

8TH ASEAN MEDICAL DEANS' SUMMIT 2019

RESEARCH COLLABORATIONS

Professor Yap-Seng CHONG

Dean, Yong Loo Lin School of Medicine

National University of Singapore

Outline

1. Updates
2. Case study: a successful, ongoing collaboration
3. Proposed Framework for Collaboration in Research
4. NIC ASEAN Research Collaboration Fund

UPDATES

PROGRESS OF RESEARCH PROJECTS

Project	Collaborators	Core Participants	Progress in years	Results/ Outcomes
Dengue	<ul style="list-style-type: none"> Jamunarani S Vadivelu (UM) Justin Chu (NUS) 	✓ (8)	3 (started in 2015)	No updates since 2018 due to lack of funding. To organise the first ASEAN Medical Deans' Dengue Symposium cum workshop by NUS Medicine.
Healthy Campus Initiative	<ul style="list-style-type: none"> Maznah Dahlui (UM) Teo Yik Ying (NUS) 	✓ (2)	3 (started in 2015)	No updates since 2017 due to lack of funding.
Tuberculosis	<ul style="list-style-type: none"> Nicholas Paton (NUS) Teo Yik Ying (NUS) 	✓ (16)	3 (started in 2015)	<ul style="list-style-type: none"> Established academic proposal-development group Secured funding from USAID to organise A-TRACTION Symposium in 2019/2020 on "Solutions to Asian TB problems through regional collaborative research", with big emphasis on attracting abstracts from junior researchers. On-going multicenter TRUNCATE-TB trial involving 4 countries

CASE STUDY: A-TRACTION

**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	<ul style="list-style-type: none">• OVERALL AIM: a network to foster and coordinate TB clinical research in Asia• SPECIFIC PROJECTS:<ol style="list-style-type: none">1) Regional database<ul style="list-style-type: none">• MDR – TB surveillance• MDR-TB clinical outcomes• Epidemiology of drug resistance2) Regional Genomics platform3) Regional Clinical trials: TRUNCATE-TB – new TB clinical trial done in Asia funded by Wellcome Trust (£5m)
Timeframe for completion	Around 5 years
Contact of Lead PI (Name, Country, Institution, Department, Email)	Prof Nicholas Paton (Singapore), Prof Teo Yik Ying (Singapore)



Asian Tuberculosis Research And Clinical Trials Integrated Organizational Network

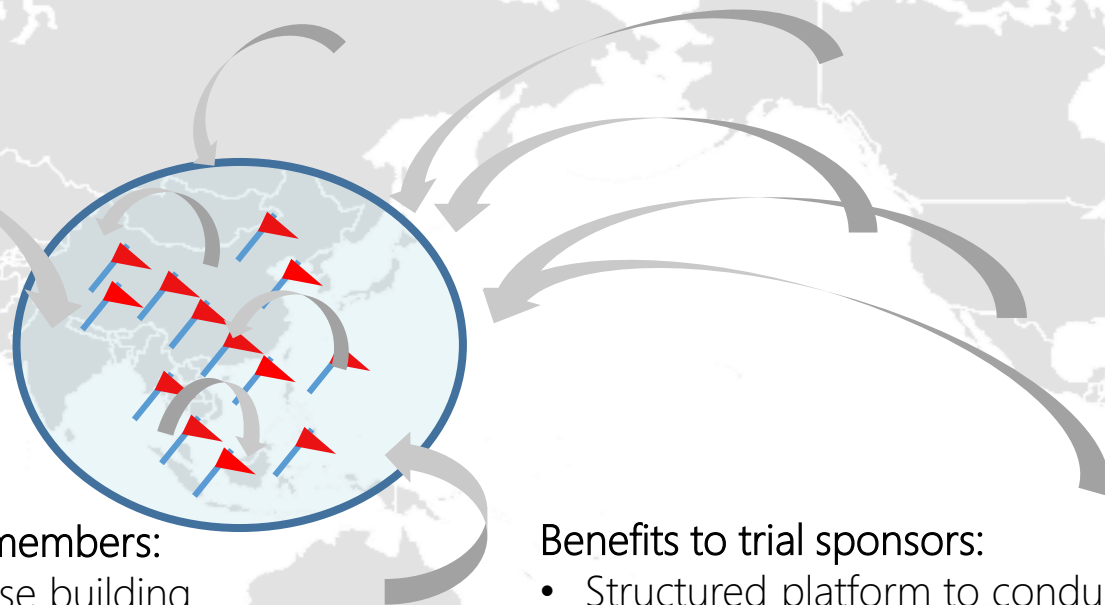
Professor Nicholas Paton
SPRINT-TB Programme Director
nick_paton@nuhs.edu.sg
+65 6772 6988





