomes.

The initiative was successful and led to increased, consolidated funding for biomedical research from the Singapore government.

Furthermore, the completion of the Biopolis, conceived in the early 2000s, saw many multi-national pharmaceutical and medical device companies relocate their headquarters to Singapore. With this boost to Singapore's profile as a global hub of research excellence, NMRC's role in coordinating world-class translational and clinical research in Singapore could only become more important to the nation's economic success.

I am confident that NMRC can continue to elevate Singapore's prominence in the global biomedical research arena.



## **PROF WOO KENG THYE** **CHAIRMAN OF NMRC (2003 - 2006)**

Talent is the key to the success of any research initiative, and thus NMRC's top priority since its inception. But Singapore's achievements in growing its dedicated pool of research talent could not have been unlocked without collective effort from the National Research Foundation (NRF). Its establishment in 2006 helped boost the infrastructure and funding to attract top scientists and clinicians to sink roots into our rapidly flourishing Biopolis.

I am proud to say that our scientists and clinician scientists now number among the best in terms of their achievements with publications, patents and inventions. They are sought after for their skills and expertise in numerous collaborative projects locally and overseas. Encouragingly, their industrial prowess has enabled our biomedical industry to maintain a steady stream of profit. These more than justify Singapore's spending and investment in biomedical research over the years.

Singapore continues to present top opportunities for our scientists, clinician scientists and technical experts. Many have found their firm footing in lucrative partnerships and startup companies, and even more are benefiting from the relocation of large-scale clinical trials involving giant pharmaceutical companies to Singapore's Industrial Parks.

Ensuring that we sustain our own pipeline of research talent is crucial for Singapore's continuing success in biomedical research. As we work towards achieving our target number of 160 national clinician scientists, we must ensure that they are retained in the system and their numbers remain adequate for the future.

I am hopeful that, with the stewardship of NMRC, NRF and other lead agencies, biomedical research in Singapore to continue to flourish and create economic impact in the years to come.



## **DR EDWIN LOW** **EXECUTIVE DIRECTOR OF NMRC (2006 - 2011)**

As NMRC's first Executive Director, I had the good fortune to work alongside Prof Edward Holmes, our first Executive Chairman. It was a challenging yet exciting direction for us, as NMRC expanded its role with the incorporation of clinical research as part of MOH's mandate.

New grant schemes were needed then to fund initiatives and promising research in translational and clinical research (TCR). With the \$550 million committed by the NRF and MOH over five years, we proceeded to set up new grants. These include the TCR Flagship Programme and the Clinician Scientist Awards.

A key challenge for us was to ensure that existing grant schemes such as Individual Research Grants and Fellowship awards were not unduly affected. This could not have been possible without the great team that we had built up over the first two years, as well as support from the BMS EXCO leadership.

We were also grateful for the opportunity to take on many interesting projects, including the transition of Block Grants to Centre Grants, the revamp of the grant review process and the development of the new national electronic grant management system. With the increase in our staff strength, we moved to our new premises at Biopolis - one that we proudly sourced for and designed.

I am heartened to see that the culture of collaboration amongst local researchers has strengthened over time, in part fostered through the many grant frameworks. It is also great to see how the critical mass of clinician scientists has grown nationally and how the two Academic Medicine Centres have matured over the years. Much will depend on the collective ability of NMRC and the AMCs to continue to grow and develop this talent pool through grants, mentoring and good career development.



## **PROF EDWARD HOLMES** **EXECUTIVE CHAIRMAN OF NMRC (2006 - 2010)**

It was exceptionally fulfilling to work hand-in-hand with Dr Edwin Low in growing the role of NMRC and contributing to the growth of Singapore as a world-class translational research centre.

Singapore has experienced extraordinary growth in the HBMS ecosystem following the government's decision to make this an area of emphasis 15 years ago. With the shift to focus on translational and clinical research in 2005, the HBMS ecosystem ascended new heights through the internationally competitive TCR programme that NMRC has these been instrumental in shaping, managing and funding.

To date, Singapore has developed a strong cadre of clinician scientists and clinician investigators; implemented a competitive set of grant schemes to support promising research; built and equipped state-of-the-art infrastructure; established two Academic Medical Centres; and launched two new medical schools. Few countries can claim such progress in the span of only 10 years.

With its excellent infrastructure, resources and talent, Singapore is making its name on the global stage as a world-class translational research centre. One area in which Singapore is particularly well-positioned to carve out a niche for itself is in the study of diseases affecting Asian populations – an emphasis of the HBMS domain in RIE2020. These can range from infectious diseases prevalent in the region to cancers that are particularly common among Asians.

Our work at NMRC is never done as global competition in translational and clinical research becomes ever more intense. I am certain that the efforts of everyone at NMRC will help the HBMS domain deliver even more in the way of health and economic returns for Singapore in the next 10 years.



## **A/PROF TAN SAY BENG** **EXECUTIVE DIRECTOR OF NMRC (2011-2015)**

The growth and development of NMRC has mirrored that of the national BMS initiative. When NMRC was formed in 1994, it administered a relatively modest budget of about \$80 million over three years. This was nevertheless a significant amount of funding. With the increased emphasis on TCR under the S&T2010 and RIE2015 funding tranches, NMRC's influence and ability to make a real difference in supporting research in the healthcare family also grew.

I had the privilege of serving as Executive Director of NMRC during much of the RIE2015 period. It was an exciting time for NMRC as we started to see impactful outcomes arise from initiatives such as the TCR Flagship Programme and the STaR Investigator Awards. RIE2015 also saw the establishment of important new initiatives, including a dedicated clinical trials grant scheme and a revamped Centre Grant Programme.

Within NMRC, there were also important organisational changes that took place during this period. In particular, MOH's research strategy and policy functions were consolidated within NMRC, along with the administration of the Health Services Research (HSR) Grant. These developments facilitated the formulation of the first ever MOH Healthcare Research Strategy, which in turn influenced the national RIE2020 HBMS strategy of increased emphasis on HSR and the identification of priority disease areas for research.

With the transition to RIE2020, NMRC remains a critical stakeholder in the HBMS landscape. Researchers, particularly in the healthcare system and medical schools, depend more than ever on NMRC to provide the necessary leadership and support to champion research and ensure that the HBMS initiative is able to deliver its potential of generating health and wealth benefits for Singapore.



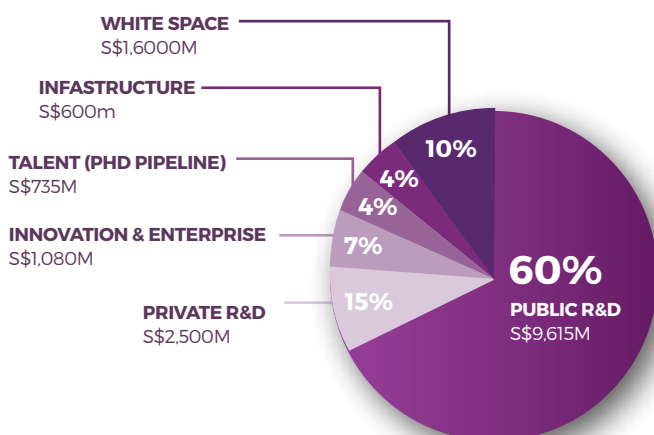
## OVERVIEW OF RIE2015 FRAMEWORK (FY2011 - FY2015) ADVANCING HEALTH AND WEALTH BENEFITS FOR SINGAPORE



Public investment in research and innovation continues to grow, as Singapore progresses into an innovation-driven, knowledge-based economy and society.

Under the RIE2015 Plan<sup>2</sup>, \$16.1 billion had been committed from 2011 to 2015 to advance the human, intellectual and industrial capital necessary to establish Singapore as a world-class R&D hub. This marked a 20% increase from the \$13.6 billion allocated between 2006 and 2010.

### RIE2015 PORTFOLIO



#### RIE2015 had six key thrusts:

1. Continued investment in new knowledge and ideas
2. Continued emphasis on the attraction and development of scientific talent
3. Greater emphasis on competitive funding
4. Greater synergies across various R&D performances
5. Larger proportion of R&D focused on economic outcomes
6. Strengthened support for commercialisation of basic research

A \$1.6 billion White Space fund was also introduced under RIE2015. Accessible to all agencies, the new fund provided Singapore the leverage to respond more swiftly to emerging opportunities and challenges during the five-year period.

Boosted by RIE2015, NMRC's funding commitment to develop Singapore's research talent pipeline had also grown from just \$94.3 million in 2010 to \$353.3 million in 2014.

<sup>2</sup> RIE Secretariat, MTI (2011). Research, Innovation, Enterprise 2015: Singapore's Future. Retrieved from <https://www.mti.gov.sg/ResearchRoom/Documents/app.mti.gov.sg/data/pages/885/doc/RIE2015.pdf>



## NMRC'S FUNDING PORTFOLIO UNDER RIE2015 - AT A GLANCE



### ENABLERS & INFRASTRUCTURE

- CBmE
- SCRI
- IMUs
- IRBs
- Research Space Funding



### RESEARCH GRANTS

#### Strategic/Thematic Research

- TCR Flagship
- CG
- CTG
- MOH-IAF

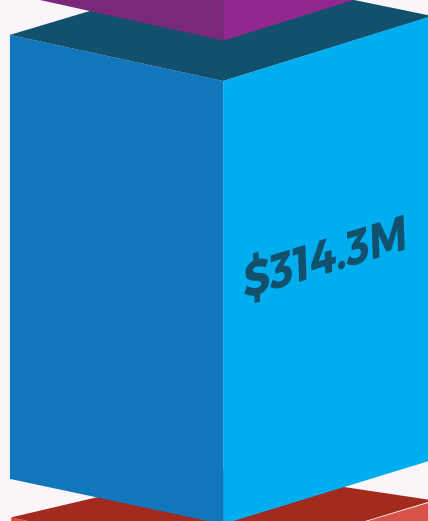
#### Investigator-Led Research

- CS-IRG
- HSRG
- CBRG
- NIGs (CS-IRG-NIG, CBRG-NIG, HSR-NIG)
- B&B



### TALENT DEVELOPMENT PROGRAMMES

- NMRC Research Training Fellowship
- MOH Healthcare Research Scholarships (PhD & MCI)



### HUMAN CAPITAL AWARDS

- STaR
- CSA
- TA
- CS/CISSP





HUMAN CAPITAL AND 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 Scientist/Investigator Salary Support Programme (CS/CISSP)
- **Talent Development Programmes**
  - MOH Healthcare Research Scholarship (PhD)
  - MOH Healthcare Research Scholarship – Master of Clinical Investigation (MCI)
  - NMRC Research Training Fellowship

## HUMAN CAPITAL AWARDS

### Singapore Translational Research (STaR) Investigator Award

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

### Clinician Scientist Award (CSA)

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

### Transition Award (TA)

The Transition Award is designed to help budding clinician scientists who have just completed formal research training. This award provides research funding and salary support to help recipients build up their research capabilities by facilitating their transition to a stable, independent research position, which in turn will enhance their ability to successfully obtain independent research support later on. The Transition Award is non-renewable, as awardees are encouraged to apply for national-level independent research grants after they have completed this award.

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

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

### Achievements under the RIE2015 Tranche

Name of Award	No. of Awards	Funding Allocation (\$ mil)
STaR Investigator Award	14	129.50
Clinician Scientist Award	47	104.64
Transition Award	46	45.87
CS/CISSP	151	34.31

# HUMAN CAPITAL AWARD RECIPIENTS 2015



## SINGAPORE TRANSLATIONAL RESEARCH (STAR) INVESTIGATOR AWARD RECIPIENTS

Results of recent clinical studies have unequivocally demonstrated that immune cells can be used to treat cancer. Our objective is to develop new ways to improve the anti-cancer capacity of immune cells and bring these technologies to the clinic. Research supported by the STaR Investigator Award started in August 2011. It produced 6 peer-reviewed articles, 5 clinical trials, 3 patent applications and the funding of a new company.

In our renewal application, we shall further our research based on new and exciting preliminary results. First, we will focus on receptors that can direct immune cells towards cancer cells and stimulate their killing capacity, a technology pioneered in our laboratory and proven to work in patients. We have identified ways to further improve upon these receptors and expand their use, ultimately creating an off-the-

shelf "living drug". Next, we will obtain large numbers of natural killer (NK) cells – a subset of immune cells – and coaxed them to kill NK-resistant tumours. Lastly, we propose to complete our 5 ongoing immune cell-based clinical studies for cancer patients, as well as to start new ones guided by encouraging laboratory results.

### **Professor Dario Campana** Cell Therapy of Cancer

Mrs Lee Kong Chian Chair in Advanced Cellular Therapy

Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System



### **Professor Patrick Tan** Epigenomic Profiling of Altered Chromatin States in Gastrointestinal Cancer

Professor  
Duke-NUS Medical School

Senior Principal Investigator  
Cancer Science Institute of Singapore, NUS

Cancer is often thought of as solely a genetic disease. Recent work has revealed that, besides DNA aberrations, epigenetic alterations are also frequent in cancer. Epigenetics is a process where specific DNA sequences and DNA-associated proteins become chemically modified in a way that preserves the DNA sequence, but causes the cell to interpret the sequence differently. Importantly, several regions

in the cancer genome exhibiting such epigenetic alterations were shown to be key "trigger sequences" for activating and repressing gene and protein functioning in cancer.

Here, we seek to comprehensively map the global repertoire of epigenetic alterations in gastric cancer (GC) – the third most fatal cancer globally. A major strength of our application involves the use of highly sensitive novel technologies, which will allow us to map epigenetic alterations directly from patient samples. An analysis of these GC epigenetic alterations will provide us insight on critical pathways used by cancer cells to induce widespread changes in gene and protein expression, ultimately leading to malignancy. We will also highlight new approaches for detecting GC early and how drugs targeting the cellular epigenetic machinery could be harnessed for GC treatment.





**CLINICIAN SCIENTIST AWARD (SENIOR INVESTIGATOR) RECIPIENTS**

**Associate Professor Goh Boon Cher**

**Development of Novel Therapy for Head and Neck Cancer**

Senior Consultant  
Department of Haematology-Oncology, NUH  
  
Associate Professor  
Yong Loo Lin School of Medicine, NUS

Senior Principal Investigator  
Cancer Science Institute of Singapore, NUS  
  
National University Health System



Prognosis for head and neck cancer has been invariably poor. Even with disfiguring surgery, chemotherapy and radiotherapy, the rate of relapse and mortality for patients remains high. Nose cancer, or nasopharynx cancer (NPC), is the most common head and neck cancer in Singapore, and is associated with the Epstein-Barr virus. The virus seizes control of normal immune cells and subvert them to promote cancer. Not many novel treatments are available for NPC.

to derive novel strategies to treat this cancer type. We will also elucidate key laboratory findings for squamous cell carcinoma of the head and neck, the next most common head and neck cancer. These findings will be studied in our proposal so as to develop new treatments for patients. We hope that our research will provide the basis for the development of more treatment options for NPC patients, especially those facing a relapse or whose cancer has metastasised.

We propose to study in greater detail the genetic mechanisms and immune system that govern the development of NPC, and



**Professor Tazeen Jafar**

**Management of Hypertension and Multiple Risk Factors to Enhance Cardiovascular Health – A Cluster Randomised Trial in Singapore’s Polyclinics**

Professor  
Duke-NUS Medical School  
  
Visiting Consultant  
Singapore General Hospital

Hypertension is a serious public health issue that can lead to heart attack, stroke and kidney failure.

antihypertensive medication; (iii) motivational conversation for high-risk patients; and (iv) telephone-based follow-up by a team of physician-supervised nurses and nurse practitioners. Changes in blood pressure will be compared between intervention and control groups.

One in three Singaporean adults has hypertension. We propose a cluster randomised trial in eight of Singapore’s polyclinics – four will implement a structured, multi-component intervention while the other four will deliver usual care. A total of 1,000 adults with uncontrolled hypertension will be followed for two years.

We propose that structured intervention will be more effective than usual care in lowering blood pressure for patients with uncontrolled hypertension. Such programmes are also likely to be more cost-effective. If successful, the findings will be informative for policymakers to roll out intervention in polyclinics and primary care centres across Singapore, as well as other countries with similar healthcare infrastructure.

