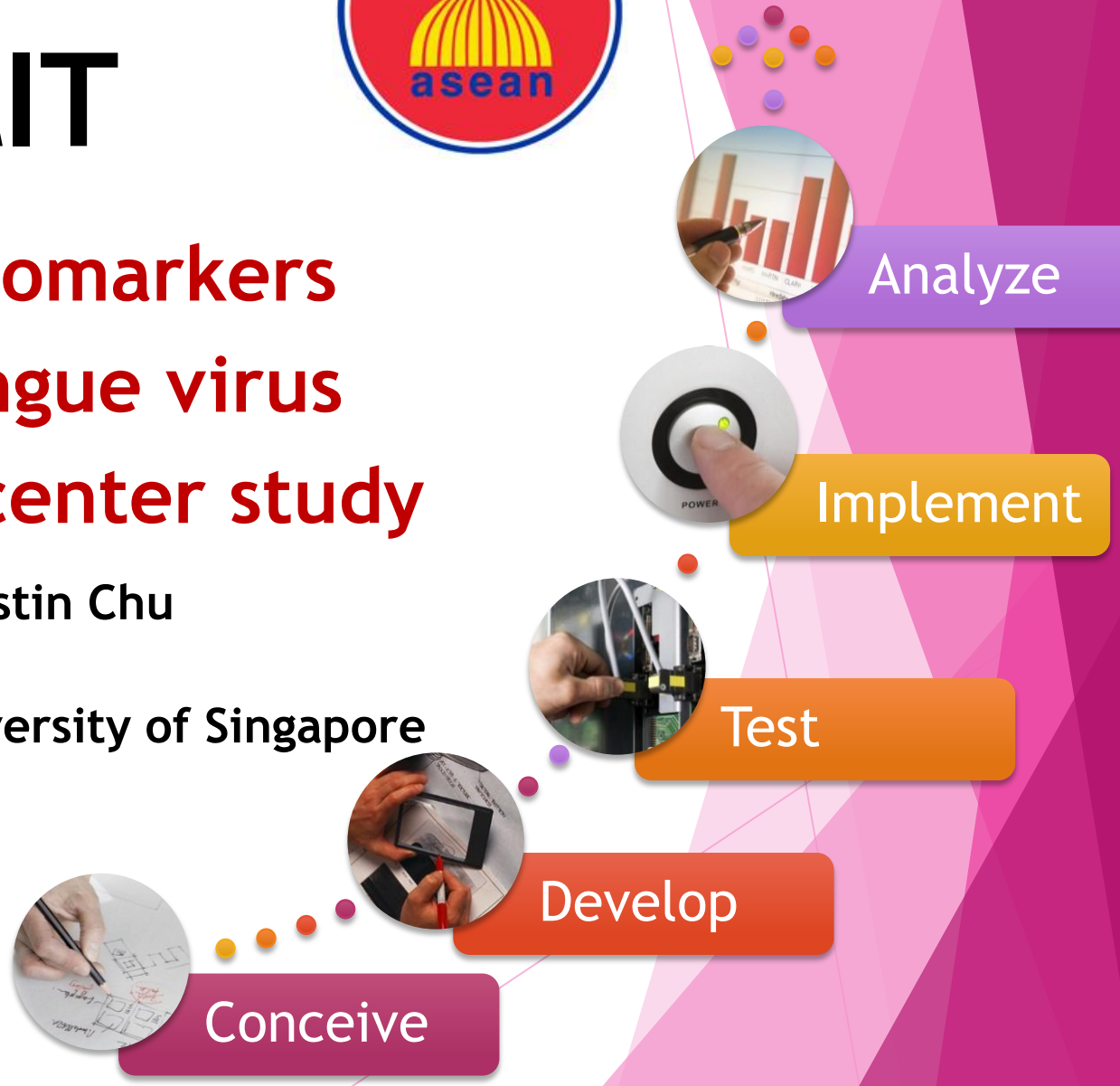
7TH ASEAN MEDICAL DEANS' SUMMIT

Clinical prediction and biomarkers related to severity of dengue virus infection in ASEAN: A Multicenter study

Prepared by Associate Professor Justin Chu

Yong Loo Lin School of Medicine, National University of Singapore



The Dengue Fighter Team:

- Prof Jamunarani (UM, Malaysia)
- Associate Professor Justin Chu (NUS, Singapore)
- Prof Datin Indra (UM, Malaysia)

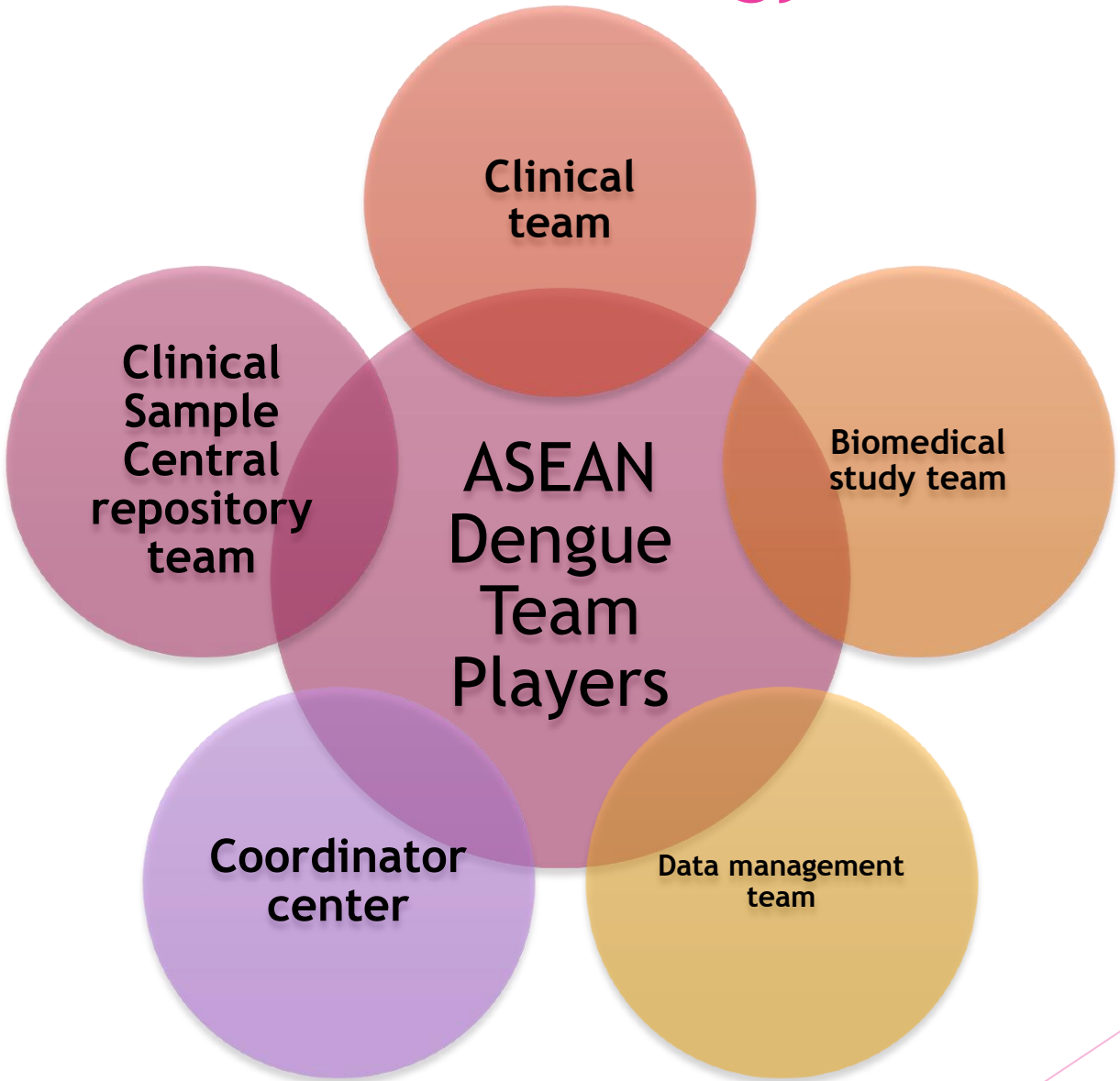
Principal Investigators from ASEAN:

- 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

- To reduce mortality of dengue virus infection in ASEAN
- 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

Research Plan and Strategy



Research Plan and Strategy

- Establish longitudinal cohort of dengue virus infected patients among ASEAN countries
- Subjects: paediatric and adult dengue virus infection cases in 9 ASEAN countries based on WHO 2009 and 2010 criteria, WHO standard or local standard care
- Biomarkers discovery: NK receptor, Dengue NS1 quantitation, CRP, other metabolomics markers
- Immunity markers: neutralizing and cross-reactive antibodies, inflammatory cytokines
- Host and viral genetics (Genome-wide association studies and personalized genomic medicine)
- Host and viral miRNA, proteome and genomic expression profile

What we have achieved:

New Paradigm for Dengue Control

UNIVERSITY OF MALAYA
The Leader in Research & Innovation

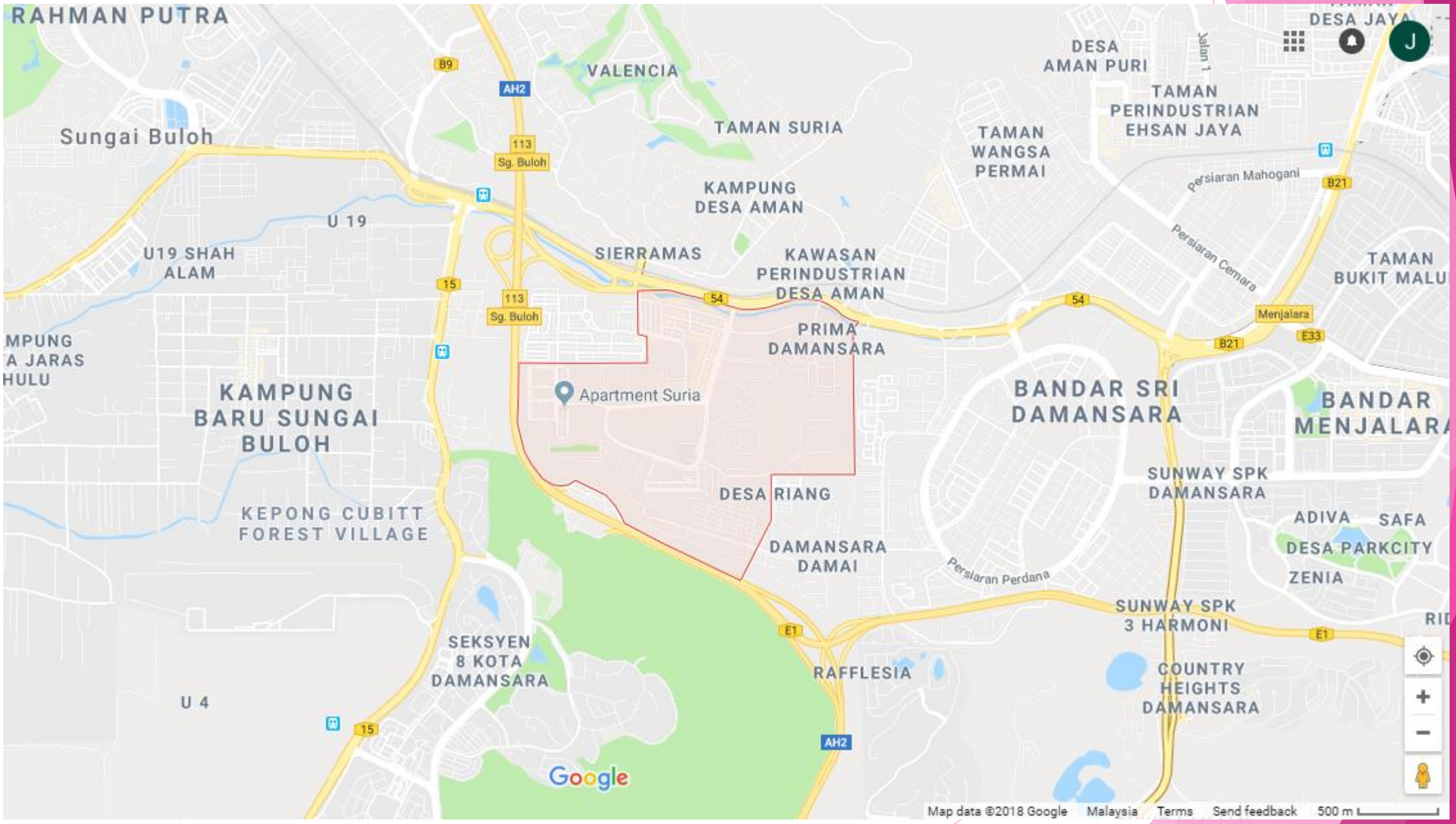
A clustered randomized control trial at PJU10, PJ for 2 years, to test the efficacy of an *Aedes* and dengue surveillance method