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

How to achieve regional TB networking?

Clinical trials provide best opportunity for networking and capacity-building

- Need multiple sites (and usually countries) to recruit
- Rigorous protocols (that include prescriptive clinical care)
- Challenging – people can learn from each other
- Budgets are high enough to foster meaningful collaboration

Two approaches:

- Ground-up: start with a trial, build collaboration
- Top down: start with the collaboration and structure, develop trials

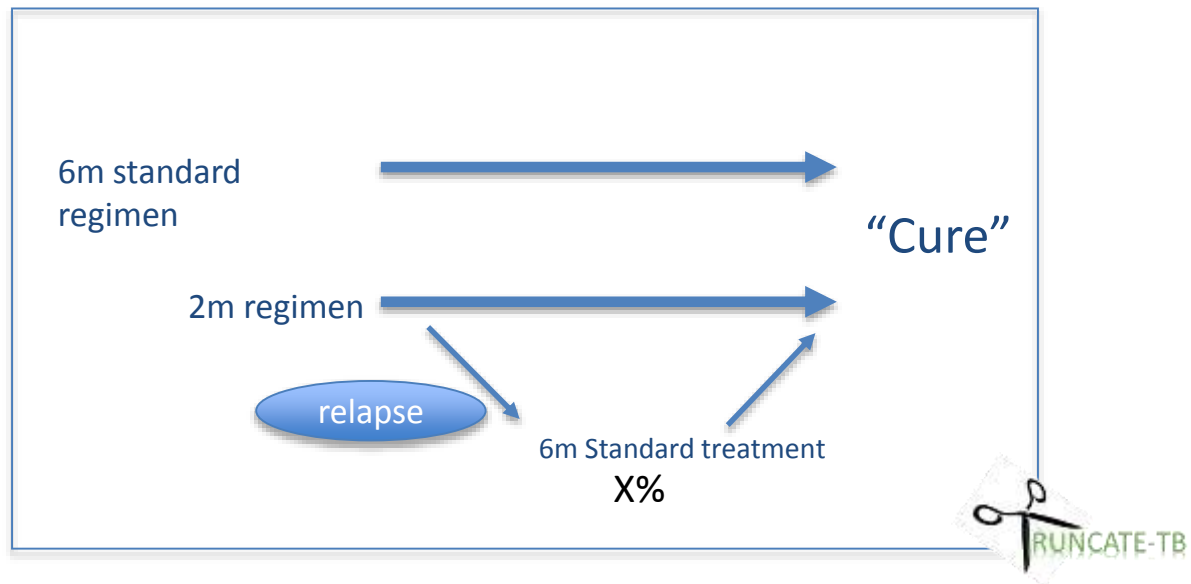
Initial project for regional collaboration:

**Two-month Regimens Using Novel
Combinations to Augment Treatment
Effectiveness for drug-sensitive
Tuberculosis (TB):**

The “TRUNCATE-TB” Trial

Funded by UK MRC/ DfID/Wellcome Trust (~\$10M) and Singapore NMRC (~\$2M)