The intervention includes (i) an algorithm-driven antihypertensive treatment – fixed-dose combination (FDC) for all patients, and lipid lowering drugs for high-risk patients; (ii) subsidy on FDC

**Associate Professor Lee Soo Chin**

**Developing Experimental Therapeutics and Understanding Mechanisms of Drug Resistance in Asian Breast Cancers**

Senior Consultant  
Department of Haematology-Oncology, NUH  
  
Associate Professor  
Yong Loo Lin School of Medicine, NUS

Senior Principal Investigator  
Cancer Science Institute of Singapore, NUS  
  
National University Health System



Effectiveness of treatment in breast cancer is hampered by the adaptation and evolution of cancer cells, resulting in drug resistance. In the last five years, we have built a breast cancer programme with clinical trials to test novel therapies; tissue and blood biobanks to test predictive biomarkers; a translational laboratory to test drug levels and effects; and a pilot study to increase the detection limit of circulating tumour cells (CTCs).

In the next five years, we will continue to design and execute clinical trials for new treatments. We will focus on combining new targeted agents with conventional chemotherapy or anti-hormonal therapy, and testing a novel patented immunotherapy approach to activate

and boost the number of natural killer cells to enhance host response towards cancer. Residual 'resistant' tumours will be collected after anti-cancer therapy for in-depth analysis and generation of patient-derived cell lines. This will allow us to better understand the mechanisms of drug resistance and uncover potential therapeutic targets to guide treatment of 'resistant' tumours. Lastly, we plan to develop an assay to test drug sensitivity on enriched CTCs for use in the clinic.



### **Associate Professor Raymond Seet Chee Seong**

#### **Detection of Occult Paroxysmal Atrial Fibrillation following Ischaemic Stroke in a Multi-Ethnic Asian Population and Elucidating Their Significance in Relation to Recurrent Stroke Outcomes**

Senior Consultant  
Division of Neurology, NUH

Associate Professor  
Yong Loo Lin School of Medicine, NUS

Senior Principal Investigator  
Cancer Science Institute of Singapore, NUS

National University Health System

Detecting paroxysmal atrial fibrillation (PAF) in patients with ischaemic strokes presenting in sinus rhythm is challenging, as PAF episodes are often short, random occurrences and frequently asymptomatic. Limited data is available on the incidence of undiagnosed PAF among Asian stroke patients. Our preliminary data reveals a high incidence of undiagnosed occult PAF of 16% among stroke patients in Singapore. These patients were older and presented higher biomarker levels relating to heart function, inflammation and blood viscosity. The long-term significance of these findings is not known.

We will, through this study, assess the frequency of PAF occurrences in Asian stroke patients, and evaluate whether biomarker and echocardiographic predictors can improve the detection of AF in stroke. This study, which transects across several multidisciplinary platforms in stroke neurology, digital health and translational medicine, aims to deliver key data on the burden of undiagnosed PAF and unlock the causes of stroke among Asians. Data derived from this study will provide critical insights on the mechanisms of AF and stroke, and guide targeted screening of high-risk stroke patients for undiagnosed PAF.

### **Associate Professor Tina Wong**

#### **Development of a Layer-by-Layer Nanoparticle-Sustained Delivery System for Nucleic Acid Therapeutics**

Senior Consultant  
Glaucoma Department, Singapore National Eye Centre

Head  
Ocular Therapeutics and Drug Delivery Research Group, Singapore Eye Research Institute

Associate Professor  
Duke-NUS Medical School



Use of gene-based therapeutics is a fast-moving field of research, with major scientific and commercial interests. The prospect of silencing key genes responsible for diseases opens the door to therapy for many intractable disorders. Through an increased understanding of disease aetiology, specific gene products whose suppression may bring therapeutic benefits have been identified. RNA inhibition can be explored as a potential treatment strategy. A major challenge of gene silencing in RNA therapeutics, however, is their delivery into the human body. Stable and sustained expression of the siRNA is desirable in therapeutic application.

To address this challenge, we will design and develop nanoparticles specifically for sustained siRNA delivery. Wound healing is a highly orchestrated event. Anti-fibrotic therapy ideally targets the early and late stages of wound healing for the best clinical outcome. In this study, we will use an animal model of post surgical fibrosis. We propose that a one time local application of the siRNA delivery system – containing two different siRNAs to target two critical stages of wound healing, released sequentially into the target tissue – will provide an improved and novel therapeutic approach to treating fibrosis.



## CLINICIAN SCIENTIST AWARD (INVESTIGATOR) RECIPIENTS



### Dr Louis Chai Yi Ann

#### Augmentation and Modulation of Host Immune Response for Optimised Management of Invasive Fungal Diseases

Consultant  
Department of Medicine, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System

An increasing number of patients face higher risk of infections due to systemic illnesses or the need to receive treatments that inadvertently lower their immunity. An important group of infections that cause significant disease burden in immunosuppressed patients, despite rigorous intervention, are the invasive fungal diseases.

To increase the chances of successful anti-fungal treatment

in immunosuppressed patients, we will propose modalities that enhance the ability of their immune system to respond appropriately to fungi infections. This is achieved either through a specific boost of the patient's immunity prior to the start of the immunosuppressive treatment, or through careful control of the permissible level of inflammation in the infected organ. Positive findings from this research will hopefully complement current conventional anti-fungal drug treatments and achieve improved outcomes in immunosuppressed patients with invasive fungal diseases.

### Associate Professor Mark Chan Yan Yee

#### Sphingolipids as Serial Biomarkers of Disease Progression in Acute Myocardial Infarction

Consultant  
Department of Cardiology, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System

Heart attack is responsible for many deaths globally each year. Sphingolipids are a class of fat molecules in the body that may predispose a person to blockage of blood vessels and heart attacks. Some sphingolipids, such as ceramides, may be harmful to the heart, while others, such as sphingosine-1-phosphate (SIP), may be cardioprotective. We previously measured ceramide and SIP levels in more than 1,000 patients with a recent heart attack. Our findings indicated that higher ceramide levels and lower SIP levels were associated with higher rates of death, stroke and a second heart attack.

We will now measure ceramides and SIP repeatedly, in the same group of healthy individuals and patients with a recent heart attack, to test if repeated measurements can pre-empt impending or subsequent heart attacks. We also aim to compare different isoforms of ceramides and SIP in healthy and diseased individuals, and assess their value in predicting early blood vessel blockage.



### Associate Professor Ronald Lee Chi-Hang

#### Sleep Study-Guided Multidisciplinary Therapy for Patients Presenting with Acute Coronary Syndrome

Senior Consultant  
Cardiac Department, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System

(OSA) is linked to coronary artery disease and can predict adverse cardiovascular events, particularly among the elderly and obese. Our aim is to determine if a Sleep Study-Guided Multidisciplinary Therapy (SGMT) for patients with an acute coronary syndrome will improve cardiovascular outcome. We hypothesise that, after undergoing SGMT, patients will have lower (i) plasma NT-proBNP levels; (ii) 10-year risk of cardiovascular death; and (iii) rate of cardiovascular events.

In this study, 180 patients with an acute coronary syndrome will be randomly sorted into SGMT or non-SGMT groups. Both groups will receive guideline-mandated treatment for their acute coronary syndrome. However, only the SGMT group will undergo an overnight sleep study to check if they have OSA. Those found to have OSA will attend the SGMT clinic and receive treatment for their OSA. After six months, we will compare the parameters (i) to (iii) between both groups. Our findings will help advance understanding of the cardiovascular benefits of screening for and treating OSA.



### Dr Lawrence Lee Soon-U

#### Application of an Expanded Whole Blood Bactericidal Activity Platform to Evaluate Pharmacokinetic and Pharmacodynamics Relationships of Novel Anti-Tuberculosis Drugs and Combination Regimens

Consultant  
Department of Medicine, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS

National University Health System

Tuberculosis remains a major health problem in Singapore, Asia and globally. There is an urgent need to improve anti-tuberculosis therapy. We aim to discover whether co-trimoxazole, a combination antibiotic, and rosuvastatin, an anti-cholesterol drug, will have anti-tuberculosis activity. We will also study the anti-tuberculous activity of higher doses of rifampicin, a drug with newly realised potential, in combination with linezolid, a promising antibiotic with the potential to treat extensively drug-resistant tuberculosis.

The whole blood bactericidal activity (WBA) method is a laboratory test done on human blood that studies the combined drug and host effects of killing different strains of tuberculosis bacteria. We will plan three clinical trials involving Asian volunteers and one trial involving tuberculosis patients. The WBA and drug concentrations of rifampicin, co-trimoxazole, rosuvastatin and linezolid will be compared alone and in combination. We will also study the WBA of higher dose rifampicin with the above drugs. The results will hugely impact tuberculosis treatment and benefit patients worldwide.

### Associate Professor Melvin Leow Khee Shing

#### The Role of Thyroid Status in Regulating Brown Adipose Tissue Activity, White Adipose Tissue Partitioning and Resting Energy Expenditure (TRIBUTE)

Senior Consultant  
Department of Endocrinology, Tan Tock Seng Hospital

Associate Professor  
Lee Kong Chian School of Medicine

Recent years has seen greater research interest in examining the role of brown adipose tissue (BAT) in regulating metabolism in health and disease. In particular, BAT volume and activity may be important in regulating the physiological state of patients with thyroid disease. Assessment of BAT may improve understanding of the euthyroid state.

To this end, we will develop a new method to assess BAT volume and activity using infrared (IR) thermography and MR imaging. This method will be compared against current methods that are expensive and utilise ionising radiation, and be used to determine

the effect of thyroid status on BAT, white adipose tissue, body composition and metabolic state. Once validated, the new method will help guide anti-thyroid drug therapy in patients with hyperthyroidism. Our findings will (i) offer insights into the nature of BAT functionality and body composition according to thyroid and physiological state; (ii) establish IR thermography and MR imaging as the standard for assessing BAT volume and activity; (iii) facilitate future metabolic research addressing obesity and diabetes.



### Dr Citra Nurfarah binte Zaini Mattar

#### Educating Maternal Immunity to Improve Donor Cell Engraftment: The Kinetics of Maternal Immune Cell Trafficking and a Novel Therapeutic Strategy in a Murine Model of Allogeneic Intrauterine Haemopoietic Stem Cell Transplantation

Consultant  
Department of Obstetrics and Gynaecology, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS

National University Health System

Intrauterine haemopoietic stem cell transplantation (IUHSCT) may treat numerous single gene disorders which begin during pregnancy. The foetus has unique advantages as a patient: size, which improves therapeutic efficiency where cell quantity is limited; relative immune-naïve status; and

enhanced permeability of tissue barriers to migrating stem cells. Yet, consistent donor cell engraftment remains a challenge in clinical trials of IUHSCT, possibly due to a combination of low initial chimerism and rejection of donor cells instigated by maternal immune cells trafficked across the placenta.



In this experimental model, we hypothesise that depletion of maternal antigen-presenting cells (APC) will educate other maternal immune cells to better tolerate donor cells and allow for improved engraftment. We will probe into the kinetics of maternal cell trafficking to the foetus after IUHST and determine if transient depletion of maternal APC can improve

long-term engraftment and foetal response to postnatal re-transplantation. This is important to our understanding of how we can increase the success of IUHST and develop novel therapies to benefit foetal patients with major haemoglobinopathies and other relevant genetic diseases.

### Associate Professor Jodhbir Singh Mehta Therapeutic Target for Corneal Endothelial Cell Survival

Senior Consultant  
Corneal and External Eye Disease Department, Singapore National Eye Centre  
Associate Professor  
Duke-NUS Medical School



Corneal is the most commonly transplanted tissue. The number of patients requiring corneal transplants is increasing due to an ageing population. But there has been a shortage of donors in Singapore and worldwide. The most common indication for corneal transplantation is due to diseases that affect the corneal endothelium cells. The survival of these cells is influenced by oxidative stress. Following cumulative oxidative stress, due to ageing or otherwise, the cells die. The cornea then becomes swollen, leading to blindness. We recently found a specific class of antioxidant proteins called peroxiredoxins on the corneal endothelial cell.

This study will elucidate the exact mechanisms of how oxidative stress affects these endothelial cells. We will examine the role of how corneal endothelial peroxiredoxins mitigates the effects of oxidative stress. Their stimulation may be able to promote cell survival. We will also investigate the role of oxidative stress in an animal model of a common human corneal endothelial disease. This may allow us to treat patients of corneal disease with a medical therapy that can promote cell survival, as the alternative to undergoing invasive and costly transplantation surgery.



### Dr Ng Oon Teck Clinical Translation of Whole Genome Sequencing to Inform Infection Control and Decrease Mortality and Morbidity from Carbapenemase-Producing Enterobacteriaceae Infection

Senior Consultant  
Infectious Disease Department, Tan Tock Seng Hospital  
Assistant Professor  
Saw Swee Hock School of Public Health, NUS

Carbapenemase-producing Enterobacteriaceae, or CPEs, are a multidrug-resistant superbug, against which there is no reliable, safe and effective antibiotic. CPEs are increasing in prevalence in Singapore and worldwide, with a mortality rate of between 40% to 80%. Infection control of CPE spread is our main defence. One of the major challenges of stopping CPE spread is determining their transmission routes. One technology that has been shown to help, mainly in theoretical studies, is whole genome sequencing (WGS). Combining WGS with routine infection control

information may be the key to understanding CPE transmission.

Our team was recently successful in developing new methods to overcome some of the technical barriers in the use of WGS to track CPE spread. We seek to use WGS to provide useful information for on-the-ground infection control by bringing together a team of scientists and infection control doctors, and establishing the necessary protocols to guide action. Additionally, we will evaluate if application of the new technology results in reduced CPE spread in the Tan Tock Seng Hospital and provide results informing on the best use of WGS for CPE prevention.



## TRANSITION AWARD RECIPIENTS

### Dr Chao Yinxia

#### The Role of Monocytes in the Pathogenesis of Parkinson's Disease

Associate Clinician Scientist (Research)  
National Neuroscience Institute

Assistant Professor  
Duke-NUS Medical School



Inflammation may be a pathogenic factor in the onset and progression of Parkinson's disease (PD) – a common neurodegenerative disorder. Leucine-rich repeat kinase 2 (LRRK2) gene is the most important cause of familial and sporadic PD. Genome-wide association studies have found an association between LRRK2 and Crohn's disease, an autoimmune disease, as well as with PD, suggesting that these two diseases share common pathways. Our unpublished data indicated that LRRK2 is abundantly expressed in immune cells, with the most found in monocytes. Also, we found that circulating monocyte populations doubled in PD patients than healthy controls. Our gene expression studies revealed numerous dysregulations of signalling pathways in human dopaminergic neurons carrying

LRRK2 mutations.

We hypothesise that LRRK2 mutations in PD lead to monocyte dysregulation, promoting the demise of dopaminergic neurons. As such, immune pathways may be therapeutic targets. Utilising PD LRRK2 variants in diseased and healthy controls, we will investigate the role of LRRK2 in monocyte activation and underlying signalling pathways, and evaluate potential immune-mediated targets. Our study will provide new pathophysiologic clues on the link between LRRK2 and immune pathways to facilitate novel therapeutic approaches in PD.



### Dr Calvin Chin Woon Loong

#### Response of the Myocardium to Hypertrophic Conditions in the Adult Population

Consultant  
Department of Cardiology, National Heart Centre Singapore

Assistant Professor  
Duke-NUS Medical School

Aortic valve stenosis and hypertension are two important conditions that cause thickening of the heart muscles, or left ventricular hypertrophy, which is initially adaptive to maintain optimal heart function. Ultimately, heart failure occurs as a result of progressive muscle cell death and scarring (myocardial fibrosis). Our previous work had demonstrated the importance of myocardial fibrosis in aortic stenosis. Dedicated techniques using cardiovascular MRI and novel high-sensitivity cardiac troponin blood assays are potential markers to detect myocardial fibrosis. As current reference ranges of heart function and mass were based on

Caucasian populations, we will establish normal ranges locally to accurately define heart disease in Singapore.

We will, through this study, extend our previous findings and focus on high-risk patients with aortic stenosis to better predict heart function recovery after valve replacement. While hypertensive heart disease is very common in Singapore, the significance of myocardial fibrosis is not well understood. We will address this critical knowledge gap by studying myocardial fibrosis in 500 patients with hypertension. This will be the largest study using state-of-the-art MRI to examine the importance of myocardial fibrosis in hypertensive heart disease.

### Dr Nicholas Francis Grigoropoulos

#### Synergistic Genetic Lesions in Diffuse Large B-Cell Lymphoma Tumour Tissue and Peripheral Blood

Consultant  
Department of Haematology, Singapore General Hospital

Assistant Professor  
Duke-NUS Medical School



Diffuse large B-cell lymphoma (DLBCL) is a common cancer of the lymph glands. With chemotherapy, around 50% of DLBCL patients can be cured. The reason for which some patients do not respond to chemotherapy remains unknown. Understanding this may thus enable us to predict patient response and offer alternative therapeutic regimens, as well as provide clues for new drug development. Despite the cancer's genetic heterogeneity, it was found that, in general, DLBCL patients who have certain deleterious point mutations or more than one DNA translocation tend to do badly with chemotherapy.

