7TH ASEAN MEDICAL DEANS' SUMMIT 2018

RESEARCH UPDATE

LAU Tang Ching

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

Outline

1. Current Projects
2. Updates
    - Dengue (Prof Jamuna)
    - TB (Koh DR on behalf of Prof Nick Paton)
    - Precision Oncology (Prof Pithukpakorn)
3. Developing a Nationwide Research Programme

UPDATES

PROGRESS OF RESEARCH PROJECTS

Project	Collaborators	Core Participants	Progress in years	Results/ Outcomes
Dengue	• Jamunarani S Vadivelu (Uni of Malaya) • Justin Chu (NUS)	✓ (8)	3 (started in 2015)	A clustered randomized control trial at Damansara Damai, Petaling Jaya, Selangor, for 2 years, to test the efficacy of an Aedes and dengue surveillance method.
Healthy Campus Initiative	• Maznah Dahlui (Uni of Malaya) • Teo Yik Ying (NUS)	✓ (2)	3 (started in 2015)	No updates since 2017: Due to the budget cut, we are not able to continue with the implementation and subsequent evaluation of the interventions. We are looking for grant from other sources.
Tuberculosis	• Nicholas Paton (NUS) • Teo Yik Ying (NUS)	✓ (16)	3 (started in 2015)	• Inaugural meeting on 19 to 20 Mar attended by over 30 key opinion leaders, clinical researchers and policy makers from 13 regional countries. • Network Steering Comm consisting of 11 regional reps formed in July 2018. • A-TRACTION Project Development Meeting on 10 to 11 Sep – to develop collaborative proposals that can be conducted under the Network and to submit for grant funding. • A-TRACTION Symposium in 1st quarter 2019 "Solutions to Asian TB problems through regional collaborative research".
Precision Oncology	• Manop Pithukpakorn (Mahidol Uni)			Siriraj is working with several university hospitals and research institutes under the 'Cancer Precision Medicine Network' in Thailand and currently focusing on 3 cancer types; breast cancer, head and neck cancer, and brain tumor. The project has been ongoing for 2 years now.

Dengue

Theme 1: Communicable Diseases (Dengue)	
Project Title: Host and Viral Factors that contribute to Dengue Susceptibility and Severity.	
Participating Countries	Indonesia, Singapore, Malaysia, Laos, Myanmar, Vietnam, Philippines
Specific Aims / Scope	• Based on cohort field collection of existing population studies in ASEAN. Host and viral factors will be investigated by genomic and proteomic platform technologies for disease severity outcomes. • Public Health and Surveillance program sharing among ASEAN countries for dengue virus infection.
Timeframe for completion	Around 5 years
Contact of Lead PI (Name, Country, Institution, Department, Email)	Prof Jamunarani S Vadivelu (Malaysia) and A/Prof Justin Chu (Singapore)

DENGUE

Jamunarani S Vadivelu

Faculty of Medicine, University of Malaya, Malaysia

TUBERCULOSIS

Koh Dow Rhoon

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

Tuberculosis

Theme 1: Communicable Diseases (TB)	
Project Title: A-TRACTION Asian Tuberculosis Research and Clinical Trials Integrated Organizational Network	
Participating Countries	Indonesia, Singapore, Thailand, Philippines, Malaysia, Cambodia
Specific Aims / Scope	• OVERALL AIM: a network to foster and coordinate TB clinical research in Asia • SPECIFIC PROJECTS: 1) Regional database • MDR – TB surveillance • MDR-TB clinical outcomes • Epidemiology of drug resistance 2) Regional Genomics platform 3) Regional Clinical trials: TRUNCATE-TB – new TB clinical trial done in Asia funded by Wellcome Trust ($10m)
Timeframe for completion	Around 5 years
Contact of Lead PI (Name, Country, Institution, Department, Email)	Prof Nicholas Paton (Singapore), Prof Teo Yik Ying (Singapore)

ATRACTION

Asian Tuberculosis Research And Clinical Trials Integrated Organizational Network

Professor Nicholas Paton
SPRINT-TB Programme Director
nick_paton@nuhs.edu.sg
+65 6772 6988