'Treat-Follow-Relapse-Re-treat' Strategy





Initial project for regional collaboration

THAILAND

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

PHILIPPINES

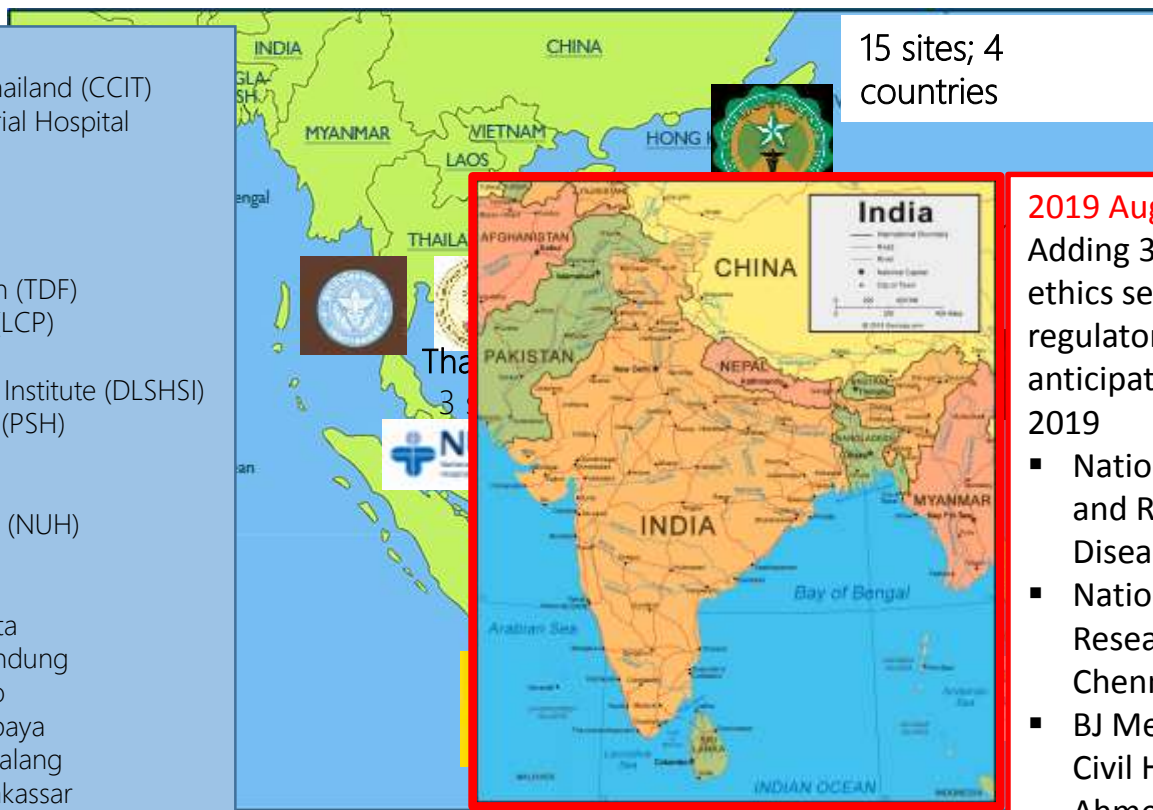
Tropical Disease Foundation (TDF)
Lung Center of Philippines (LCP)
Quezon Institute (QI)
De La Salle Health Sciences Institute (DLSHSI)
Perpetual Succour Hospital (PSH)

SINGAPORE

National University Hospital (NUH)