Our study aims to discover the effects of having a translocation and a point mutation at the same time in DLBCL patients. Pilot data has shown that a gene called DDX3X is more frequently mutated in DLBCL patients who did not respond to treatment. We wish to confirm this finding in a large patient group and find out how these mutations can promote lymphoma. Finally, we will try to identify mutations through the use of the patient's blood as this may improve diagnosis and monitoring.

**Dr Javed Iqbal**

**Study of Interactions between Immune Response and Hypoxia-Related Genes in Triple Negative Breast Cancer and Potential Role in Prognosis in a Singaporean Patient Population**

Senior Consultant  
Division of Pathology, Singapore General Hospital

Assistant Professor  
Duke-NUS Medical School

Research Director  
Pathology Academic Clinical Programme, SingHealth



Breast cancer attracts leucocytes that, depending on the type of cells, either support or destroy the tumour. Lymphocytes may help in preventing tumour growth. Meanwhile, some cells like macophages can have the opposite effect on tumour cells. Presence of 'good' white blood cells (WBC) can mediate chemotherapy efficacy in some types of breast cancer.

It has been found that hypoxia can promote tumour growth in breast cancer by influencing the function of tumour-related leucocytes. The understanding of how these 'good' or 'bad' leucocytes are attracted to tumours during hypoxic conditions can therefore help us increase the presence of 'good' WBCs and

eradicate 'bad' WBCs. Similarly, the effect of hypoxia on tumour-inducing WBC can be targeted by controlling the degree of hypoxia to attract the 'good' WBC.

In our study, we aim to achieve this by (i) studying the quantity of proteins involved in establishing low oxygen conditions and increasing WBCs; and (ii) to identify genes that are either active or inactive in these two conditions. By identifying patients with good leucocytes in less hypoxic conditions, we can promote tumour destruction and thus improve survival and quality of life for cancer patients.



**Dr Angela Koh Su-Mei**

**Characterising and Elucidating Pathways of Cardiac Ageing in an Asian Population**

Consultant  
Department of Cardiology, National Heart Centre Singapore

Assistant Professor  
Duke-NUS Medical School

bodily functions, which will lead to reduced physical abilities. Heart function is a major determinant of one's ability to function independently in society. Understanding how the heart undergoes ageing will, therefore, allow us to adopt measures to retard the ageing processes that lead to poor heart function.

The population in Singapore is rapidly ageing. An ageing population faces a greater risk of ill health due to age-related deterioration in overall

Our study aims to define the key ageing processes of the heart that occur with different stages of ageing. We will also investigate how the heart ages by comparing blood tests obtained in midlife with those obtained in old age. We will perform detailed heart imaging tests and blood tests on participants. The results of this study will provide new knowledge on cardiac ageing among Asians and lead to targeted therapies that can be used in midlife to prevent or retard the heart's ageing process.

**Dr Lek Ngee****The Role of the BIM Deletion Polymorphism in Type I Diabetes**

Consultant, Endocrinology Science  
KK Women's & Children's Hospital

Clinical Senior Lecturer  
Yong Loo Lin School of Medicine, NUS

Assistant Professor  
Duke-NUS Medical School

Type 1 diabetes (T1D) is a debilitating disease that commonly presents during childhood. As beta cells are damaged by the body's own immune system, patients with T1D require multiple daily insulin injections for life and face significant risk of serious diabetes-related health problems.

To develop better therapeutic alternatives, further understanding of the underlying mechanisms of immune-mediated beta cell death is needed. We postulated that some East Asian individuals harbour beta cells that survive autoimmune attack better due to a genetic variant called the BIM deletion polymorphism. We previously tested our hypothesis on 87 Singaporean ethnic Chinese children with T1D and found promising results. Eight of the children carrying this genetic variant were diagnosed with

T1D about five years later than the other 79 children without it.

In this study, we aim to (i) confirm the delay in T1D onset by genetically testing a larger population of T1D patients; and (ii) determine through laboratory experiments, whether human beta cells bearing the BIM deletion polymorphism are indeed resistant to immune-mediated damage. Our findings, taken together, will increase the understanding of beta cell survival and lead to the development of novel cell-based treatment of T1D.

**Dr Baskaran Mani****Clinical, Mechanical and Histological Characterisation of Trabecular Meshwork in Ocular Hypertensive Primates – Exploring Mechanical Strain in Glaucoma**

Senior Clinical Research Fellow  
Singapore Eye Research Institute

Assistant Professor  
Duke-NUS Medical School

Glaucoma is a progressive eye disease affecting the optic nerve and a major cause of irreversible blindness. The

trabecular meshwork is a structure located at the front of the eye responsible for aqueous humour drainage. The resistance to flow of aqueous humour in the eye through this tissue can cause a rise in intraocular pressure and eventually lead to glaucoma. However, little is known about the trabecular meshwork in terms of its structural and functional aspects.

With access to SERI's animal facility, we aim to studying the nature of the trabecular meshwork in live animals, i.e. monkeys with naturally occurring high eye pressure, as well as in animals that had died of natural causes. We will assess the tissue biomechanics, ultrastructure and flow of fluid through the trabecular meshwork using microscopic techniques. This will allow us to learn the causes of glaucoma and be of immense use in the future development of medications and gene therapy for treating glaucoma.

**Dr Ng Chin Teck****The Role of Circulating Pathogenic-Like CD4+ T Cells in Early Rheumatoid Arthritis**

Consultant  
Department of Rheumatology and Immunology, Singapore General Hospital

Assistant Professor  
Duke-NUS Medical School

Rheumatoid arthritis (RA) is the most common autoimmune chronic inflammatory arthropathy and is characterised by inflammation of the joint lining. If left untreated, the disease ultimately leads to bone and cartilage destruction. Erosion, which leads to disability, can occur as early as four months after onset of disease. Despite advances in treatment in the last one to two decades, many patients are still suffering from this condition. Approximately 30% to 40% of RA patients do not respond to methotrexate, the anchor drug of therapy, and need to escalate to more expensive biological treatments. This suggests that we still do not fully understand the underlying pathogenesis.

Our study focuses on a group of newly discovered cells called circulating pathogenic-like lymphocytes (CPLs). Using state-of-the-art technologies, we will examine the role of CPLs in early RA and improve our understanding of this debilitating disease. We also aim to relate CPLs to disease activity and treatment response. The potential of CPLs in stratifying treatment response will positively impact medication selection, help patients save time and reduce healthcare cost in the long run.





**Dr Monisha Esther Nongpiur**  
**Investigating the Role of Inflammation in Primary Angle-Closure Glaucoma**

Senior Clinical Research Fellow  
 Singapore Eye Research Institute

Assistant Professor  
 Duke-NUS Medical School

Primary angle-closure glaucoma (PACG) is one of the leading causes of blindness worldwide, particularly in Asia. The disease progresses through three stages: primary angle-closure suspects

(PACS), primary angle-closure (PAC) and finally PACG. However, the cause of disease progression is currently unknown. A feature of PAC/PACG eyes is the presence of permanent scarring of the angle structures called peripheral anterior synechiae (PAS).

Typically, PAS formation is associated with uveitis – an inflammation of the eye’s uvea, where the leakage of proteins and inflammatory

cells is responsible for PAS development. Since PAS is also present in some PAC/PACG eyes, albeit of a lesser magnitude than in uveitis, we hypothesise that an underlying low-grade inflammation is present in these eyes, and is responsible for the development and progression of the condition.

In this study, we aim to determine if inflammation is a primary component in angle-closure eyes, and if it is associated with the progression of PACS and PAC to PACG. We will perform a comprehensive evaluation of inflammatory markers in different eye tissues obtained from the entire spectrum of angle-closure disease stages.

**Dr Catherine Ong Wei Min**  
**Host Inflammatory Responses Driving Immunopathology in Human Central Nervous System Tuberculosis**

Associate Consultant  
 Division of Infectious Diseases, NUH

Assistant Professor  
 Yong Loo Lin School of Medicine, NUS

National University Health System



The incidence of tuberculosis is increasing globally. Central nervous system tuberculosis (CNS-TB) is particularly virulent with death rates of untreated patients reaching 100%. Brain inflammation and tissue destruction can be very extensive despite a lack of infection. But the mechanisms resulting in this immune-mediated destruction is unclear. There is emerging evidence that host immunity drives inflammation in CNS-TB. We hypothesise that host factors contribute to CNS-TB neurological deficit and death in patients.

We aim to investigate tissue destruction in human CNS-TB by examining the cerebrospinal fluid and blood of patients for various host immune markers. We will determine the diagnostic

and prognostic markers for CNS-TB. Patients with TB, viral and bacterial meningitis and febrile seizures will be recruited from Singapore and Malaysia. Patient data, biological specimens and brain imaging will be collected. Immune markers will be analysed. A mouse model of CNS-TB will be used to investigate the mechanism of tissue destruction. This study is crucial in the identification of key human immune markers driving pathology in CNS-TB. Determining the role of these host factors may help identify therapies that can improve patient outcome.



**Associate Professor Poh Kian Keong**  
**Cardiovascular Structure and Function in Mildly Overweight Asian Subjects of Mixed Ethnicity Following Early Versus Delayed Lifestyle Intervention – A Randomised Controlled Study (CASMES)**

Clinical Director (Research) and Director (Postgraduate Education)  
 Department of Cardiology, National University Heart Centre, Singapore

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

Associate Professor  
 Yong Loo Lin School of Medicine, NUS  
 National University Health System

Cardiovascular structural changes and dysfunctions commonly occur in the morbidly obese. While also present in some mildly overweight Asian individuals, these changes can only be detected and measured through newer, more sensitive echocardiographic

techniques and blood assays.

The aim of our study is to assess the effects of six months of lifestyle intervention (LSI)-comprising diet and exercise programmes, on

cardiovascular structure and function in mildly overweight Asian adults free of overt cardiovascular disease at baseline. We will randomise 100 subjects, 21-year-old and older, with BMI 23 to 27.5 kg/m<sup>2</sup>, into Early and Delayed LSI groups. Their heart will be assessed through the use of echocardiography and new parameters that can detect subclinical dysfunction. Additionally, we will perform assays on circulating progenitor cellular markers as surrogates for vascular health.

Our study will provide a more complete understanding of how cardiac dysfunction and circulating cellular derangements may be affected by weight loss. This may be used to develop new therapeutics. By demonstrating that simple lifestyle changes can improve cardiovascular function, we will be able to push for a reduction in obesity and achieve better health outcomes for all.

### Dr Colin Tan Siang Hui

#### Non-Invasive Optical Coherence Tomography Angiography for Deep Phenotyping and Diagnosis of Polypoidal Choroidal Vasculopathy

Senior Consultant  
Department of Ophthalmology, Tan Tock Seng Hospital

Clinician Researcher  
Lee Kong Chian School of Medicine



Polypoidal choroidal vasculopathy (PCV), a form of age-related macular degeneration, is one of the most important eye diseases globally. PCV occurs more commonly in Asia, and in Singapore. To confirm the presence of PCV, an injection of the dye indocyanine green (ICG) is required in order to take images of the eye in a technique called ICG angiography. The images will allow doctors to identify abnormal blood vessels that may lead to a loss of vision.

abnormal blood vessels without the need for dye injection. It is thus safer and also much faster as compared to ICG angiography.

Optical coherence tomography (OCT) angiography is a new, non-invasive imaging technique that can produce similar images of

In our research study, we will assess the accuracy of OCT angiography in diagnosing PCV and compare this against ICG angiography. Our findings will enable doctors to use this new and safer imaging technique to detect and categorise PCV, thereby improving the quality of patient care.



### Dr Tan York Kiat

#### Musculoskeletal Bioimaging Comprehensive Programme (A Themed Approach) – Developing a Musculoskeletal Ultrasound Programme as an Intervention to Improve Disease-Modifying Anti-Rheumatic Drug Adherence in Rheumatoid Arthritis: A Randomised Controlled Trial

Consultant  
Department of Rheumatology and Immunology, Singapore General Hospital

Assistant Professor  
Duke-NUS Medical School

Clinical Senior Lecturer  
Yong Loo Lin School of Medicine, NUS

Many rheumatoid arthritis (RA) patients do not adhere to their medications. Disease-modifying anti-rheumatic drugs (DMARDs) are the mainstay of treatment for RA patients. Adherence rate is frequently reported to be below 70%. Non-adherence needs to be urgently addressed as it can lead to suboptimal treatment with poor disease outcome. The subsequent need for more aggressive therapy and treatment of disease-related complications can translate into increased healthcare utilisation and costs.

To improve DMARDs adherence, we will implement a randomised controlled trial to test out an innovative intervention to improve medication adherence among low adherers. This intervention involves the use of a musculoskeletal ultrasound programme (MUSP), which allows RA patients to visualise their joint inflammation and damage real-time while treatment adherence is simultaneously reinforced. Through this, we hope to improve the patient's understanding of their joint disease and motivate them to adhere to their medications.

### Dr Tey Hong Liang

#### Keloids: Therapy with Drug-Free Solid and Steroid-Laden Hyaluronic Acid Dissolving Microneedles

Consultant  
Medical Department, National Skin Centre

Head of Research  
National Skin Centre

Clinician Researcher  
Lee Kong Chian School of Medicine



Keloids are raised overgrowths of scar tissue that occur at the site of a skin injury. The goal in treatment is to flatten the keloid so that it is more like the surrounding normal skin, and to diminish any accompanying pain or itch. Many conventional treatments exist, such as injecting steroids. But they are frequently inconvenient, expensive, painful and prone to frequent recurrences.

Our previous laboratory studies utilised recent advancements in microneedle technology to develop novel treatments that circumvent many problems of conventional treatments. We found that both drug-free solid microneedles and steroid-containing hyaluronic acid-based dissolving microneedles

demonstrated therapeutic properties and efficacy comparable to the traditional subcutaneous route of administration.

We will hereby investigate the efficacies and mechanism of action of these two novel methods, and concurrently compare them against standard steroid injections, in terms of changes in the size of keloids, relief of pain and itch, and improvement in appearance. In the laboratory studies, we will examine the mechanism of how microneedles stop the growth of cells in keloid, which possibly occurs due to altered cellular communications. Our research will help pave the way for better treatment options for keloids.



### Dr Yeo Wee Song

#### Profiling and Monitoring of Risk Factors for the Development of Post-Transplant Lymphoproliferative Disorder in Paediatric Renal Transplant Recipients

Consultant  
Department of Paediatric Medicine, NUH

Assistant Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System

Post-transplant lymphoproliferative disorder (PTLD) is a significant cause of morbidity and mortality

in transplant recipients. It encompasses conditions ranging from benign infections to malignancies like lymphomas. Chronic infection by the Epstein-Barr virus (EBV) is a well-recognised risk factor, accounting for more than 90% of PTLDs. The risk factor for chronic EBV infection is, in turn, over-immunosuppression. Interestingly, not all transplant recipients with EBV will develop PTLD, nor are all PTLDs associated with EBV infection. Notably, our local paediatric renal transplant population has a higher incidence of PTLD, compared to that in the West. There must, therefore, be other underlying factors, such as genetics, that predispose these patients to PTLD.

Our study aims to comprehensively identify immunologic and genetic risk factors for PTLD. This will be achieved respectively through a series of quantitative and functional tests on various components of the immune system, and the identification of genetic abnormalities through high throughput sequencing. We will evaluate the usefulness of immunoglobulin/immune cell receptor gene rearrangements in facilitating early detection of PTLD. Our results will assist in the identification of transplant recipients at high risk of PTLD, and possibly provide guidance on the use of immunosuppressants (personalised medicine).

### Dr Yu Na

#### Using Glycosaminoglycan-Enriched Demineralised Bone Matrix in Regeneration of Periodontal Tissues

Senior Dental Surgeon  
Department of Restorative Dentistry, National Dental Centre Singapore  
Assistant Professor  
Duke-NUS Medical School

Periodontal disease is a leading cause of tooth loss. It is an inflammatory disease that causes progressive breakdown of the gum line. It is highly prevalent and associated with other systemic diseases, including diabetes and heart disease. Current standard of care focuses on mechanical debridement to arrest the progression of tissue destruction, which does not regenerate lost tissues.

An emerging treatment option involves the application of bioactive demineralised bone matrix (DBM) containing growth factors and cytokines into the defect area, which is considered superior in promoting tissue restoration. Its efficacy is however inconsistent, and reliant on the quantity and quality of growth factors present in the DBM preparation. These parameters also

depend on the donor's age and health status, as well as the method of preparation and administration.