Pauline Yoong, Ph.D.
SPRINT-TB Programme Manager
mdcpy@nus.edu.sg
+65 6601 6352

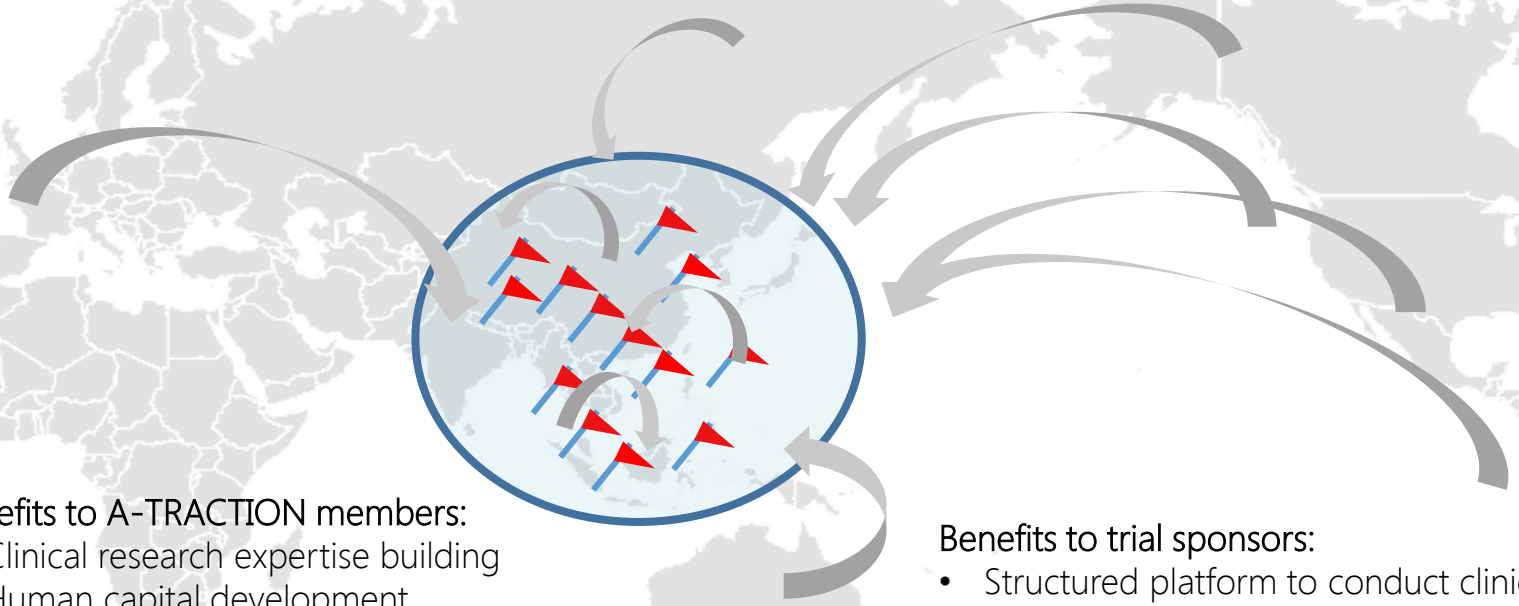
SPRINT TB
SINGAPORE PROGRAMME OF RESEARCH INVESTIGATING NEW APPROACHES TO TREATMENT OF TUBERCULOSIS

NUHS
National University Health System

A-TRACTION

OVERALL AIM

A network to foster and coordinate TB clinical research in Asia



Benefits to A-TRACTION members:

- Clinical research expertise building
- Human capital development
- Clinical trials infrastructure building
- Flow of funds for TB research into economies
- TB burden reduction in the long run

Benefits to trial sponsors:

- Structured platform to conduct clinical trials
- Shorter time to complete TB research projects
- Faster & more efficient answers to research questions

A-TRACTION Inaugural Meeting

Singapore, 19-20 March 2018

Attended by >30 key opinion leaders, clinical researchers and policy makers from 13 regional countries

Main outcomes of meeting:

- Sharing information on existing regional TB sites and national networks
- Sharing information on ongoing projects, national funding opportunities and how these could be synergistic
- Agreeing on a governance structure for the Network and to hold an annual symposium for regional TB Clinical research
- Agreeing on research focus (clinical research) and mechanism for establishing collaborative proposals (Project Development Meeting)

Funded by:

APEC Asia-Pacific Economic Cooperation · NUS National University of Singapore · SPRINT TB · Ministry of Health Singapore · NMRC National Medical Research Council Singapore · USAID · The Union International Union Against Tuberculosis and Lung Disease · Vital Strategies · An affiliate of the International Union Against Tuberculosis and Lung Disease

Network Steering Committee

Formed in July 2018

11 regional representatives with strong research credentials & national research leadership

Roles of the Steering Committee include:

- Providing expert oversight of Network
- Reviewing/approving research proposals/projects to be conducted under the Network
- Program committee for annual symposium
- Advise on developments within member countries/research networks
- Publicize the Network at national meetings & with key stakeholders in country
- Identify new opportunities for research collaboration & funding opportunities

A-TRACTION Project Development Meeting

10-11 September 2018, in Singapore

Will be attended by 11 senior established clinical researchers from 10 regional countries

Purpose of meeting is to develop collaborative proposals that can be conducted under the Network and to submit for grant funding

A-TRACTION Symposium

"Solutions to Asian TB problems through regional collaborative research"
Planned for 1st Quarter of 2019, with target size of 100-150 attendees

Symposium will include keynote speakers, and plenary sessions on topics including:

- TB Immunology Clinical Research
- TB Clinical Trials in Asia
- Latent TB
- Multi-drug resistant TB
- TB Diagnostics

A big emphasis on attracting abstracts from junior researchers

Funding and in-kind support

- Network initially supported under SPRINT-TB program (Singapore NMRC-funded program)
- In 2016 secured additional funding support (US$150,000) from APEC to initiate the A-TRACTION network
- Established partnership for in-kind support for A-TRACTION network with International Union Against TB and Lung Disease (the main international TB NGO)
- USAID agreed to fund the Project Development Meeting (US$30,000)
- Currently seeking additional financial support for the symposium (APEC funds restricted in their use)