INDONESIA

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



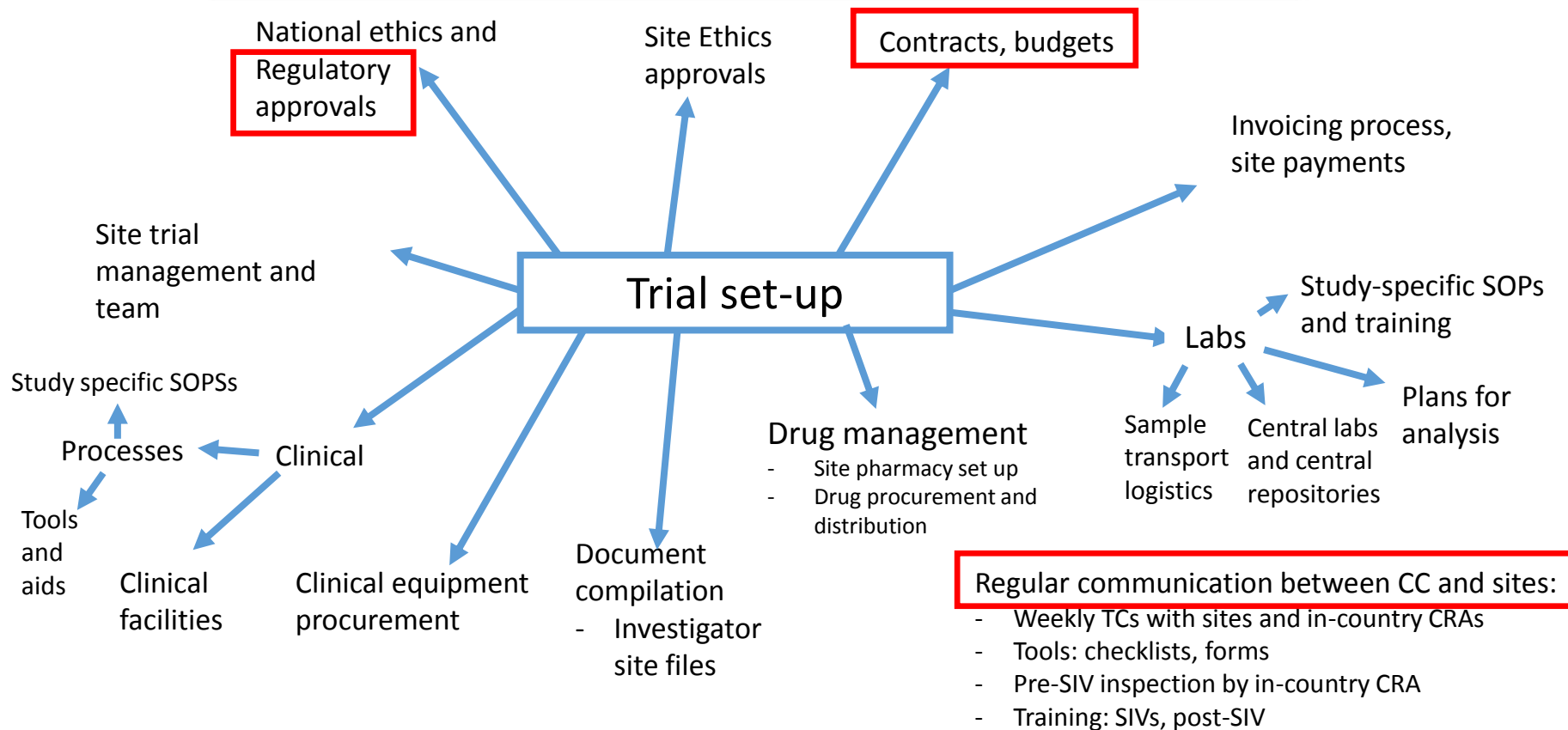
15 sites; 4 countries

2019 August update:

Adding 3 sites in India – ethics secured, awaiting regulatory approval; anticipated start Sept 2019