Our study seeks to engineer the sugar glycosaminoglycan that can significantly promote and sustain the activity of pro-healing growth factors present in DBM, with a view to provide dentists with a novel mouldable supplement for the treatment of periodontal tissue damage. This will translate into reduced rate of tooth loss, improved oral function and better quality of life for patients.



## TALENT DEVELOPMENT PROGRAMMES

### NMRC Research Training Fellowship

The NMRC Research Training Fellowship aims to provide doctors and health science professionals with the training necessary to become clinician scientists. Medical doctors registered with the Singapore Medical Council, dental surgeons registered with the Singapore Dental Board, health science professionals and biostatisticians are all eligible to apply. The fellowship covers both overseas research training and graduate research degree programmes at local or overseas institutions. Awardees of the fellowship receive funding for salary and tuition fees for local graduate degree programmes, or allowances and other benefits in line with the host institution's policies for overseas research attachments.

### MOH Healthcare Research Scholarship (PhD)

This scholarship provides support to Basic Specialist Trainees, Advanced Specialist Trainees and Residents who wish to enrol in a PhD programme locally or overseas. It is targeted at young clinicians who wish to pursue a career in translational and clinical research. The scholarship provides funding for salary, tuition fees and maintenance allowance (for overseas PhDs), as well as protected time for research during the clinical training period. The programme will be merged with the NMRC Research Training Fellowship under RIE2020.

### 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 the tuition and research fees for the programme.

### Achievements under the RIE2015 Tranche - Talent Development Programmes

Programme	No. of Awards	Amount Committed (\$ mil)
NMRC Research Training Fellowship	57	13.92
MOH Healthcare Research Scholarship (PhD and MCI*)	47	0.80
		7.99

\*as of FY13-FY15

## AWARDEES FOR TALENT DEVELOPMENT PROGRAMMES 2015

### NMRC Research Training Fellowship

There were 20 awardees under the NMRC Research Training Fellowship.

Name	Institution and Type of Training	Project
<b>Dr Chen Yong</b>	<b>KKH</b> Overseas Attachment	Feeding-Related Bowel Ischaemia in Necrotising Enterocolitis
<b>Ms Chin Lay Fong</b>	<b>TSSH</b> PhD (Part-time, local)	Protocolised Early Upper Limb Intensive Repetitive Task-Specific Practice to Achieve Optimal Functional Outcomes after Stroke
<b>Dr Dawn Chong Qingqing</b>	<b>NCCS</b> Master's Degree (Full-time, overseas)	Mendelian Randomisation Study of Adiponectin and Colorectal Cancer Survival
<b>Ms Chong Sheue Lih</b>	<b>NUHS</b> Master's Degree (Full-time, local)	Impact of Hearing Loss on Significant Others and Intervention through Hearing Aids
<b>Mr Gu Qinglong</b>	<b>KKH</b> Master's Degree (Full-time, overseas)	Evaluation of Susceptibility-Enhanced Contrast-Optimised (SECO) T1-Weighted Images with Bowsher Prior for Quantitative PET Brain Imaging
<b>Dr Mohamad Farid bin Harunal Rashid</b>	<b>NCCS</b> Master's Degree (Part-time, overseas)	A Psychosocial Intervention Programme for Adolescent and Young Adult (AYA) Cancer Patients at National Cancer Centre Singapore (NCCS): A Pilot Study



Name	Institution and Type of Training	Project
<b>Dr Amit Jain</b>	<b>NCCS</b> Master's Degree (Part-time, local)	Cell-Based Therapies in Lung Cancer
<b>Dr Lee Eng Sing</b>	<b>NHGP</b> PhD (Part-time, overseas)	Encounters of Patients Who Have Multimorbidity with the Healthcare System: A Phenomenological Study
<b>Dr Katy Leung Ying Ying</b>	<b>SGH</b> Overseas Attachment	A Randomised Controlled Trial of Colchicine for Symptom and Inflammation Modification in Knee Osteoarthritis
<b>Dr Sarah Li Weiling</b>	<b>NUHS</b> Master's Degree (Full-time, overseas)	Caesarean Delivery Rates following Induction of Labour in an Asian Cohort
<b>Dr Joline Lim</b>	<b>NUHS</b> Overseas Attachment	Synergising Targeted Therapy by Combination Use - Addition of Novel PI3K Inhibitor Pictilisib to CDK4/6 Inhibitor Palbociclib in Treatment of Solid Tumours
<b>Dr Eric Lim</b>	<b>NHCS</b> Overseas Attachment	Defining the Genetic Basis of Brugada Syndrome (BS) in a Geographically and Ethnically Diverse Cohort
<b>Dr Ng Chin Hin</b>	<b>NUHS</b> Overseas Attachment	Taking PI3K Inhibition to the Clinic in Haematological Malignancies: Rational Combinations and Patient Selection
<b>Ms Soh Wei Jie</b>	<b>IMH</b> Master's Degree (Full-time, local)	Resilience in Singaporean Caregivers of Individuals with Autism Spectrum Disorder: The Effects of Hope, Self-Efficacy and Chronic Stress on Life Satisfaction
<b>Dr Raghav Sundar</b>	<b>NUHS</b> Overseas Attachment	Development of Novel Targeted Therapy in the RAS-RAF-MEK Pathway in Advanced Solid Tumours
<b>Ms Tan Woan Shin</b>	<b>NHG HQ</b> PhD (Part-time, local)	Home is Where I Would Like to Be: A Multi-Method Study Aiming to Increase the Number of People Who Wish to Die at Home is Honoured
<b>Dr Tay Sen Hee</b>	<b>NUHS</b> PhD (Part-time, local)	Multimodal Analysis of Anti-N-Methyl-D-Aspartate Receptor Subunit NR2A/B Antibodies Mediating Cognitive Dysfunction in Systemic Lupus Erythematosus
<b>Ms Esmeralda Teo Chi Yuan</b>	<b>SGH</b> Overseas Attachment	Evaluation of the Synergistic Cytotoxicity of Busulphan, Melphalan, Gemcitabine, SAHA and Decitabine in Lymphoma Cell Lines.
<b>Dr Tu Tian Ming</b>	<b>NNI</b> Overseas Attachment	Neuroprotective Pentapeptide Improves Outcome after Ischaemic Stroke
<b>Dr Etienne Wang Cho Ee</b>	<b>NSC</b> PhD (Full-time, overseas)	JAK-STAT Signalling in the Murine Hair Cycle

### MOH Healthcare Research Scholarship (MCI)

There were 19 awardees under the MOH Healthcare Research Scholarship (MCI).

Name	Institution and Department	Project
<b>Dr Dedrick Chan Kok Hong</b>	<b>NUHS</b> Surgery	A Multi-Centre Case-Control Study Evaluating Biomarkers for an Increased Risk of Colorectal Cancer
<b>Dr Diana Chan Xin Hui</b>	<b>SGH</b> Anaesthesiology	Single-Shot Paravertebral Block to Reduce Morphine Requirement in Cytoreductive Surgery (CRS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Infusion: A Randomised Controlled Trial

Name	Institution and Department	Project
<b>Dr Kelven Chen Weijing</b>	<b>NUHS</b> Urology	Macroscopic Haematuria: A Novel Method for Objective Measurement and Impact on Clinical Practice
<b>Dr Chia Jun Yang</b>	<b>NUHS</b> Urology	Validating the Effectiveness of Extracorporeal Shockwave Therapy for Erectile Dysfunction: A Combination of International Index of Erectile Function and PEDRA
<b>Dr Chin Hui-Lin</b>	<b>NUHS</b> Paediatrics	Validating the VEDALAB FRT-CHECK-1 Device for Capillary Ferritin to Screen for Iron Deficiency in Infants in Singapore
<b>Dr Tiffany Priyanthi Hennedige</b>	<b>NCCS</b> Oncologic Imaging	Use of Intravoxel Incoherent Motion for the Detection of Metastatic Regional Nodes in Pelvic Carcinomas
<b>Dr Jonathan Lee Wei Jie</b>	<b>NUHS</b> Gastroenterology & Hepatology	Gut Dysbiosis Associated with Obesity
<b>Dr Li Hao</b>	<b>TTSH</b> Otorhinolaryngology	Is Connexin Overexpression Implicated in the Impaired Healing of Skin and Mucosa in Head and Neck Surgery Performed after Radiotherapy?
<b>Dr Greg Li</b>	<b>SingHealth</b> Investigational Medicine Unit	A Pilot Study to Develop a Novel Algorithm to Risk Stratify Medical Inpatients in an Acute Hospital General Medical Ward
<b>Dr Lim Beng Leong</b>	<b>NTFGH</b> Emergency	Identifying Crucial Factors Associated with Hyperoxemia among Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease in the Emergency Department
<b>Dr Lim Hui Fang</b>	<b>NUHS</b> Medicine	The Mechanistic Relationship between Insulin Resistance and Glucocorticosteroid Resistance in Obese Asthmatics
<b>Dr Aishworiya Ramkumar</b>	<b>NUHS</b> Paediatrics	Predictors of Outcome of Autism Spectrum Disorder
<b>Dr Iris Rawtaer</b>	<b>NUHS</b> Psychological Medicine	In-Home Sensors for Assessment of Cognitive and Psychological Health of Older Adults: A Pilot Study
<b>Dr Kiattisa Sommat</b>	<b>NCCS</b> Radiation Oncology	Fluorine-18-Labelled Fluoromisonidazole Positron Emission Tomography (18F-FMISO PET) Guided Intensity-Modulated Radiotherapy (IMRT) in Nasopharyngeal Carcinoma: A Feasibility Study
<b>Dr Balamurugan Vellayappan</b>	<b>NCCS</b> Radiation Oncology	Identifying Immunological Predictors of Response in Rectal Cancers
<b>Dr Sinead Wang Zhen</b>	<b>SingHealth Polyclinics</b> (Marine Parade)	Diabetes and Health Outcomes Study: A Cohort Study of Type 2 Diabetics in Primary Care
<b>Dr Yeo Tianrong</b>	<b>NNI</b> Neurology	Prevalence of CNS Autoantibodies in Patients with Epilepsy of Undetermined Cause and Insights into Treatment Effect: A Pilot Study
<b>Dr Zhong Youjia</b>	<b>NUHS</b> Paediatrics	Identifying Oncogenic Mutations in Epstein-Barr Virus Associated With Post-Transplant Lymphoproliferative Disorder in Children
<b>Dr Zhuang Kun Da</b>	<b>SGH</b> Radiology	Combination of Cutting and Drug-Eluting Balloon for Treatment of Resistant AVF Stenosis

# CLINICIAN SCIENTISTS IN THE SPOTLIGHT 2015

## A Vision to Succeed

Imagine a future where the body's immune system can be reliably recruited to target and fight off the scourge of cancer cells. Cancer patients will benefit from less drastic and debilitating side effects of traditional treatments, such as chemotherapy and radiation therapy, in which healthy cells are killed as collateral damage. This is particularly important for children with cancer.

Prof Dario Campana's research focuses on the cell therapy of cancer. He and his team are currently developing new ways to improve the anti-cancer capacity of immune cells and bring the technologies into the clinic. These include receptors that mark cancer cells for destruction by immune cells, and stimulating natural killer (NK) cells – a subset of immune blood cells – to kill NK-resistant tumours. Preliminary results have proven promising.

Prof Campana was awarded renewal of the STaR Investigator Award. "I feel honoured to receive such a prestigious award and am very grateful for NMRC's continued support in my mission to improve treatment outcome for cancer patients. This provides our team the opportunity to further the work that we have achieved during the first funding cycle enabled by my previous STaR Investigator Award," said Prof Campana.

But it was not simply a case of 'second time lucky' for the distinguished professor. He has produced 6 peer-reviewed articles, implemented 5 clinical trials, filed 3 patent applications and funded a new company within the five years since his first STaR Investigator Award.

"The STaR Investigator Award is the main source of grant support for my laboratory. It funds our manpower, facility and operating expenses. We now have room to focus on creative and serious research work without a constant scramble for grants, while also finding the time and resources to train the next generation of translational researchers," shared Prof Campana on how the STaR Investigator Award has been critical for his research to move forward.

Exciting research developments are already underway at Prof Campana's laboratory. With the next five-year funding tranche secured, he aims to complete the five ongoing immune cell-based clinical studies for cancer patients, as well as starting new ones guided by encouraging laboratory results.

Prof Campana is optimistic about the clinical potential of immunotherapy, which he lamented had been often

neglected (and at times derided) in the past.

With its prominence propelled by dramatic results of successive clinical trials, he is glad that the potential of immunotherapy has been recognised and is set to become an integral component of cancer treatments in the future.

He added, "through our research, we hope to offer treatment options that are more effective than those available today to improve cure rates and quality of life during and after treatment. Our vision is for immunotherapy to succeed where all other treatments have failed."

## STAR Award

### Professor Dario Campana

Mrs Lee Kong Chian Chair in Advanced Cellular Therapy

Professor  
Yong Loo Lin School of Medicine, NUS  
National University Health System



## Scaling New Heights

Epigenetics is rising in prominence as a key puzzle in treating cancer. Cancer used to be thought of as solely a genetic disease. Recent research has however revealed that, epigenetic alterations can also act as key “trigger sequences” for activating or repressing genes and proteins functioning in cancer, and thus be a viable target for cancer screening and treatment.

Prof Patrick Tan has always had a keen interest in gastric cancer. That gastric cancer is the third leading cause of global cancer death spurs Prof Tan to further his research on its early detection and possible targets for treatment.

It was Prof Tan’s outstanding research on mapping the global epigenomic profiles associated with gastric cancer that won him the prestigious STaR Investigator Award in 2016. He has also previously published high impact research on various genetic and epigenetic models of tumourigenesis.

“I feel very humbled and honoured to receive the award. It is an affirmation of the impact and quality of the research that our incredible team of clinicians and scientists has done throughout the years. We are spurred to redouble our efforts in tackling this deadly disease, so that we can improve outcomes for patients with gastric cancer,” shared a delighted Prof Tan.

Through his research, Prof Tan and his team obtained invaluable insight on new approaches to the early detection of gastric cancer, reduction of treatment toxicities, and how drugs targeting the cellular epigenetic machinery could be harnessed for treatment. This will go a long way towards improving the survival rates of patients with gastric and other cancers.

According to Prof Tan, the award is critical for his research to scale new heights. Its five-year nature will allow him to initiate longer-term projects with more comprehensive scientific and clinical impact. Additionally, he will be able to assemble a suite of novel technology platforms to study the process of cancer epigenomics. Such platforms will not only accelerate his own research, but also contribute towards the cancer research efforts of other investigators worldwide.

“Our research bore fruit at the right time. Pharmaceutical companies are developing drugs to inhibit various types of epigenetic enzymes deregulated in gastric and other cancers. We are also excited to combine our knowledge of the epigenome with immunotherapy. It may be challenging to identify the right subset of patients who will respond to such drugs. But we believe that

this can be overcome through a robust interrogation of the cancer epigenome,” explained Prof Tan on the translational prospects that his research entails.

“The main focus of our research over the past 15 years has always been the patient,” added Prof Tan on his vision for the future of medicine. “No two patients and their cancer are the same. Each has developed under the influence of different molecular and environmental conditions. By understanding these processes, patients can benefit from more personalised and efficacious treatments. This is the future that our research aims to advance towards.”

## STAR Award

### Professor Patrick Tan

Professor  
Duke-NUS Medical School

Senior Principal Investigator  
Cancer Science Institute of Singapore, NUS



## An Eye for the Patient's Needs

Gene-based therapeutics is poised to become the next frontier of medical research. Silencing key genes responsible for diseases will open new doors to therapy for many intractable disorders. One way this can be achieved is through the use of small interfering RNA (siRNA), which directs the degradation of the mRNA necessary for translation of the target gene.

But the biggest roadblock to this mechanism lies in the first step. The chemically synthesised siRNA has to be safely delivered into the human body and released in a sustained manner into the right cells, without which the target genes cannot be silenced exogenously.

This key challenge of gene-based therapeutics is what A/Prof Tina Wong's research aims to overcome. Her research focuses on the design and development of nanoparticles for sustained siRNA delivery into wound tissues in the eye.

A/Prof Wong was awarded the CSA-INV award in 2011 and subsequently the CSA-SI award in 2015. "It gives me the opportunity to continue and pursue my research in wound healing, which is a highly complex and orchestrated event in which there is an unmet need for ground-breaking research. By silencing fibrosis in the early and late stages of wound healing, my research can help surgery patients achieve the best clinical outcome by minimising post-operative scarring."