Initial project for regional collaboration

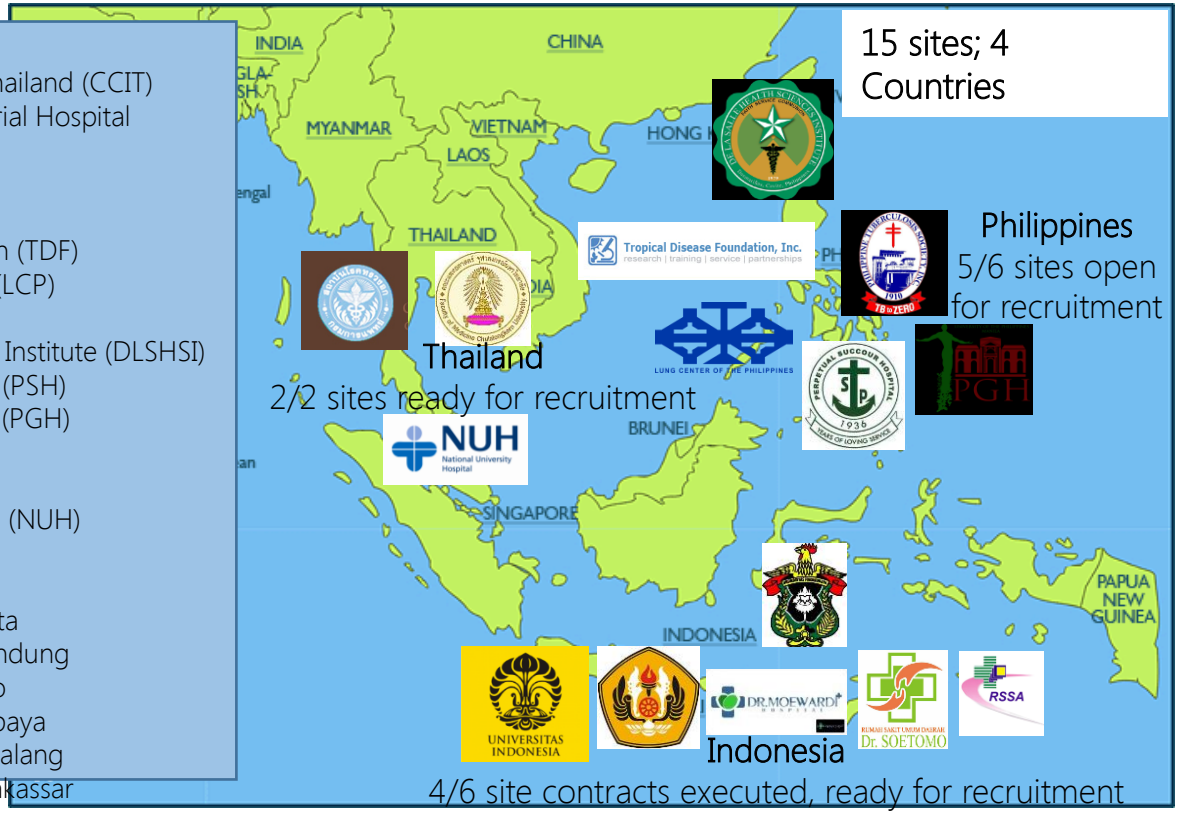
11 sites open for patient recruitment

THAILAND
Central Chest Institute of Thailand (CCIT)
King Chulalongkorn Memorial Hospital (Chula)

PHILIPPINES
Tropical Disease Foundation (TDF)
Lung Center of Philippines (LCP)
Quezon Institute (QI)
De La Salle Health Sciences Institute (DLSHSI)
Perpetual Succour Hospital (PSH)
Philippine General Hospital (PGH)

SINGAPORE
National University Hospital (NUH)

INDONESIA
Universitas Indonesia, Jakarta
Universitas Padjadjaran, Bandung
Dr. Moewardi Hosptial, Solo
Dr Soetomo Hospital, Surabaya
Dr Saiful Anwar Hospital, Malang
Universitas Hasanuddin, Makassar



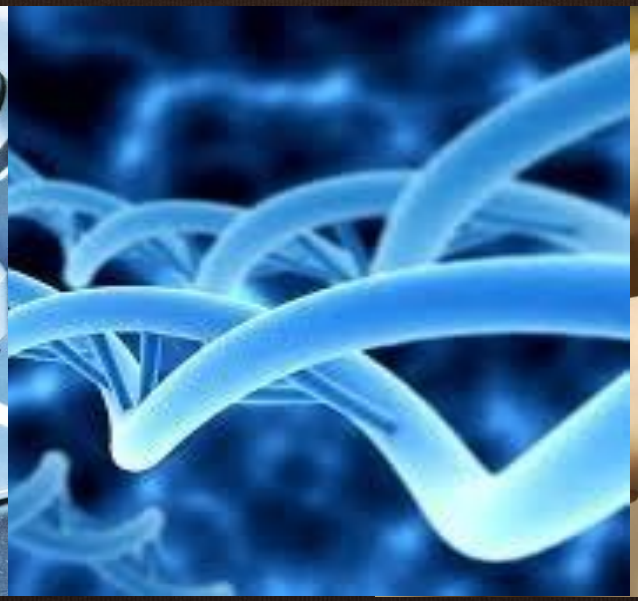
Precision Oncology

Theme 1: Non-communicable Diseases (Precision Oncology)	
Project Title: To be discussed	
Participating Countries	To be discussed
Specific Aims / Scope	• Biorepository & Bioinformatics: precision oncology set up for ASEAN Medical School network • Shared data • Decrease mortality rate and increase survival rate: selected cancers (Tm resistant) • Early detection and monitoring tool, R&D
Timeframe for completion	To be discussed
Contact of Lead PI (Name, Country, Institution, Department, Email)	Prof Manop Pithukpakorn (Thailand)