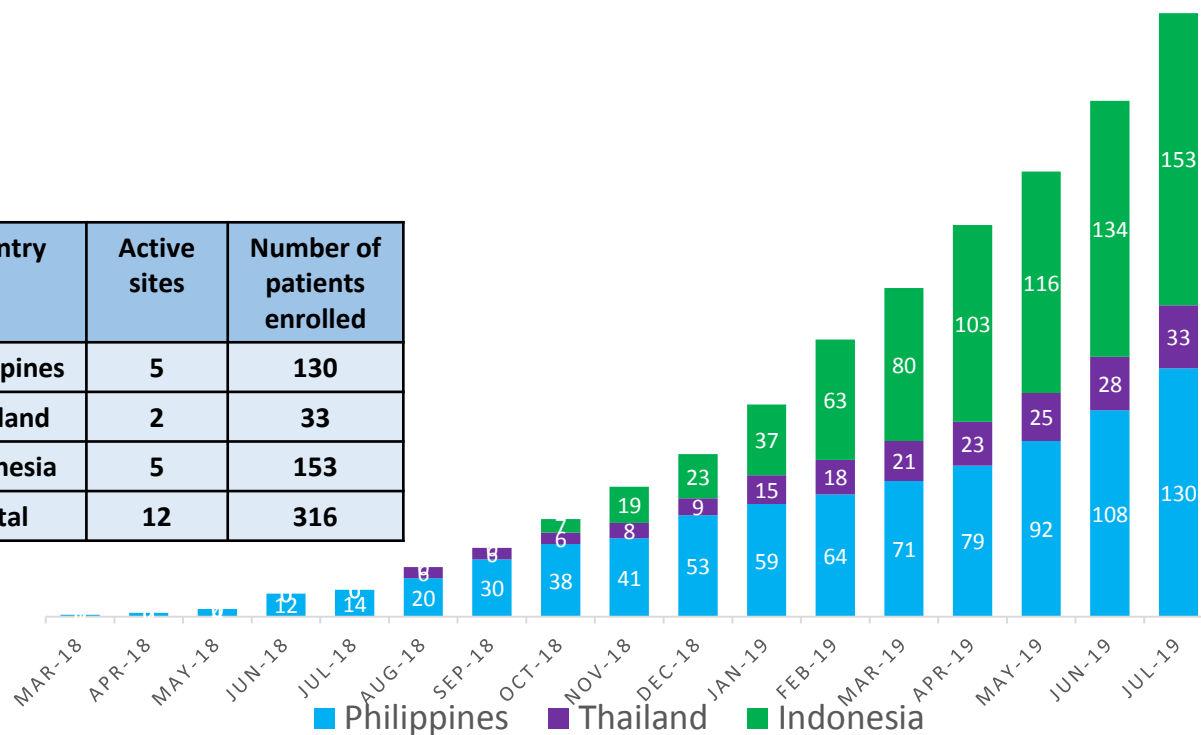
- National Institute of TB and Respiratory Diseases, Delhi
- National Institute for Research in TB, Chennai
- BJ Medical College and Civil Hospital, Ahmedabad

Trials build research capacity: TRUNCATE-TB site set-up



Recruitment (as of end July 2019)

Country	Active sites	Number of patients enrolled
Philippines	5	130
Thailand	2	33
Indonesia	5	153
Total	12	316



How to achieve regional TB networking?

Clinical trials provide best opportunity for networking and capacity-building

- Need multiple sites (and usually countries) to recruit
- Rigorous protocols (that include prescriptive clinical care)
- Challenging – people can learn from each other
- Budgets are high enough to foster meaningful collaboration

Two approaches:

- Ground-up: start with a trial, build collaboration
- Top down: start with the collaboration and structure, develop trials

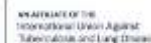
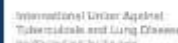
A-TRACTION Inaugural Meeting

Singapore, 19-20 March 2018

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



Funded by:



A-TRACTION Inaugural Meeting

Singapore, 19-20 March 2018

Main outcomes of meeting (specific):

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

A-TRACTION 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, Singapore

Was attended by senior established clinical researchers from 10 regional countries