In the next five years, A/Prof Wong intends to work with collaborators to fine-tune the technology and develop a new sustained delivery platform for gene-based therapies. The work will involve detailed and extensive studies in disease models to validate the delivery platform in different systems. She hopes that the novel therapy will help reduce the need for patients to visit the clinic, as well as the inconvenience of adhering to a strict medication regimen.

"The award will go a long way toward bringing my research to the next step - translating it into clinically meaningful outcomes for patients that maximise their convenience and quality of care. Looking back, the past three years had been a challenging yet exciting journey of benchwork to prove our concept of being able to deliver nucleic acids in sustained manner. To date, this is still a rare clinical feat."

A/Prof Wong's belief in research that delivers clear benefits to patients has always guided her approach to translational and clinical research. She subscribes to the tenet of "whatever we do in our research has to be

something that patients want". This, she asserts, is the key principle for her continued success as a clinician scientist renowned for her understanding of her patient's needs.

## CSA-SI Award

### Associate Professor Tina Wong

Senior Consultant  
Glaucoma Department, Singapore National Eye Centre

Head  
Ocular Therapeutics and Drug Delivery Research Group,  
Singapore Eye Research Institute

Associate Professor  
Duke-NUS Medical School



## No Magic Formula

Most people may have a negative perception towards body fat. But not all adipose tissues are created equal. Clinician scientists are increasingly examining a type of adipose tissue known as brown fat, and its emerging role in metabolic health and diseases like diabetes.

A/Prof Melvin Leow has been studying brown fat volume and activity in patients with thyroid disease. Brown fat metabolism is closely regulated by the level of thyroid hormones and thus can be a reliable indicator for the clinical diagnosis of abnormal thyroid function.

But assessing brown fat volume and activity often requires expensive equipment and consumables. PET-CT is presently deemed the gold standard for imaging brown fat. It is, however, a prohibitively expensive imaging method that also exposes patients to vast quantities of ionising radiation.

To address this gap, A/Prof Leow established infrared (IR) thermography as a new method of interrogating brown fat volume and activity. Its greater accessibility, safety and cost-effectiveness, compared to current methods, is set to overhaul the process of thyroid drug development and future metabolic research addressing obesity and diabetes.

"I am delighted to have achieved the CSA-INV award. It is a well-known fact that the award is so competitive that even prominent researchers with top-notch projects and strategic grantsmanship may not be guaranteed success. There is simply no magic formula to it."

A/Prof Leow also shared his gratitude to the NMRC for the funding support, which has been critical for him to progress further in his research. "The overall project cost is staggering. Every aspect of the study is hungry for funds: the manpower; the imaging equipment and consumables; compensation for the research subjects. The award has been a tremendous help. I can now focus full-time on my research."

While he foresees brown fat's potential in tackling the growing global scourge of obesity and diabetes, A/Prof Leow is aware that his research would first need to elevate thermal imaging from its infancy in brown fat visualisation and quantification. As such, he has teamed up with scientific experts on image processing to address the technical challenges involved and refine his methodology.

"We have already published, just this year, our preliminary findings on stimulating brown fat activation with capsinoids and quantifying the resultant thermal effects

through IR thermography. Its success gives me realistic assurance that we can extend our study to correlate the heat output measurements against current methods of PET scan, fat fraction MRI and whole body calorimetry. I hope that, with our efforts, IR thermography can eventually supersede PET-CT as the gold standard in metabolic studies. When that happens, this can accelerate the discovery and development of functional food or drugs that increase both brown adipose tissue quantity and activity as a means of managing obesity, and perhaps even diabetes."

## CSA-INV Award

### Associate Professor Melvin Leow Khee Shing

Senior Consultant  
Department of Endocrinology, Tan Tock Seng Hospital

Associate Professor  
Lee Kong Chian School of Medicine

Associate Professor  
Yong Loo Lin School of Medicine, NUS



## A Passion for Bench and Bedside

Type 1 diabetes (T1D) is an autoimmune disease that commonly presents during childhood. With no known cure nor optimal treatment options, patients with T1D face the debilitating prospect of multiple daily insulin injections for life and serious diabetes-related health problems.

Dr Ngee Lek is passionate about helping young patients with T1D through his expertise in paediatric endocrinology and diabetes. Straddling both bench and bedside, Dr Lek seeks to better understand the underlying mechanisms of immune-mediated beta cell death in T1D in order to develop better therapeutic alternatives to insulin replacement.

In his research, Dr Lek found that a deletion polymorphism in BIM – a promoter of apoptosis – confers the beta cells of some East Asian individuals with T1D greater resistance to autoimmune attack. The findings set forth new possibilities in treating T1D.

“I feel extremely honoured and privileged to receive the Transition Award. It symbolises NMRC’s faith in my research and my mission to uplift the lives of patients with type 1 diabetes. Despite my limited training in formal bench work, I will now have the time and funds to complete my research and grow my competencies as a clinical scientist,” remarked Dr Lek, who felt humbled by the experience.

For Dr Lek, it was a research journey fraught with challenges and uncertainties. He had ventured the path where few scientists went, employing novel molecular techniques and working on a slow-growing cell line that had only recently become available through a sole supplier. But he remain unfazed, and yet all the more excited, by the prospect of being able to help young patients with T1D

“It was also a huge challenge for me to look for the right research mentors, as well as basic scientists whom I can collaborate with for maximum impact. But I succeeded after much trial and error, and am now fortunate to work with and learn from top local scientists in the domain,” added Dr Lek.

His findings have helped facilitate greater research interest and action on T1D in Singapore. The KK Women’s and Children’s Hospital, where Dr Lek currently consults at, has replicated a similar study involving more than 100 young patients with T1D. The results will be further validated in the laboratory, as well as in 200 patients across other hospitals in Singapore. Once validated, the collective findings will be used to develop novel cell-based replacement therapy to treat T1D, and potentially the more prevalent type 2 diabetes.

“Medical research is a test of one’s passion and commitment towards bench and bedside. It may be an arduous journey strapped with uncertainties. However, the success achieved at the end of the journey makes all our hard work worthwhile. Because as clinician scientists, we know that our efforts in the clinic and the laboratory will improve and benefit the lives of many,” said Dr Lek in his encouragement towards fellow aspiring clinician scientists.

## Transition Award

### Dr Lek Ngee

Consultant  
Department of Endocrinology Science,  
KK Women’s & Children’s Hospital

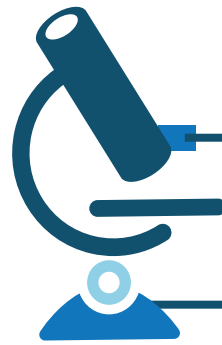
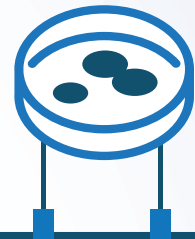
Assistant Professor  
Duke-NUS Medical School

Clinical Senior Lecturer  
Yong Loo Lin School of Medicine, NUS



RESEARCH

# GRANTS





## FUNDING TRANSLATIONAL AND CLINICAL RESEARCH

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

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

1. Investigator-led research
2. Strategic/Programmatic research

The first category supports different types of investigator-led studies via the following grant schemes:

- Clinician Scientist Individual Research Grant (CS-IRG)
- Clinician Scientist Individual Research Grant New Investigator Grant (CS-IRG-NIG)
- Cooperative Basic Research Grant (CBRG)
- Cooperative Basic Research Grant New Investigator Grant (CBRG-NIG)
- Bedside & Bench Grant (B&B)
- Health Services Research Competitive Research Grant (HSR-CRG)
- Health Services Research Competitive Research New Investigator Grant (HSR-NIG)

The second category supports programme-level research and strategic studies via the following grant schemes:

- TCR Flagship Programme
- Clinical Trial Grant (CTG)
- Ministry of Health Industry Alignment Fund (MOH IAF)
- Centre Grant (CG)

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

## ACHIEVEMENTS UNDER THE RIE2015 TRANCHE

NAME OF GRANT	NO. OF GRANTS AWARDED	FUNDS COMMITTED (\$ MIL)
CS-IRG	117	153.49
CS-IRG-NIG	72	16.00
CBRG	108	138.00
CBRG-NIG	52	11.95
B&B	20	38.16
HSR-CRG	44	21.71
HSR-NIG	16	1.79
CG	17	178.38
CTG	21	49.63
MOH-IAF	73	49.65
TCR	11	174.14

## INVESTIGATOR-LED RESEARCH

### Clinician Scientist-Individual Research Grants

Clinician Scientist-Individual Research Grants (CS-IRGs) are provided to clinician scientists to enable them to carry out medical research on a specifically defined topic for a period of three years in a local public institution. The focus of the research should be translational and clinical in nature. The quantum supported for CS-IRGs is up to \$1.5 million over a period of three years. CS-IRG grant calls are made twice per year, with closing dates on 1 June and 1 December.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2014	43	10	23.3%	15.90
May 2015	80	16	20.0%	23.17
Nov 2015	67	12	17.9%	17.39
<b>TOTAL</b>	<b>190</b>	<b>38</b>	<b>20.0%</b>	<b>56.46</b>

### CS-IRG New Investigator Grants

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

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2014	19	9	47.37%	1.79
May 2015	29	13	44.83%	2.92
Nov 2015	25	7	28.00%	1.60
<b>Total</b>	<b>73</b>	<b>29</b>	<b>120.2%</b>	<b>6.31</b>

### Cooperative Basic Research Grants

Cooperative Basic Research Grants (CBRGs) are provided to non-clinician researchers to carry out basic and translational clinical research that is relevant to human health, as well as research that looks at the causes, consequences, diagnosis and treatment of human diseases. CBRGs also aim to promote basic biomedical sciences (BMS) research collaborations across institutions in Singapore. The quantum supported for CBRGs is up to \$1.5 million over a period of three years. CBRG grant calls are made twice a year, with the closing date on 1 June and 1 December.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2014	96	14	14.6%	17.72
May 2015	116	13	11.2%	17.97
<b>Total</b>	<b>212</b>	<b>27</b>	<b>12.7%</b>	<b>35.69</b>

## CBRG New Investigator Grants

The CBRG New Investigator Grant (CBRG-NIG) is a sub-category of the CBRG that is targeted specifically at new non-clinical investigators. The CBRG-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 CBRG-NIGs is up to \$200,000 over a period of two years.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2014	25	8	32.0%	1.85
May 2015	32	8	25.0%	1.91
<b>Total</b>	<b>57</b>	<b>16</b>	<b>28.1%</b>	<b>3.76</b>

## Bedside & Bench Grants

Bedside & Bench (B&B) Grants aim to foster closer interactions between basic scientists and clinicians in order to translate scientific discoveries in the laboratory into clinically useful and commercially viable applications to improve health outcomes.

For B&B Grants, each Co-Principal Investigator must provide symmetrical intellectual inputs for the project. Partnerships with industry collaborators are strongly encouraged and additional consideration will be given to proposals that demonstrate industrial interest or engagement. The scheme supports up to \$5 million per project depending on the host institutions of the Co-Principal Investigators, with funding provided for up to three years. B&B grant calls are made once a year, with the closing date in mid-January.

GRANT CALL	LETTERS OF INTENT RECEIVED	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2014	28	19	4	21.1%	8.23

## Health Services Research Competitive Grants

The Health Services Research Competitive Research Grant (HSR CRG) is a MOH research grant established in 2009. This Competitive Research Grant aims to promote the conduct of HSR and enable the translation of HSR findings into policy and practice. The quantum supported for HSR CRG is up to \$1 million over a period of two years. HSR CRG grant calls are made once a year, with the closing date on 1 June.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
May 2015	39	8	20.5%	4.75

## HSR New Investigator Grants

The Health Services Research New Investigator Grant (HSR NIG) sub category of the HSR CRG was launched with the aim to support new HSR researchers. The quantum supported for this new subcategory is \$100,000 over 2 years. The HSR NIG grant calls are made once a year, with the closing date on 1 December.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	SUCCESS RATE	AMOUNT COMMITTED (\$ MIL)
Nov 2015	14	1	7%	0.12

## STRATEGIC/THEMATIC RESEARCH

### Centre Grant Funding Framework

The aim of the revised Centre Grant (CG) funding framework is to provide core funding support to the public hospitals and national disease-specific centres to build up their core research capabilities in terms of common research platforms, shared equipment and core research manpower. One of the key aspects of the CG funding model is to also provide longer-term research funding to sustain core research activities in the eligible research institutions.

The revised CG funding framework adopts a competitive performance-based mechanism to award funding. It evolved from two previous NMRC research funding frameworks: the Institutional Block Grant/Enabling Block Grant (IBG/EG) and the Centre Grant/Programmatic Project Grant (CG/PPG), with integration of key successful components from the previous models.

NMRC launched the first grant call of the revised CG funding framework in August 2012 and received applications from 17 eligible centres/institutions. Each application underwent two levels of evaluation: first, looking at the institution's research performance over the past three years; and second, assessing the institution's proposed four-year strategy for building up its core research capabilities. The 17 centres/institutions were awarded funding quanta ranging from \$3 million (for developing centres) to \$26 million (for established centres) for a funding period from 1 April 2013 to 31 March 2017.

The Centre Grant Scientific Advisory Board (CG-SAB), comprising members from the NMRC Board and International Expert Panel, was formed to conduct a mid-term review on how the various centres/institutions have progressed with their CG programmes. CG-SAB will work with the funded entities to ensure appropriate utilization of the research funds, and where necessary, provide guidance to redirect them back on track to their proposed CG research.

### Clinical Trial Grant

The Clinical Trial Grant (CTG) is a strategic initiative that was launched by NMRC in late 2012 to support clinicians carrying out clinical trial studies for the development of novel therapies, moving promising ideas from bench to bedside, to improve health outcomes. There are three schemes under the CTG programme:

1. **The Co-Development Scheme (Co-D)** supports clinical trial projects carried out via a public-private partnership (PPP) model, in which a clinician collaborates with an industry partner. The clinician can apply for Co-D funding for 50 percent or less of the total project cost. An industry partner must provide co-investment (either cash or in-kind contributions) representing 50 percent or more of the total project cost. The quantum for Co-D funding is up to \$5 million over five years. The Co-D scheme is open throughout the year.
2. **The Investigator-Initiated Trials - Early Phase Scheme (IIT-E)** supports investigator-initiated Phase I and II clinical trials carried out by clinicians. The scheme should preferably support the development of locally produced assets, ideas and compounds. Partnership with industry for carrying out the trial is optional. The quantum for IIT-E funding is up to \$7 million over five years. The IIT-E scheme grant calls are made twice a year, with closing dates on 1 June and 1 December.
3. **The Investigator-Initiated Trials - Late Phase Scheme (IIT-L)** supports investigator-initiated Phase III and IV clinical trials carried out by clinicians. Partnership with industry for carrying out the trial is optional. The quantum for IIT-L funding is up to \$4 million over five years. The IIT-L scheme grant calls are made twice a year, with closing dates on 1 June and 1 December.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	TOTAL SUM AWARDED (\$ MIL)
FY2015	17	5	24.75

<sup>3</sup> Launched in 1994, the IBC/EG scheme provided annual block funding to national disease-specific centres and research units in public hospitals.

<sup>4</sup> Implemented in 2009 to replace the IBC/EG scheme, the CG/PPG scheme was awarded through a competitive scientific review process involving a team of investigators who worked towards central research themes. It was also awarded to administration units.

## Ministry of Health Industry Alignment Fund

The Ministry of Health Industry Alignment Fund (MOH IAF) is a strategic initiative that was launched by NMRC to strengthen public-private collaboration in biomedical sciences (BMS) research and encourage commercially relevant research for better health outcomes. This programme was jointly developed with the Singapore Economic Development Board and comprises two schemes:

1. **The Category 1 (Cat 1)** funding under the MOH IAF was launched in early 2013 to support both clinicians and non-clinicians in their partnerships with industry in pre-clinical and clinical research. Joint funding from industry is a prerequisite, with an industry partner covering at least 70 percent of the total project cost via cash or in-kind contributions. The quantum for MOH IAF Cat 1 funding is up to \$500,000 for pre-clinical projects and \$1 million for clinical projects. In the case of projects involving both pre-clinical and clinical research, the funding quantum is up to \$1.5 million. Cat 1 funding is provided for up to two years. The Cat 1 funding is open throughout the year.