Mahidol University
Faculty of Medicine
Siriraj Hospital

Cancer Precision Medicine

ASEAN Medical School Network

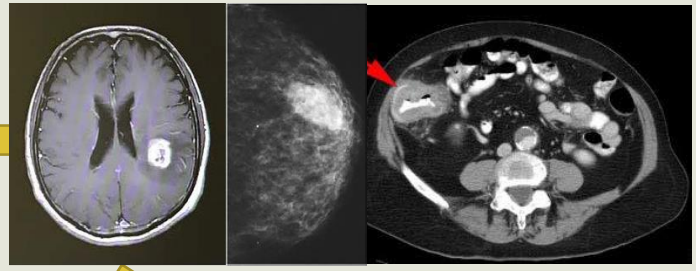


Manop Pithukpakorn, MD
Division of Medical Genetics
Department of Medicine

CANCER
PRECISION MEDICINE

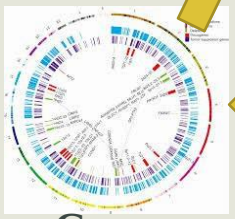
Databases/AI

REDCap
Research Electronic Data Capture



Patients

SiCORE PRECISION MEDICINE



Genome Landscape

Bioinformatics

Germline, cfDNA, biomarkers

Blood test

Surgery/Biopsy

Pathologist

Frozen specimens

Biobanking

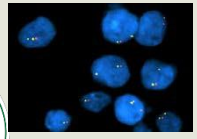
Genome Sequencing

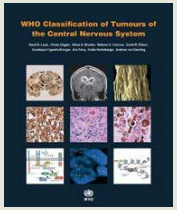
Diagnostics

Standard &Advanced Lab

Treatment selection

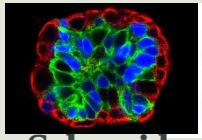
Advanced immunostaining





Cancer cell lines

Clinical Cohorts/Clinical Trials



Spheroid Organoid

Orthotopic xenograft

Zebrafish Model

Collaboration

RESEARCH UNIVERSITY NETWORK THAILAND

กระทรวงสาธารณสุข MINISTRY OF PUBLIC HEALTH

สวทช NSTDA

Drug testing/Tailored regimen

Genome Institute of Singapore A*STAR

National Neuroscience Institute SingHealth

DANA-FARBER CANCER INSTITUTE

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

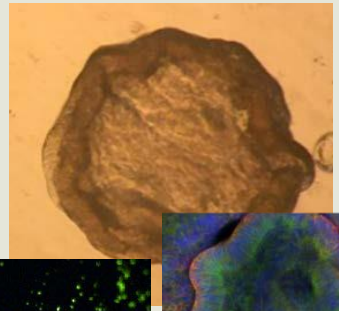
CANCER PRECISION MEDICINE

RESEARCH UNIVERSITY NETWORK THAILAND

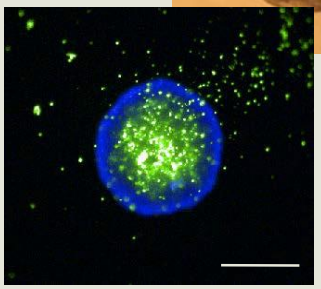
Network Resource

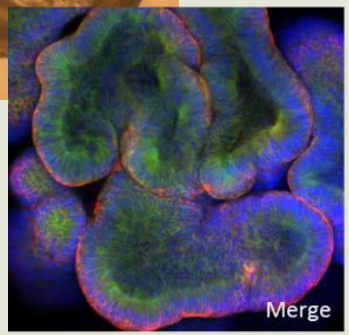
Clinical Database & Biospecimens from >3,000 patients