Trap adult *Aedes* → test mosquito for dengue virus → search and destroy → test residents for dengue virus

Clustered randomized controlled trial (2 Years)

- To establish proactive vector surveillance using the GOS + NS1 antigen kit
- To develop strategies and understanding for active engagement of the community and health staff
- To determine the effectiveness of this method in reducing dengue cases in the community

Map of PJU10, Damansara Damai, Petaling Jaya, Selangor,



Study sites (Apartments

Control

Interventio n

No.	APARTMENT	No. of Blocks	No. of Units	No. of cases 2015	No. of cases 2016	No. of cases 2017
Control						
1	APT LESTARI PJU 10	9	2000	29	41	18
2	APT PERMAI PJU 10	12	1428	27	72	36
3	APT VISTA PJU 10	12	750	8	11	5
4	APT INDAH PJU 10	2	120	65	28	10
Intervention						
5	APT SURIA PJU 10	4	440	7	7	2
6	APT HARMONI PJU 10	19	2273	72	85	57
7	APT BAYU PJU 10	8	960	7	7	5
8	PARK AVENUE PJU 10	3	315	6	6	8

Study protocol

Intervention arm

4 clusters comprising 34 blocks, 3988 residential units

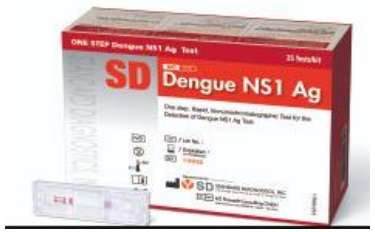
Control arm

4 clusters comprising 35 blocks, 4298 residential units

Baseline Entomological survey

KAP study + Baseline serology of community

Weekly surveillance of *Aedes* mosquito for dengue virus (GOS trap + NS1 kit)



Monthly surveillance of *Aedes* mosquito

Routine dengue surveillance and control by health staff

When dengue-positive *Aedes* is found,

Alert and inform residents via banners and flyers. For clean up, search and destroy

Proactive case detection of residents within 50 m radius from where dengue-positive mosquito was found

Pre-emptive measures are taken before a case is reported.

Dengue-positive mosquito as predictive “markers” before dengue clinical cases

Education is an on-going activity, especially during

a) KAP survey
b) Site visit/notification when infected mosquito is found
c) Planned roadshows/seminar/engagement with community

We will also recruit volunteers from the community to be responsible as contact persons

Endpoints for evaluation

Entomological evaluation

- *Aedes* density
- *Aedes* infection

Epidemiological evaluation

- Cases of dengue reported within the study period
- NS1 positivity
- Serology at baseline and end point

Additional study

Proactive case detection of residents within 50 m radius from where dengue-positive mosquito was found. If subject is positive and not symptomatic additional blood will be collected to feed mosquitoes.

This is to test if asymptomatic people are more infectious than symptomatic people

Team

- Entomology
  - Prof Datin Indra
  - Dr Wan Yusoff
  - Dr Jonathan
- Virology
  - Prof Jamuna
- Public Health/Community
  - Dr Rafdzah
  - Prof Yvonne Lim
- Medical Doctor
  - Assoc. Prof Dr Si Lay Khaing
  - Dr Neha Sethi
- MBPJ
- With support from Selangor Health Department

Funded by MOHE FRGS

Looking forward:

- Action plans:
  - To secure research funding from international funding agencies (eg.Wellcome Trust) to support ASEAN dengue virus research agenda.

Thank you