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	TOTAL SUM AWARDED (\$ MIL)	INDUSTRY DOLLARS ATTRACTED (\$ MIL)
FY2015	38	38	21.70	82.40

2. **The Category 2 (Cat 2)** funding under the MOH IAF was launched in late 2013 to support both clinicians and non-clinicians in pre-clinical and clinical research that will pre-position Singapore as a desirable location for industry to undertake TCR activities. Industry interest is a prerequisite. Cat 2 funding is up to \$3 million and is provided for up to three years. There is one pilot grant call in 2013 (future call is to be confirmed).

GRANT CALL	PROPOSALS REVIEWED	GRANTS AWARDED	TOTAL SUM AWARDED (\$ MIL)
May 2015	19	2	5.91

## Translational and Clinical Research (TCR) Flagship Programme

The TCR Flagship Programme is a strategic initiative that was launched by NMRC in 2007 to fund TCR in key disease areas of clinical relevance to Singapore. The programme's aims are:

- To bring together the best complementary research strengths in hospitals, national disease centres, universities and A\*STAR research institutes to focus on diseases or research themes of strategic importance.
- To build up a critical mass of experienced high-level researchers to facilitate a broader research platform, and increase collaboration both locally and internationally.
- To establish Singapore as a global leader in the study of key strategic medical research fields by integrating, coordinating and leveraging the full spectrum of research capabilities in Singapore, from basic science to clinical research, in a comprehensive manner.

In view of the success of the early programmes funded under the Science and Technology (S&T2010) framework, further funding of \$175 million has been secured from the National Research Foundation's (NRF) Research, Innovation and Enterprise 2015 (RIE2015) Open Collaborative Funds (OCF). This helps provide opportunities for new programmes to be funded and existing programmes to be renewed on a competitive basis.

Under RIE2015, two tiers of TCR Flagship Programme funding are available

- Tier-1: Capped at \$9 million, inclusive of indirect costs, over a period of five years.
- Tier-2: Capped at \$25 million, inclusive of indirect costs, over a period of five years.

A total of 11 TCR Flagship Programmes were awarded – six Tier-1 and five Tier-2 programmes. Three of the Tier-2 programmes awarded were renewals.

### Overview of TCR Flagship Programmes Awarded in FY2015

Title	Research Area	Lead PI (Institution)	Year of Award
The Eradication of Chronic Hepatitis B	Infectious Disease (Hepatitis B)	Prof Lim Seng Gee (NUHS)	2015 (Tier-2)
Precision Medicine in Liver Cancer across an Asia-Pacific Network	Oncology (Liver Cancer)	Prof Pierce Chow Kah Hoe (NCCS)	2016* (Tier-1)
Targeting Brain Tumours: Improving Lives through Precision Medicine	Oncology (Brain Tumour)	A/Prof Christopher Ang Beng Ti (NNI)	2016* (Tier-1)

\* refers to Tier-1 projects capped at \$7.5mil (incl. of IRC) instead of \$9mil (incl. of IRC).

## TCR FLAGSHIP ACHIEVEMENTS UNDER RIE2015

### Genetic Predisposition, Epigenetic Change, microRNA Profiling and Experimental Therapies in Heart Failure

The Tier-1 TCR Flagship Programme aims to improve the understanding of inherited risk factors for heart failure, with a view to improve the prediction of heart disease and to identify new treatments. This will be achieved through genetic studies and the identification of specific gene products.

#### Milestones

- Made important progress in: (i) the recruitment of key disease cohorts for genomic and epigenomic studies; (ii) the identification and characterisation of non-coding RNA species (particularly miRNAs) in heart failure groups; and (iii) focused mechanistic studies in laminin A- and Sun1-mediated cardiac pathology.
- Established the first landscape of circular RNAs in human heart tissue.
- Discovered at least two long non-coding RNAs that influence the cardiac cell cycle and cardiomyocyte regenerative potential.
- Collected preliminary data in vitro and in vivo on newly characterised microRNAs that could be manipulated to ameliorate cardiac response to ischaemic injury.
- Built collaborative linkages within and beyond Singapore, which ignited a nationwide integration of cardiovascular (especially heart failure) research best exemplified by the newly initiated and funded "ATTRaCT" consortium of the two heart centres and five basic research institutes. The initiative aims to address the biology and clinical epidemiology of heart failure, which had attracted multiple connections and partnerships with the industry.
- Progressed biomarker and genotyping contracts with AstraZeneca and Bayer HealthCare.



Principal Investigator:  
**Professor Arthur Mark Richards**

Yong Loo Lin School of Medicine,  
National University of Singapore

### Non-Small Cell Lung Cancer: Targeting Cancer Stem Cell and Drug Resistance

The Tier-1 TCR Flagship Programme focuses primarily on individuals with lung cancer who have never smoked (termed "never-smokers"). The programme aims to conduct a comprehensive analysis of the cancer genome, look for novel genomic mutations that can be treated by new targeted agents, address mechanisms of therapeutic resistance and develop appropriate intervention strategies to improve survival outcomes.

#### Milestones

- The plethora of trials of genome-directed targeted therapies and immunotherapies in lung cancer have helped us understand the tremendous benefits and also the limitations of the novel drugs. Ceritinib is now commercially available for a lung cancer subset, adding yet another treatment option to this erstwhile untreatable disease when standard options are exhausted.
- Initiated and implemented many early phase clinical trials of genome-directed targeted therapies and immunotherapies in lung cancer, to expand treatment options for lung cancer patients.



Principal Investigator:  
**Associate Professor Tan Eng Huat**

National Cancer Centre Singapore

- Secured investments for trials from multinational pharmaceutical companies such as Novartis. The availability of these trials have also attracted a higher proportion of foreign patients seeking novel therapies while the access to a larger collection of lung cancer tissues, both local and overseas, allowed a better understanding of the genomic landscape of lung cancers in the country, making Singapore in the league of the first-world nations.

## Eye Surgery and Innovative Technologies (EyeSITE)

The Tier-2 TCR Flagship Programme is a continuation of the previous eye diseases TCR Flagship Programme titled “Translational Research Innovations in Ocular Surgery (TRIOS)” carried out from July 2008 to July 2013. It builds upon the notable achievements of the previous Programme, and aims to develop novel clinical therapies and diagnostic applications to help alleviate ocular morbidity from major eye diseases.

### Milestones

- Developed the world’s first sustained-release nanomedicine through the nanoliposomal latanoprost formulation, which was a technological breakthrough in the field of sustained-release nanotechnology and applicable also to other ophthalmic conditions. Also incorporated a spin-off company - Peregrine Ophthalmic Pte Ltd.
- Developed three novel synthetic antimicrobial molecules, through the AntiMicrobial against Ocular Pathogen (AMOP) project, with vast potential applications in disinfection systems, and incorporated an NIAID-funded spin-off to accelerate drug development.
- Established a robust and reproducible system for in vitro cell culture of corneal endothelial cells with the ability to passage the cells, hence treating many patients with fewer donors. Only one of only two laboratories worldwide have performed this technique and a clinical trial had been applied for.
- Developed the lenticular storage concept, and patented a novel femtosecond laser-assisted ocular surgery system in 2010 as the only reversible refractive procedure with first-in-man treatments. Clinical trials and negotiations are currently underway for licensing this technology to a well-known Singapore-based tissue banking company.



Principal Investigator:

**Professor Donald Tan**

Arthur Lim Professor  
Singapore National Eye Centre



## Singapore Gastric Cancer Consortium – Redefining Gastric Cancer Management

The Tier-2 TCR Flagship Programme is a continuation of the previous gastric cancer TCR Flagship Programme carried out by the Singapore Gastric Cancer Consortium (SGCC) from August 2007 to January 2013. It builds upon the notable achievements of the previous Programme, and aims to improve the management of gastric cancer and patient outcomes.

### Milestones

- Established the Gastric Cancer Epidemiology Programme (GCEP) comprising 3,000 pre-disease high-risk subjects aged 50 years and above, to explore the feasibility of early detection of gastric cancer through screening.
- Became the first programme in Singapore to diagnose early Stage 0 and Stage 1 gastric cancer through screening. The screening and resection provided secondary prevention, which has likely saved the lives of participants whose gastric cancer would otherwise not be detected by routine clinical care, and also avoided the direct costs of treating advanced gastric cancer.
- Developed the world's first real-time in vivo molecular diagnostic system to improve speed and cost-effectiveness for patients undergoing endoscopic examinations for diagnosing in real time pre-cancerous tissue in the gastrointestinal tract during endoscopic examination. Based on Raman spectroscopy, a vibrational spectroscopic technique used to collect a unique chemical fingerprint of molecules, the system can potentially improve the patient's prognosis as a result of early diagnosis.



**Principal Investigator:**  
**Associate Professor**  
**Yeoh Khay Guan**

Yong Loo Lin School of Medicine,  
National University of Singapore

## Singapore Programme of Research Investigating New Approaches to Treatment of Tuberculosis (SPRINT-TB)

The Tier-1 TCR Flagship Programme focuses on new approaches to discovering, developing and delivering improved treatments for tuberculosis (TB) – an infectious disease that sees 10.4 million new cases each year, with nearly 60% occurring in Asia.

### Milestones

- Published 25 peer-reviewed papers in top-ranked journals, presented nearly 50 abstracts in local and international scientific events and filed three provisional patent applications.
- Identified bortezomib, a multiple myeloma drug, as a potent new target for TB. This promising and now patented compound is currently undergoing lead optimisation, along with several other identified leads.
- Completed several studies aimed at implementing PET-CT and PET-MRI imaging with existing and novel ligands as a method to improve the monitoring of TB treatments.
- Initiated a large-scale Phase 2/3 trial to test novel TB combination regimens, which, together with other regional trials run by the programme, led to the founding of the Asian TB trials network.
- Expanded collaborative network to include multiple academic, clinical and industry partners in Singapore, as well as regionally and internationally.



**Principal Investigator:**  
**Professor Nicholas Paton**

Yong Loo Lin School of Medicine,  
National University of Singapore

## National Lymphoma Translational Research Programme: From Genomics to Therapeutics

The Tier-1 TCR Flagship Programme, which focuses on lymphoma, aims to sequence nasal NK/T-cell lymphoma (NKTCL) and achieve a deep understanding of genomic alterations associated with this cancer.

### Milestones

- Took the lead on whole genome sequencing studies of T-cell and NK-cell lymphoma (NKTCL), representing Singapore in the International Cancer Genome Consortium (ICGC).
- Published findings extensively across top-ranked journals, including The Lancet Oncology, The Lancet Haematology, Leukaemia (Nature) and Blood.
- Completed the genomic and functional studies on monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) and identified two important survival pathways – JAK/STAT and MEK/ERK – in this disease. There are clinical drugs targeting these pathways and in vitro studies have documented the response of patient-derived MEITL primary cells to these drugs.
- Made tremendous progress in the development of diagnostic markers for NKTCL, having established gene expression signatures with our collaborators in NIH that could effectively differentiate various subtypes of T-cell lymphoma with clinical significance, leading to potential plans to co-develop the gene signatures using the NanoString platform and validate with archived FFPE samples.
- Completed the preclinical study in collaboration with US-based pharmaceutical company, Principia Biopharma, of a novel Jak3 – specific inhibitor. This will potentially lead to a trial given the encouraging preliminary results.
- Established strategic collaborations with multinational pharmaceutical companies, such as Bayer HealthCare and ASLAN Pharmaceuticals.



Principal Investigator:

**Professor Lim Soon Thye**

National Cancer Centre Singapore

## Developmental Pathways to Health and Disease: Metabolic, Neurodevelopment and Related Outcomes

The Tier-2 TCR Flagship Programme is a continuation of the previous TCR Flagship Programme titled “Developmental Pathways to Metabolic Disease”, carried out from June 2009 to May 2014. It builds upon the notable achievements of the previous programme, and aims to understand how pregnancy and early childhood conditions may affect later growth and development, as well as metabolic, neurodevelopmental and other disorders, which have major public health and economic importance, not only in Asia, but globally.

### Milestones

- Influenced the screening policy of Gestational Diabetes Mellitus (GDM) in public hospitals through recommendations of universal screening and lifelong post-diagnosis follow-up, to allow early disease detection and intervention, thereby improving the long-term health of mother and child. The recommendation stemmed from findings that GDM is much more prevalent than previously thought, affecting up to 1 in 5 GUSTO women. Even in the absence of GDM, higher fasting glucose levels can affect infant adiposity and neural development, suggesting that surveillance is needed at levels below the formal diagnostic criteria.
- Established (i) microbial profile development in newborns as a potentially useful predictor of obesity risk later in life; and (ii) a catechol-o-methyltransferase (COMT) gene-environment interaction as a critical factor for brain development in susceptible infants and children.
- Observed that six-month-old GUSTO bilingual infants had enhanced ability to process new information and recognise familiar objects compared to monolingual infants, suggesting a potentially strong neurocognitive advantage for Singaporean children outside the domain of language.
- Found through MRI the first evidence that the development of the prefrontal and parietal cortex, brain regions critical for executive functioning and sensory processing, of GUSTO neonates born to anxious mothers is modifiable by the COMT gene, suggesting the importance of a nurturing environment during the child's early years.



Principal Investigator:  
**Associate Professor  
Chong Yap Seng**

Yong Loo Lin School of Medicine,  
National University of Singapore

## Translational Clinical Research Programme in Parkinson's Disease

The Tier-2 TCR Flagship Programme, which focuses on Parkinson's Disease (PD), aims to reduce the economic burden of PD through identifying factors or markers that can facilitate early diagnosis, disease monitoring, drug screening and development, patient-centred individualised treatment regimens, and cellular replacement therapies.

### Milestones

- Published more than 30 peer-reviewed papers across top-ranked clinical, genetics and basic science journals since the launch of the Programme.
- Developed the world's first 3D live human organoid bearing features of the human midbrain, and pioneered a novel method to differentiate human pluripotent stem cells (hPSCs) into a large multicellular organoid-like structure that contains distinct layers of neuronal cells expressing markers characteristic of the human midbrain. The method allows detection of electrically active and functionally mature mDA neurons and dopamine production in our 3D midbrain-like organoids (MLOs). The MLOs bearing features of the human midbrain will provide a tractable model system to study the human midbrain and its related diseases. The pioneering work would build the groundwork for other region-specific 3D brain cultures for modelling and elucidating novel aspects of brain diseases.



Principal Investigator:  
**Professor Tan Eng King**

National Neuroscience Institute, Singapore

## The Eradication of Chronic Hepatitis B

The Tier-2 TCR Flagship Programme, which focuses on chronic Hepatitis B (CHB), aims to reduce the economic and disease burden of Hepatitis B on patients and the healthcare system, by developing new treatments and strategies to eradicate the disease.

### Milestones

- Presented latest research breakthroughs (seven abstracts, including an oral presentation) at the recent International Meeting of the Molecular Biology of Hepatitis B Viruses in Korea, where we demonstrated the heterogeneity of T cell exhaustion markers at different stages of chronic viral infection. Complementing this is a study that found differing levels of toll-like receptor (TLR) expression levels in patients before, during and after HBeAg seroconversion. An examination of liver-specific immune cells in a mouse model showed pro-inflammatory responses to bacterial TLR agonists that we modulated via oral antibiotic treatment, suggesting a direct involvement of intestinal microbiota in liver injury.
- Established (i) microRNA as a suitable target for antiviral therapy by using a novel computational tool One-SENSE to show how selected microRNAs affect viral replication; (ii) a mannose-functionalised polyethylenimine (PEI) macromolecule as a potential antiviral drug, with the optimisation of a new mouse model and clinical studies currently underway.



Principal Investigator:  
**Prof Lim Seng Gee**

Yong Loo Lin School of Medicine,  
National University of Singapore

## Precision Medicine in Liver Cancer across an Asia-Pacific Network

The Tier-1 TCR Flagship Programme, which focuses on hepatocellular carcinoma (HCC), aims to develop an internationally competitive research programme that leverages cutting-edge technologies and research expertise in genomics and immunology, as well as an established collaborative multinational trials group, the Asia-Pacific Hepatocellular Carcinoma (AHCC), to advance therapeutic strategies for HCC. This includes meeting the pressing need for efficacious drugs, as well as bringing precision medicine to patients with HCC. The TCR will form the basis of a strategic HCC platform that informs and guides strategies in drug development and precision medicine programmes.

### Milestones

- Launched the world's first longitudinal HCC genomics, immunological and clinical study to resolve the challenges of intratumoural heterogeneity in lung cancer, with clinical sites across Asia-Pacific and mirroring the scale of the multi-site TRACERx study in Europe.
- Developed deep immunomics analyses that will enable the HCC study to potentially become the first in the world to identify mechanistic links between genomics and immunomics in HCC.