REDCap
Research Electronic Data Capture



>300 cancer genome sequencing data





>30 primary cancer cell lines/organoids

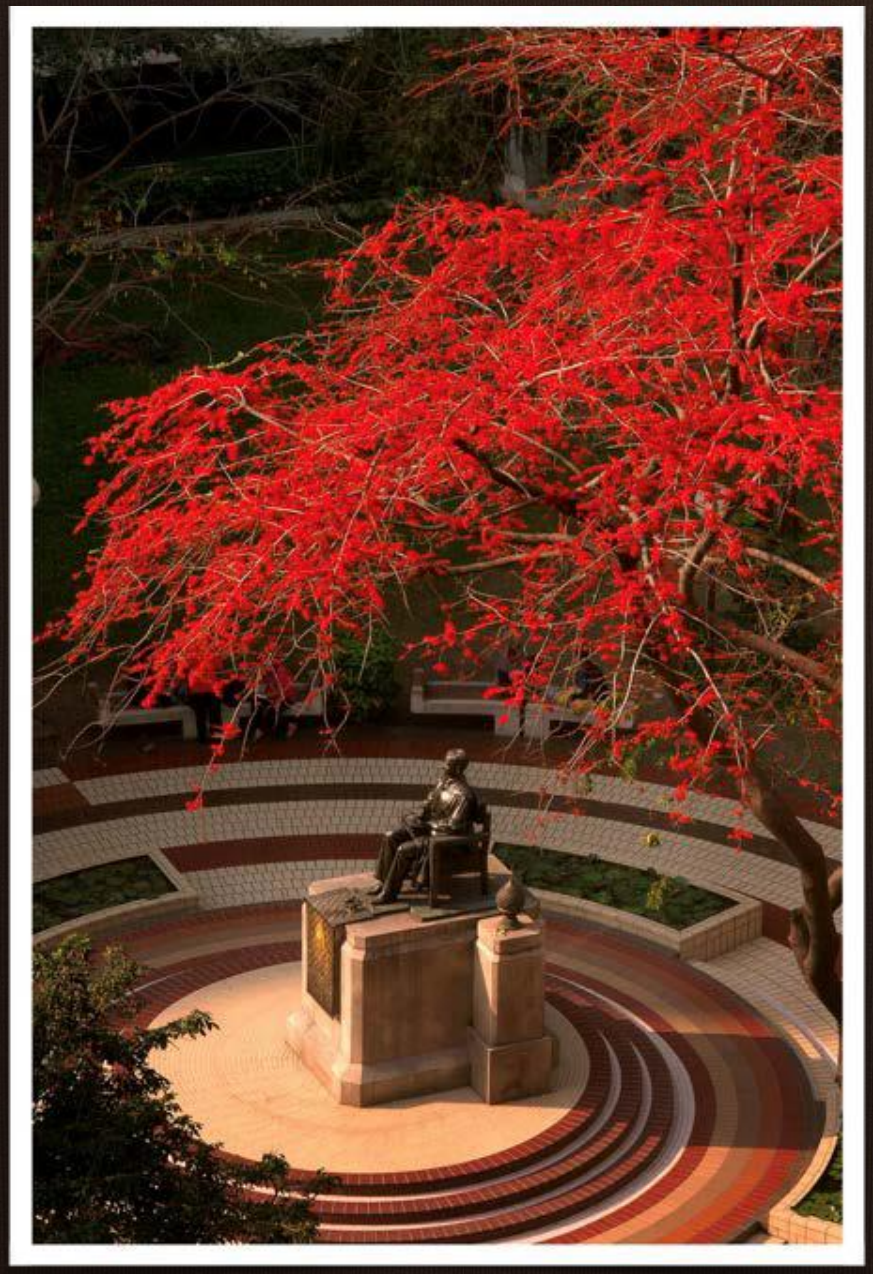
Multi-gene panel testing

Zebrafish model and drug testing platform

CANCER PRECISION MEDICINE

Scope of Research Network

- Focus on selected cancers (breast cancer, H&N cancer, colorectal cancer) with unique clinical/population aspect
- Set up biorepository: blood (serum/plasma, DNA), tissue
- Establish multidisciplinary databases: clinical data, pathological data, multi-omics data, cell line, PDX, drug screening data
- Data sharing policy
- Clinical implementation: individual cancer care, clinical trials, clinical guidelines/policies
- Capacity building
- Start with the most capable topic then gradually expand