Aims

- 1) To develop a small number of new research proposals that can be conducted under A-TRACTION
- 2) Plans for securing funding
- 3) Plans for implementation



Outcome from project development meeting

- Multiple concepts proposed and discussed
- Trust established – safe to share ideas
- Group coalesced around two proposals
- Developed and submitted as outline concepts for funding to UKMRC/Wellcome Trust
- Neither approved, but exercise established collaboration on grant proposals and plan to repeat.... perhaps too ambitious with initial proposals:

Proposal 1: Options for preventive treatment of children exposed to MDR-TB

Which countries: Indonesia (Prof Rovina “Nina” Ruslami, at Universitas Padjadjaran), Bandung , India, Vietnam, Philippines, Cambodia, Thailand, China

Duration: 60 months overall trial timeline (including 36 month duration of treatment/follow-up)

Principal research question to be addressed:

- Whether combination therapy with a quinolone and ethambutol offers any advantage over a quinolone alone in children under 5 years who are a close household contact of an index case with MDR-TB patients

Study design and sample size:

- Randomised, double-blind, parallel arm superiority trial; children < 5 years from 1600 households with MDR-TB index case (estimate 2400 children)

Total budget requested: £3.9 million including overheads

Proposal 2: Randomised controlled trial of 1HP vs 6H for treatment of patients with end-stage renal disease requiring renal replacement therapy

Countries: Malaysia (Prof Adeeba Kamarulzaman, University of Malaya Medical Centre), India, Vietnam, Philippines, Cambodia, Indonesia, Thailand, China, Taiwan, Singapore

Duration: 54 months (4 years 6 months)

Principal research question to be addressed: To determine whether a 1-month course of daily rifapentine plus isoniazid is non-inferior to the 6-month daily isoniazid course for prevention of active tuberculosis in patients who have latent TB infection and end-stage renal disease requiring renal replacement therapy (haemodialysis or peritoneal dialysis)

Study design and sample size: Randomised, double-blind, parallel-group, non-inferiority trial with an active control arm. Sample size 2100 patients (1050 per arm)



Funding and in-kind support

- **Singapore:** NMRC: supported organization of network through funding for SPRINT-TB program; support coordinating centre for TRUNCATE-TB in Singapore
- **Regional:** APEC provided funding support (US\$150,000) for development of network
- **International (cash):**
 - USAID agreed to fund the Project Development Meeting (US\$30,000, no strings attached) and committed an additional US\$50,000 (no strings attached) as part-funding for symposium or for project development meeting.
 - UK MRC/ Wellcome Trust provide funding for regional sites in Philippines, Indonesia, Thailand and India in TRUNCATE-TB trial
- **International (in-kind):** International Union Against TB and Lung Disease (the main international TB NGO) have provided organizational support for the meetings and for fund-raising (including assistance in securing USAID funding)

A-TRACTION current status: summary

- Established contacts between key opinion leaders of national TB research networks and major research institutions
- Have one major regional collaboration on a multinational clinical trial (TRUNCATE-TB) that has recruited > 320 patients in Indonesia, Thailand and Philippines and is in the process of expanding to include India
- Established academic proposal-development group
- Have secured funding from USAID for a further research proposal development meeting (or part funding for symposium) planned for end of 2019

What are the lessons learnt?

1. Ground-up collaborations yield results faster
 - Specific projects focus and galvanise efforts
 - Strong Lead PIs needed
2. Top-down support important to seed efforts
3. Extramural funding critical for take-off
4. Ability to get international funding advantageous
5. Many local and cross-border processes to sort out
6. Trust and collegiality among collaborators essential



Great things can happen when
you don't care who gets the
credit.