Principal Investigator:  
**Professor Pierce Chow  
Kah Hoe**

National Cancer Centre Singapore

## Targeting Brain Tumours: Improving Lives through Precision Medicine

The Tier-1 TCR Flagship Programme, which focuses on Glioblastoma (GBM), will define the subtypes of GBM with respect to prognosis and treatment, with the ultimate aim of matching patients to specific chemotherapies (i.e. precision medicine) to extend survival and quality of life. The programme capitalises on high-content genomic information for GBM from The Cancer Genome Atlas, USA. Biological validation of patient data-driven computational hypotheses can therefore be realised by tapping into the brain tumour resource at NNI – the only such international resource comprising patient cells, their matched animal tumours and primary tissues with clinical history.

### Milestones

- Signed the Memorandum of Understanding (MOU) with Siriraj Hospital, Mahidol University – the largest and oldest hospital in Thailand, to further expand capabilities in recruiting recurrent GBM patients for the n-of-1 precision medicine-based clinical trial.



Principal Investigator:  
**Associate Professor  
Christopher Ang Beng-Ti**

National Neuroscience Institute, Singapore



# EVENTS



## NATIONAL MEDICAL EXCELLENCE AWARDS 2015

The National Medical Excellence Awards (NMEA) is held annually to honour and recognise clinicians, clinician scientists and healthcare professionals for their invaluable contributions towards medical excellence in the areas of clinical care, clinical research, clinical quality, training and mentorship in Singapore. The awards also provide an opportunity to celebrate successes and hold up role models for the younger generation of clinicians and clinician researchers.

In 2015, the NMEA recognised seven individuals and one four-member team for their outstanding contributions to medical research, training and clinical practice. Awards were given out in six categories:

- 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

The recipients of this year's awards represented a wide range of disciplines, including cardiology, metabolic diseases, neurology, paediatrics and surgery. Despite their diverse backgrounds, the award winners all share a common commitment to excellence, which is reflected in their selfless dedication to raising the standards of medicine ever higher in Singapore.

## NMEA 2015 AWARD WINNERS

### National Outstanding Clinician Award 2015

Professor Tan Puay Hoon is a dedicated pathologist and one of the key opinion leaders on breast pathology internationally. Over the past 26 years, she has been working tirelessly behind the scenes to examine and understand what ails patients. She has since lost none of the passion that she has for pathology, which she describes as an invigorating discipline that is “very forward, very cutting-edge”.

Helmed by Prof Tan, the pathology department at SGH has grown from strength to strength in the last decade, handling more than 12 million investigations each year. Today, the department is widely recognised as a regional breast pathology hub for pathologists in the region and worldwide.

Prof Tan was instrumental in spearheading many initiatives at SGH aimed at enhancing patient care and management. These include multidisciplinary meetings, courses on pathology, as well as the implementation of collaborative digital pathology that allows for real-time consultation and discussion of cases with medical experts around the world.

Despite a hectic schedule largely focused on subspecialty surgical signouts, Prof Tan dedicates time to translational research on breast and prostate cancer. She has since published more than 400 papers in peer reviewed journals and participates regularly in regional and international meetings. Under her leadership, the department is actively focused on furthering research in the various fields of pathology.

A keen teacher, Prof Tan contributes immensely to mentoring and teaching activities locally and in the region, under the auspices of the Asia-Pacific Pathology Societies. She is the Chairman of the Pathology Specialists Training Committee and is an examiner for the Royal College of Pathologists of Australasia.

Prof Tan’s international renown as a key opinion leader on breast pathology and her outstanding contributions to the field were recognised when she was invited to be a Volume Editor for the 2012 edition of the WHO Classification of Tumours of the Breast. This is a distinct honour that Prof Tan shared with four internationally renowned breast pathology experts. This edition was highly commended in the Pathology category of the 2013 British Medical Association Medical Book Awards. Her latest contribution was in the 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs.



### Professor Tan Puay Hoon

#### Professor

Duke-NUS Medical School and  
Yong Loo Lin School of Medicine, NUS

#### Chairman

Department of Pathology,  
Singapore General Hospital

#### Academic Chair

Pathology Academic Clinical Programme





## Associate Professor Tai E Shyong

### Head & Senior Consultant

Division of Endocrinology, NUHS

### Associate Professor

Duke-NUS Medical School

### Associate Professor

Yong Loo Lin School of Medicine and  
Saw Swee Hock School of Public Health, NUS

## National Outstanding Clinician Scientist Award 2015

Associate Professor Tai E Shyong has made studying how chronic metabolic diseases, such as obesity and diabetes, impact health outcomes his key priority as an endocrinologist. His clinical and research achievements are paving the way for better understanding and strategy towards tackling the growing scourge of obesity and diabetes in Singapore and Asia.

As a clinician scientist, A/Prof Tai has headed various prominent studies on metabolic disorders. One such large-scale study involved more than 5,000 Singaporeans and investigators from across institutions, like the Singapore Eye Research Institute, Khoo Teck Puat Hospital and Singapore General Hospital. This collaborative effort led to the identification of risk factors and better understanding of the impact of diabetes and other metabolic diseases on the Singapore population.

For A/Prof Tai, a key enabler of his research achievements has been collaboration, and how he is harnessing the collective expertise and synergy to advance studies that require a multidisciplinary approach. Working hand-in-hand with MOH researchers, he developed a tool to optimise cost-effectiveness in aggressive lipid-lowering therapy for patients with the highest risk of heart disease.

Additionally, A/Prof Tai has contributed immensely to the understanding of the biological basis of type 2 diabetes (T2D) and other metabolic conditions. His collaborative work uncovered numerous new genes as putative causes of T2D, some of which could serve as new drug targets. His current research involves understanding why Asians are afflicted with T2D despite their relatively leanness, so as to identify biological pathways relevant to T2D in Asians.

Together with his collaborators, A/Prof Tai has facilitated innovative translational clinical research, not only within his specialty, but also in other disease areas such as cardiovascular diseases, ocular diseases and Parkinson's disease. Throughout his illustrious career, A/Prof Tai has published over 250 papers and chalked up more than 1,500 citations.

As Head of the Endocrinology division at NUHS, A/Prof Tai leads a review of the practice of endocrinology, specifically in diabetes and other chronic diseases. As the director of the Patient-Centred Medical Home Programme at NUHS, he heads a pilot programme at the NUH-Frontier Family Medicine Clinic to develop, implement and evaluate novel models of patient care for better healthcare delivery.

## National Outstanding Clinician Mentor Award 2015



### Professor Koh Tian Hai

#### Senior Advisor and Senior Consultant

Department of Cardiology,  
National Heart Centre Singapore

Professor Koh Tian Hai led NHCS from 2003 to 2014 as its longest serving Medical Director. During his 11 years at the helm, NHCS has grown from a specialty centre with just 650 staff, to a renowned public healthcare institution in the region with more than double the staff strength. Its services and facilities have also expanded to include operating theatres and a short stay unit, housed within its 12-storey building.

Prof Koh's astute leadership has positioned NHCS at the forefront of medical advancement. Inspired by his forward-thinking approach, clinicians have over the years actively sought out new, evidence-based medicine that will enhance outcomes and the quality of life for patients. As a national specialist centre for cardiovascular disease, NHCS has introduced many 'firsts' under Prof Koh's leadership, including the novel minimally invasive treatment modalities that placed NHCS on the world stage for pioneering complex cardiovascular therapies.

An eminent supporter of education and training, Prof Koh worked tirelessly to ensure that NHCS shares its specialist knowledge via training programmes for cardiovascular practitioners. In particular, Prof Koh took the SingLIVE course to new heights by collaborating with

EuroPCR to form the AsiaPCR-SingLIVE course in 2010. AsiaPCR-SingLIVE has since earned a reputation as the premier cardiovascular interventional courses in Asia, attracting cardiologists, cardiac surgeons and healthcare professionals from around the world.

Over the years, Prof Koh has trained and mentored numerous local and overseas doctors, particularly in the field of interventional cardiology. Many of his mentees have since assumed senior leadership positions regionally as heads of department or hospital directors. Prof Koh's deep domain knowledge, judicious decision-making skills and meticulous attention to care have drawn many clinicians, such as the current Medical Director of NHCS, Professor Terrance Chua, to seek him out for guidance and mentorship.

Recognising Prof Koh's leadership, the regional cardiology community elected him as President of the Singapore Cardiac Society from 2005 to 2007 and Emeritus Fellow of the Asian Pacific Society of Interventional Cardiology in 2008. Today, he advises the executive leadership of SingHealth, as well as the Singapore Cardiac Society, as a member of their Board.

## National Outstanding Clinician Mentor Award 2015



### Professor Lee Chuen Neng

#### Senior Consultant

Department of Surgery, NUH

#### Professor

Yong Loo Lin School of Medicine, NUS

#### Deputy Director

National University Heart Centre, Singapore

#### Chairman

Centre for Healthcare Innovation and Medical Engineering, NUS

#### Chairman

University Surgical Cluster, NUHS

Professor Lee Chuen Neng is known to many in the medical community as a master clinician, a visionary leader and an outstanding mentor. As a founding leader in cardiothoracic and vascular surgery, combined with his passion for passing on his skills, Prof Lee has developed generations of cardiac surgeons and general surgeons for Singapore. His personal clinical excellence exemplifies the high values and standards that he has inculcated in his students and mentees.

As a mentor, Prof Lee has groomed a new generation of cardiac and general surgeons in Singapore and beyond. Through his teaching and leadership, he ensures that the baton is now passed to this new generation, who will in turn further the advancement of surgery. His motto "we do the best for every patient in whatever we do" has inspired many of his mentees, who include luminaries such as Prof Wan Song from the Chinese University of Hong Kong, A/Prof Vahe Gasparyan from the Erebouni Medical Centre in Armenia, and closer to home, Prof Krishnakumar Madhavan, A/Prof Michael George Caleb, A/Prof Stephen Chang, A/Prof Jimmy So and A/Prof Edmund Chiong.

In his various capacities, Prof Lee has also introduced bold new research initiatives. These include IRIS (Initiatives for Research In Surgery), helped consolidate the Department of Surgery's research efforts, and to provide medical students insight and exposure to research methodology at the early stage of their careers.

As the Professor of Surgery at NUS, Prof Lee was instrumental in shaping education across faculties. He spearheaded MERCI (Medicine Engineering Research Commercialising Initiative) to promote interprofessional learning. MERCI allows engineering students and experts to collaborate and patent new products that impact the changing healthcare landscape.

Prof Lee is also well-known internationally and for locally for his medical teaching and mentorship. He holds several appointments in the local and international professional bodies, including President and Founding Council Member of the Asian Society for Cardiovascular and Thoracic Surgery, and Member of the Founding Editorial Board of the Asian Cardiovascular and Thoracic Annals. An avid researcher, he has published more than 100 papers and contributed chapters in various medical literature.

## National Outstanding Clinician Educator Award 2015

Prof Lim Shih Hui is a renowned clinician educator who diligently pursues new knowledge and proactively developed a systematic structure to transform the practice of neurology and medicine. His efforts and expertise in clinical neurology, epilepsy and electroencephalography (EEG) have greatly contributed to Singapore's international renown in neuroscience.

As a clinician educator, Prof Lim exudes an unmatched ability and fervour to inspire, motivate and influence medical students, junior doctors and specialists. Since 1993, he has devoted much of his time to teach clinical neurology and general internal medicine, where he imparted his clinical skills, developed his students' clinical acumen, and assisted them to build good ethical behaviour and professionalism. He was both supervisor and mentor to many neurologists and physicians in Singapore from the 1990s to 2000s.

Prof Lim now continues his passion for teaching through SingHealth's Internal Medicine Residency Programme and the Neurology Senior Residency Programme at the NNI-SGH campus. Over the course of his illustrious career, Prof Lim has received numerous awards in recognition of his outstanding contributions as a clinician educator, teacher and curriculum developer.

His renown and expertise as a clinician educator has made him a highly sought-after administrator of medical education. As SingHealth's Group Director of Education, Prof Lim takes charge of the educational and professional advancement of undergraduate, graduate and postgraduate health professionals within SingHealth. He is also the co-Director of Academic Medicine, Education Institute (AM·EI) and Senior Associate Dean of Duke-NUS Medical School.

Prof Lim plays a pivotal role in specialist training, accreditation and maintenance of clinical competencies, both in Singapore and overseas. As Master of the Academy of Medicine, he co-chairs a joint committee to oversee the training and assessment of 35 medical specialties and five medical sub-specialties in Singapore. As Chairman (Commission on Asian Oceanic Affairs) of International League Against Epilepsy (ILAE) from 1997 to 2009, he helped make SGH an important training centre for epilepsy fellows in the Asian-Oceanic region. He also set the international standard of EEG practice by establishing an EEG Certification Examination in Asia.



### Professor Lim Shih Hui

#### Senior Consultant

Department of Neurology,  
National Neuroscience Institute and  
Singapore General Hospital

#### Professor and Senior Associate Dean

Duke-NUS Medical School

#### Group Director (Education)

SingHealth

#### Co-Director

Academic Medicine Education Institute (AM·EI)

#### Master

Academy of Medicine, Singapore

## National Outstanding Clinical Quality Champion Award 2015

Associate Professor Thomas Chee Swee Guan is one of Singapore's pioneering clinicians on quality improvement. In the early 2000s, he was instrumental in conceptualising a local training curriculum for the Clinical Practice Improvement Programme (CPIP), which is applied across many public and private healthcare institutions today.

A/Prof Chee's passion and unwavering dedication towards quality has since inspired like-minded clinicians to form groups that champion quality and safety improvement in patient care. His influence has been evident in clinical practice and large-scale milestone projects, such as the management of hyperkalaemia, consistently safer warfarinisation, and timely tracheostomy weaning and removal.

As the Chairman of NHG's CPIP Expert Panel from 2002 to 2013, A/Prof Chee initiated over 1,000 clinical improvement projects, and was part of the faculty that trained more than 1,600 healthcare professionals from Singapore and around the region. His commitment contributed to multinational collaborations, which in turn led to better networking, as well as safer and more efficient care in Southeast Asia.

A/Prof Chee is also a venerable leader in the local radiology community. His contributions towards advancing the specialist field of radiology over the past 30 years have led to vast improvements in safety standards and clinical quality of patient care. Returning from training overseas, A/Prof Chee managed to forge new ground in the subspecialty of musculoskeletal and spinal radiology at TTSH while the field was still in its infancy in Singapore.

As Head of the TTSH's Diagnostic Radiology Department from 1999 to 2008, he oversaw the planning and implementation of radiology services support, both within TTSH and to the polyclinics, in addition to developing related protocols, guidelines and policies. He helped establish radiology services on-site at polyclinics and implemented an information and image archiving system, which allowed the radiologists to rapidly and seamlessly share information across locations.

A/Prof Chee is currently the Clinical Director of the Office of Clinical Governance, where he continues to spearhead initiatives that encourages evidence-based clinical care, cost-effective practices and greater safety standards, so that patients can benefit from more effective and better quality care.



**Associate Professor  
Thomas Chee Swee Guan**

**Associate Professor Thomas Chee Swee Guan**

**Senior Consultant**

Department of Diagnostic Radiology,  
Tan Tock Seng Hospital

**Clinical Director**

Office of Clinical Governance,  
Tan Tock Seng Hospital

## National Outstanding Clinical Quality Champion Award 2015



### Associate Professor James Yip Wei Luen

#### Chief Medical Information Officer

National University Health System

#### Senior Consultant and Programme Director

Department of Cardiology,

National University Heart Centre, Singapore

#### Associate Professor

Yong Loo Lin School of Medicine, NUS

Associate Professor James Yip Wei Luen has, since his early days as a clinician, envisioned how the use of Information Technology (IT) could potentially transform the healthcare sector.

One of his first projects was mooted in 1998 when he was a cardiology registrar at NUH. He introduced the Cardiology Information System (CIS) to enable the amalgamation of cardiology reports and images. This improved the quality of cardiology reports, which were previously documented by hand. This ingenuity led him to receive an award for his innovative infocomm solution, which has since been implemented in local restructured hospitals.

Appointed Chairman of Medical Informatics and Chief Medical Information Officer at NUH since 2008, A/Prof Yip has championed numerous award-winning IT projects to enhance the quality of care and improve processes in local public healthcare institutions. These include the implementation of ICD-9-CM for clinical systems, the Critical Medical Information Store – a national electronic platform, and the Critical Lab Results Alert System – a collaborative effort.