Mahidol University
Faculty of Medicine
Siriraj Hospital

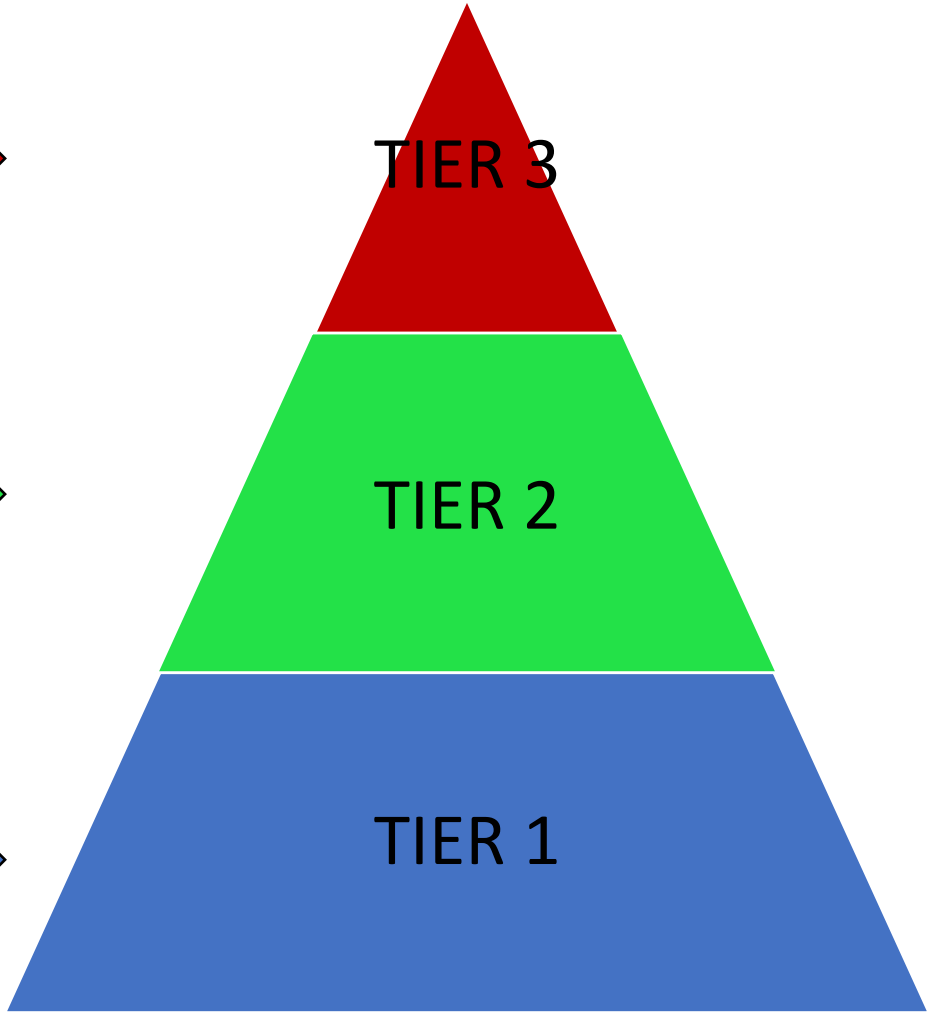
Questions & Answers

Consensus on Prioritisation of Research

Tier 3: 1 to 2 research projects of the highest importance for most member countries; most likely to engender widespread collaboration. Concerted funding from international agencies could be sought for these projects.

Tier 2: 2 to 3 research projects of high importance for several member countries; could lead to collaboration among several countries. Projects could be funded by the interested countries.

Tier 1: Multiple research project of intermediate importance for several member countries; may lead to collaboration among a few countries. Projects could be funded by the interested countries.



DEVELOPING A NATIONWIDE RESEARCH PROGRAMME

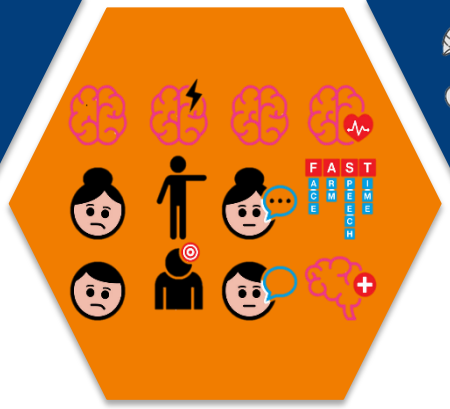
Dr Koh Dow Rhoon
Yong Loo Lin School of Medicine
National University of Singapore