– Mark Twain

FRAMEWORK FOR COLLABORATION IN RESEARCH

Factors for successful Collaboration in Research

1. Topic must be a priority area for parties involved.
2. Ground-up interest must be present – projects and Pls.
3. Top-down commitment must be secured but is not enough.
4. Sustainability requires extramural funding.
5. Multi-year planning:
 1. At least a 3-year plan for research activities
 2. Regular review of progress
 3. Need for exit planning

Proposal for Future Collaboration in Research

1. Establish processes for:

- a) Identifying priority areas
- b) Research funding across borders
- c) Data and sample sharing across borders
- d) Student & Faculty exchanges across borders
- e) Research Collaboration Agreements – 1-to-1 works
- f) Regulatory approvals critical

2. Top-down commitment :

- a) Schools should internally commit at least USD\$5,000/year for 3 years for each project.
- b) Schools should identify & facilitate extramural funding opportunities.

3. Multi-year planning:

- a) Agree a 3-year plan at outset
- b) Agree on a review process

NUSMED INTERNATIONAL COUNCIL (NIC) ASEAN RESEARCH COLLABORATION FUND

- The NIC will commit USD\$50,000 per year to the NIC ASEAN Research Collaboration Fund (NARCF).
- The NARCF will fund research collaborative efforts among ASEAN medical schools.
- ASEAN medical deans will be invited to discuss the governance structure and its funding processes.
- The Yong Loo Lin School of Medicine will serve as secretariat.

DISCUSSION

DENGUE

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

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	<ul style="list-style-type: none">• 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)

The ASEAN Dengue Fighter

- ▶ Associate Professor Justin Jang Hann CHU (NUS Medicine, Singapore)
- ▶ Prof Jamunarani (UM, Malaysia)
- ▶ Prof Ruengpung Sutthent (Mahidol, Thailand)

Principal Investigators from ASEAN:

- ▶ Dr Raul Destura (UP, Philippines)
- ▶ Dr Betty Irmawat (FMUI)
- ▶ Prof Sazaly Abu Bakar (UM, Malaysia)
- ▶ Prof Shamala Devi (UM, Malaysia)
- ▶ Associate Professor Mayfong Mayxay (UHS, Laos)
- ▶ Prof War Win Htike (UM 1, Myanmar)
- ▶ Prof May Lwin (UM 1, Myanmar)
- ▶ Associate Professor Nguyen Vu Trung (HMU, Vietnam)
- ▶ Associate Professor Bui Vu Huy (HMU, Vietnam)
- ▶ Associate Professor Aye Aye Han (UM Mandalay, Myanmar)



Aims and Objectives



- ▶ **Aim:** To reduce mortality of dengue virus infection in ASEAN.
- ▶ **Project:** To establish **longitudinal cohort of dengue virus infected patients** among ASEAN countries (severe and non-severe cases).
 - ▶ To identify clinical and biomarkers as predictive markers for severity of dengue virus infection.
 - ▶ To study host and viral genetic factors correlated with severity of dengue virus infection.

1st ASEAN Universities Medical DEANS' Dengue Symposium/Workshop

- ▶ To be funded and hosted by NUS Yong Loo Lin School of Medicine, Singapore.
- ▶ ASEAN dengue investigators to meet and discuss funding opportunities as well as collaborative action plans.
- ▶ To secure research funding from international funding agencies (eg. Wellcome Trust) to support ASEAN dengue virus research agenda.
- ▶ MOU/RCA to be signed for all ASEAN Universities involved in this multicenter dengue research program.
- ▶ This symposium will be coordinated by Assoc Prof Justin Chu (email: miccjh@nus.edu.sg), NUS Medicine, Singapore.

1st ASEAN Universities Medical DEANS' Dengue Symposium/Workshop

- ▶ Venue: School of Medicine, National University of Singapore (NUS), Singapore
- ▶ Tentative date: Late 2020 or Early 2021

Invited Speakers (1 invited speaker from each ASEAN Country)

Airfare (Economy) will be provided.

Hotel accommodation for 2 nights.

All meals and transportation for invited speakers will be provided.

A/Prof Justin Jang Hann CHU
miccjh@nus.edu.sg

THANK YOU