In collaboration with the IT team at TTSH, A/Prof Yip also developed the Electronic Inpatient Medication

Record (EIMR) system, which allows doctors, nursing staff and pharmacists to more effectively perform their daily clinical duties. He combined the EIMR system with the barcoding project for all medications and clinical decision support system, thereby developing the Closed Loop Medication Management System (CLMMS). CLMMS aims to reduce human error, enhance patient safety and improve operational efficiency. Thanks to his efforts, as many as 2/6 potential adverse drug events per hospital are avoided each day.

More recently, A/Prof Yip teamed up with a local company myHealth Sentinel, a healthcare technology company, to develop Singapore's first integrated tele-health monitoring system. The system targets patients with hypertension, heart failure and diabetes, allowing them to be cared for at home through tele-health tools that help in monitoring blood pressure, assessing blood glucose levels and titrating medications. Over the course of 10 months, close to 800 patients have benefited from better health management enabled by the system. This project was conferred the Best Project Award at the inaugural MOH Health IT Excellence Award 2015 in the category of IT Excellence in Increasing Access to Care. A/Prof Yip also won the Individual Award for Champion for Health IT Excellence.

## National Clinical Excellence Team Award 2015

Early childhood years are a significant period of growth and development. For children with developmental needs, it is crucial for intervention and support services to be provided to them and their families at an early stage, so that their developmental outcomes can be optimised.

The team from KKH's Department of Child Development (DCD) recognised a significant gap in how educational help is provided to pre-schoolers with mild developmental needs. To address this gap, they developed an innovative solution – the Developmental Support Programme (DSP).

The programme was first piloted by a Child Development Community Outreach Team within the department, with philanthropic funding from the Lien Foundation. It interfaces between health, education and social services, providing pre-schoolers with mild developmental needs learning support and therapy intervention that simulate the natural learning environments of kindergartens and childcare centres.

Now helmed and funded by the Ministry of Social and Family Development (MSF), DSP is currently provided in 300 pre-schools. The programme is slated to be made available to 1,200 pre-schools and childcare centres in Singapore over the next three to five years. The KKH DCD team has been appointed by MSF to be the consultancy team that builds capability and capacity for the pre-school landscape.

In traditional therapy services, children seek treatments in clinical settings while their parents try to generalise intervention strategies and outcomes to the children's natural learning environments. DSP is a novel programme that aims to detect and provide intervention support for pre-schoolers using an ecologically-integrated, community-based and family-centred approach. It trains and equips experienced early childhood educators with the appropriate knowledge and relevant skills to provide crucial support for these children.

Through the team's effort, children with developmental needs in Singapore will now have access to a more conducive learning environment. In addition, it empowers the community to build up its capability and capacity to support these children within their natural environment, and paves the way for other excellent programmes for children with developmental needs in Singapore.

## KK Women's and Children's Hospital Department of Child Development

### Associate Professor Lim Sok Bee

Senior Consultant and Head



### Dr Sylvia Choo Henn Tean

Senior Consultant



### Mr Tang Hui Nee

Assistant Director and  
Head Community Services



### Ms Oh Shujun

Psychologist



## NMRC AWARDS CEREMONY AND RESEARCH SYMPOSIUM 2016



In 2016, the NMRC Awards Ceremony and Research Symposium were held concurrently during a one-and-a-half day event that attracted about 300 leading clinician scientists, researchers and other key players in the field of biomedical research, and featured a total of 20 speakers from various healthcare institutions and the industry.

Held at the Suntec City Convention and Exhibition Centre on 24 and 25 February 2016, the event recognised clinicians and researchers for their achievements and contributions to the continuous improvement of care for patients. It also provided a useful platform for networking and collaboration across healthcare institutions, academia and the industry.

One of MOH's key priorities for this year is to promote research that improves care outcomes and to encourage innovative ideas that can future-proof Singapore's healthcare system. With the theme "Research for a Better Future", the event this year aims to foster stronger collaborations that lead to research excellence and better healthcare outcomes for a better future.

### Awards Presentation

The NMRC Awards Ceremony is a platform where awardees under the NMRC Human Capital and Talent Development Programmes, namely Singapore Translational Research (STaR) Investigator Award, Clinician Scientist Award (CSA), Transition Award (TA), MOH Healthcare Research Scholarship (MCI) and NMRC Research Training Fellowship, are recognised and honoured. The guest of honour was Mrs Tan Ching Yee, Permanent Secretary for Health.

This year, we invited Dr Howard Bauchner, Editor-in-Chief of Journal of the American Medical Association (JAMA), as the plenary speaker for the event's opening session, who spoke on "Precision Medicine and Big Data: Reconciling the Differences". This was followed by sharing sessions from recipients of the STaR Investigator Award, who regaled the audience with insights and experiences unique to their clinical and research background. We concluded the morning session with presentations from the lead PIs of three of the TCR Flagship Programmes, who shared their achievements and experiences thus far.



## Research Symposium

The Research Symposium is a platform to promote and inculcate the spirit of translational and clinical research in Singapore's biomedical and healthcare research landscape. For the event this year, we invited our awardees, as well as clinicians, researchers, collaborators and industry partners, to join us at the symposium for two days of intensive knowledge exchange and networking with the local research community.

Day One's concurrent sessions took off after the Awards Presentation, with parallel sessions for "Clinical Trials" and "Health Services Research". The day culminated in a Wine and Cheese Reception, which provided participants a comfortable setting to mingle, network and explore collaboration opportunities after the forum discussions.

The workshops continued on Day Two, with parallel sessions for "Medical Entrepreneurship and Innovative Technologies"

and "Career Progression for Clinician Scientists". The focus was on fostering innovative and enterprising directions that will allow Singapore's biomedical research to achieve better translational outcomes, and sustaining Singapore's pipeline of research talents.

Participants also had a chance to visit the exhibition booths during their break times, which showcased the services and latest projects undertaken by various institutions, namely:

- National Health Innovation Centre
- NUHS Investigational Medicine Unit
- NUHS TCR Programme (Metabolic Diseases)
- SERI TCR Programme (Eye)
- Singapore Clinical Research Institute
- SingHealth Investigational Medicine Unit
- Springer Nature



## BIOMEDICAL SCIENCES INTERNATIONAL ADVISORY COUNCIL MEETING 2015



On 4 and 5 May 2015, Singapore's Health and Biomedical Sciences International Advisory Council (HBMS IAC) held its annual meeting in London, UK. The meeting was brought forward from its usual schedule of November to dovetail with the broader RIE2020 planning timeline. HBMS IAC members were consulted on their views towards the development of the HBMS strategy for RIE2020.

Chaired by Sir Richard Sykes, the HBMS IAC convened to discuss the RIE2020 governance framework, budget principles and work plan. Noting the complexity of Singapore's HBMS landscape, its members commended the efforts of various agencies in developing and articulating a coherent national vision and strategy. The funding agencies will continue to work together to rally HBMS research performers towards the common goal of reaping health and economic benefits from our HBMS investments.

### Transition from RIE2015 to RIE2020

Under RIE2015, MOH has built capabilities in clinical research and fostered a strong pipeline of clinician scientists, particularly in the Academic Medicine Centres (AMCs). As the research ecosystem matures, the growth in R&D budget will be moderated for RIE2020. This will provide the impetus to focus on research areas where Singapore can achieve differentiation and global competitiveness, to facilitate collaborations amongst researchers, clinicians, funding agencies and the industry, as well as to develop a

sustainable funding framework. Improved health outcomes can be realised through a more targeted approach towards tackling diseases of high burden and relevance to Singapore. There is also a need to accelerate the economic value captured, through the creation of more R&D jobs, commercialisation of research discoveries and development of local enterprises.

### Progress in HBMS Efforts

HBMS has been a strategic initiative for Singapore since its inception in 2000 and the opening of Biopolis in 2003. Since 2000, employment in the HBMS manufacturing industry has grown threefold from 6,000 to 18,000 in 2014, while HBMS manufacturing output has increased by more than fourfold from \$6 billion to \$26 billion in 2014. The HBMS industry also plays an important role in attracting private sector investments. This is evident in the 25 percent growth of its Business Expenditure in R&D (BERD) from 2013 to 2014.

While economic outcomes remain an important measure of success for Singapore's investments in HBMS R&D, greater emphasis has been placed on health outcomes in the recent years. Efforts to translate healthcare research into clinical care will be intensified to achieve better health, better care and better life. NMRC will continue to, under RIE2020, develop and implement initiatives that facilitate the translation of research outputs into health outcomes, so as to improve the quality of life for Singaporeans.

# CHARTING AHEAD WITH RIE2020

## THE NEXT FIVE YEARS OF ADVANCING SINGAPORE'S HBMS OBJECTIVES

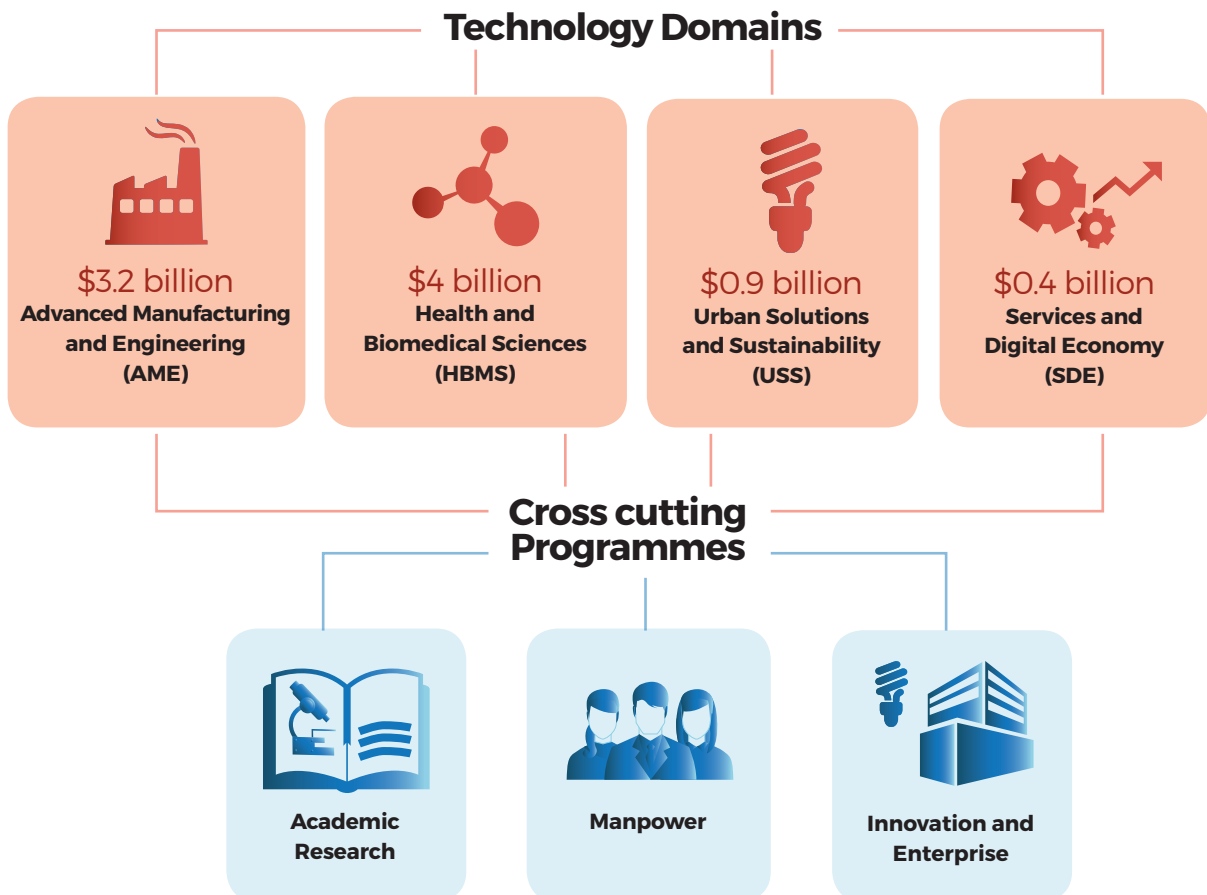
### OVERVIEW OF THE RIE2020 FRAMEWORK

Under the RIE2020 Plan<sup>3</sup>, Singapore will build upon the progress achieved under the RIE2015 Plan to reap greater value from its investment in research, innovation and interprise. Funding will be prioritised in four strategic technology domains:

- i. Advanced Manufacturing and Engineering (AME)
- ii. Health and Biomedical Sciences (HBMS)
- iii. Urban Solutions and Sustainability (USS)
- iv. Services and Digital Economy (SDE)

To ensure excellent science, a strong pipeline of skilled manpower and value creation, activities in these four domains will be supported by three cross-cutting programmes:

- i. Academic Research
- ii. Manpower
- iii. Innovation and Enterprise



<sup>3</sup> RIE Secretariat, NRF (2016). Research Innovation Enterprise 2020 Plan: Winning the Future through Science and Technology. Retrieved from: [http://www.nrf.gov.sg/docs/default-source/Publications/rie2020-publication-\(final\)ec954c68efe3678baf95ff0000030609.pdf](http://www.nrf.gov.sg/docs/default-source/Publications/rie2020-publication-(final)ec954c68efe3678baf95ff0000030609.pdf)



## ENVISIONING AHEAD IN HEALTH AND BIOMEDICAL SCIENCES

The HBMS sector is an increasingly important contributor to Singapore's economy. Fuelled by a rapidly ageing global population, demand for healthcare solutions, innovative medicines and medical devices will continue to increase. With its renown as a regional biomedical hub and strategic investments in HBMS R&D, Singapore is well-placed to leverage these market opportunities.

In addition to economic outcomes, Singapore will seek to ensure that its HBMS efforts will translate into the development of innovative healthcare services, drugs and devices that will deliver better health outcomes for Singaporeans. Greater emphasis will be placed on Health Services Research to enhance the delivery of a world-class, accessible and cost-effective healthcare system.

NMRC will work together with other HBMS agencies to develop research roadmaps, which will help determine specific problem statements and priorities for each of the identified therapeutic areas of focus. These include pathways to translate research discoveries into healthcare solutions, innovative medicines and medical devices that create value for Singapore's economy, as well as bring about greater health outcomes for Singaporeans.

## HBMS VISION

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.




## HBMS STRATEGY AT A GLANCE

### 4 Strategic Thrusts:

- **5 Therapeutic Areas of Focus** based on Singapore's scientific excellence, national needs and disease impact
  - Cancers
  - Cardiovascular Diseases
  - Diabetes and Metabolic/Endocrine Conditions
  - Infectious Diseases
  - Neurological and Sense Disorders
- **Translational Pathways** that bring research discoveries from bench to bedside, especially for the five therapeutic areas
- **Diversification beyond Pharmbio and MedTech** to grow health-related sectors
- **Increased Focus on Health Services Research** to improve the delivery of health services in Singapore discoveries from bench to bedside, especially for the five therapeutic areas

## NMRC RIE2020 FUNDING PORTFOLIO

Under the RIE2020's HBMS Domain, NMRC will continue to drive translational and clinical research through sustained and strategic investment in three key areas: human capital and talent development programmes, research grants, and knowledge exchange and enablers.

 <h3>HUMAN CAPITAL &amp; TALENT DEVELOPMENT PROGRAMMES</h3>	 <h3>RESEARCH GRANTS</h3> <table border="1"> <thead> <tr> <th data-bbox="576 918 798 1030">COMPETITIVE GRANTS</th> <th data-bbox="805 918 1024 1030">OPEN FUND</th> </tr> </thead> <tbody> <tr> <td data-bbox="576 1041 798 1635"> <ul style="list-style-type: none"> <li>Centre Grant (CG)</li> <li>CS-Individual Research Grant (CS-IRG)</li> <li>Health Services Research Grant (HSRG)</li> <li>Ageing National Innovative Challenge</li> </ul> </td> <td data-bbox="805 1041 1024 1635"> <ul style="list-style-type: none"> <li>Large Collaborative Grant (LCG)</li> <li>Individual Research Grant (IRG)</li> <li>Young Individual Research Grant (YIRG)</li> </ul> </td> </tr> </tbody> </table>		COMPETITIVE GRANTS	OPEN FUND	<ul style="list-style-type: none"> <li>Centre Grant (CG)</li> <li>CS-Individual Research Grant (CS-IRG)</li> <li>Health Services Research Grant (HSRG)</li> <li>Ageing National Innovative Challenge</li> </ul>	<ul style="list-style-type: none"> <li>Large Collaborative Grant (LCG)</li> <li>Individual Research Grant (IRG)</li> <li>Young Individual Research Grant (YIRG)</li> </ul>	 <h3>ENABLERS &amp; INFRASTRUCTURE GRANTS</h3>
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