Ministry of Health Singapore: 5 Therapeutic Areas of Focus

Infectious Diseases

Diabetes Mellitus and other Endocrine / Metabolic Diseases

Cardiovascular Diseases



Neurological and Sense Disorders

Cancers

Elements of a Nationwide Research Programme

- Leadership
- People
- Supporting infrastructure
- Grant mechanisms
  - Larger grants focused on cross-cluster collaborations between hospitals, national centres, academia and research institutes in the 5 key disease areas
- Master Agreements

Grants

Large Collaborative Projects
Supporting collaborative research aimed at 5 MOH therapeutic areas of focus

Centres, Enablers and Infrastructure
Structure basic-clinical or cross-cluster collaborations, to promote interdisciplinary projects between hospitals, national centres, academia and research institutes

Talent Development, Individual Research Projects
Various recognition and support schemes aimed to develop clinician-scientists in their research and career progression

National Innovation Challenge
Ensure that research outcomes are translatable to actual healthcare applications or public healthcare policies in short- to mid-term

Funding agencies in Singapore: National Medical Research Council: www.nmrc.gov.sg | National Research Foundation: www.nrf.gov.sg | Ministry of Education: www.moe.gov.sg

Building a nationwide research programme

Singapore Gastrointestinal Cancer Consortium

A national effort in translating science to benefit patient care

A National Effort in translating science to benefit patient care

SGCC Singapore Gastrointestinal Cancer Consortium

1st Translational and Clinical Research (TCR) Flagship Grant awarded in 2007
1st TCR grant renewal awarded in 2013

Universities

NUS National University of Singapore

NANYANG TECHNOLOGICAL UNIVERSITY

DUKE NUS GRADUATE MEDICAL SCHOOL SINGAPORE

Industry

MiRXES scire est agere "To Know is to Act"

NOVARTIS

SANOFI

BAYER

sengenics

illumina

TAIHO PHARMA SINGAPORE

RE-DEFINING THE MANAGEMENT OF GASTRIC CANCER

Strongly Facilitated by

NMRC National Medical Research Council Singapore

MINISTRY OF HEALTH SINGAPORE

NATIONAL RESEARCH FOUNDATION

A*STAR Agency for Science, Technology and Research SINGAPORE

DB singapore

Research Institutes

A*STAR Genome Institute of Singapore

NUS National University of Singapore | CSI SINGAPORE

A*STAR Institute of Medical Biology

A*STAR Experimental Therapeutics Centre

A*STAR Bioprocessing Technology Institute

A*STAR Singapore Immunology Network

Hospitals

Singapore General Hospital SingHealth

NUH National University Hospital

Tan Tock Seng HOSPITAL

Changi General Hospital SingHealth

Translation of Research to Healthcare Applications

New way to better predict stomach

- Symptoms for stomach cancer often show up late, and most cases are discovered at an advanced stage where the survivability of patients are low (5-year survival rate is at 27%).

- Researchers from the SGCC have found that DNA sequencing was more effective in detecting *Helicobacter pylori*, a key trigger for stomach cancer.

- The findings can be applied in future to better identify patients who have a high risk of developing stomach cancer.

The findings were published in Cancer Cell (2018).

Translation of Research to Outcomes
Policy Influence

Screening Pregnant women for DM

- 1 in 5 pregnant Singaporean women found to have gestational diabetes, even though half of them were thought to be at low risk and would normally not have been checked for it.
- Led to adoption of new policy by the Ministry of Health in 2017 to offer routine gestational diabetes screening for all pregnant patients.
- Detection of gestational diabetes will allow for timely medical intervention; to halt disease progression, and potentially reduce complications in newborns later in life

1. *Maternal Dietary Patters and Gestational Diabetes Mellitus in a Multi-Ethnic Asian Cohort: The Gusto Study, De Seymour et al 2016. Nutrients 8:E574*
2. *The Influence of Gestational Diabetes on Neurodevelopment of Children in the First Two Years of Life: A Prospective Study, Chai et al 2016. PLoS One 11:e0162113*
3. *Pregnancy-time diabetes may be risky for babies, Straits Times, 21 Nov 2016*

Prof Chong Yap Seng

THANK YOU

DISCUSSION