To combat 21st century global public health problems, we develop next generation vaccines against Infectious diseases and Cancer.
Introduction
2016 GHIT Grant
Development of novel dengue virus-like particle (VLP) vaccines against all four serotypes

Director Tetsuro Matano
Japan

Professor Kouichi Morita
Japan
Leading Dengue Vaccine Candidates

**Preclinical**
- Virus Like Particles
- Virus-vectored
- NS1 Protein
- DNA
- Recombinant Fusion

**Phase 1**
- Merck V180
  - Subunit
- NMRC TVDV
  - DNA
- WRAIR TDENV-LAV TDENV-PIV
  - Prime-boost

**Phase 2**
- NIAID TV003/TV005
  - Live attenuated
- GSK/WRAIR/Fiocruz TDENV-PIV
  - Live attenuated

**Phase 3**
- Takeda TDV
  - Live attenuated
- Butantan TV003
  - Live attenuated

**Approved**
- Sanofi Dengvaxia
  - Live attenuated

**Seronegative**
Advantages of VLP Vaccines for Dengue

- Approved vaccine has only indicated for 9-45 year-old populations

- VLP vaccine is appropriate for: Infants, children and adults
VLP Therapeutics Dengue Vaccine

Native Dengue Virus

Dengue VLP
VLP Therapeutics Dengue VLP Vaccine Concept

Native Dengue

Native Dengue protein composition:
- C: Capsid
- E: Envelope
- prM: Precursor membrane protein
- NS1, NS3, NS5: Non-structural proteins

Dengue VLP

Dengue VLP structure:
- F108A mutant
- kDa bands
  - Control
  - WT
  - F108A

Critical E Conformational Change During Viral Fusion

Fusion Loop

Cellular Membrane

Virus Membrane

pre-fusion

stem region

Critical E Conformational Change

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Critical E Conformational Change

Results of GHIT – VLP Therapeutics Collaboration

Immunogenicity of VLP tetravalent Vaccine and DNA Vaccine in mice

Against: DENV1

DENV2

DENV3

DENV4

Nab Titer (FRNT$_{50}$)

10,000

1,000

100

10,000

1,000

100

Detection limit

: Preimmune
: DNA_wild type
: DNA_F108A
: DENV VLP
Results of GHIT – VLP Therapeutics Collaboration

Immunogenicity of VLP tetravalent Vaccine in nonhuman primates (N=6)

Against: DENV1

Against: DENV2

Against: DENV3

Against: DENV4

- 12.5 µg each VLP + Alum
- 1.25 µg each VLP + Alum
- 0.125 µg each VLP + Alum
About VLP Therapeutics - Intellectual Property

Three Issued Patents

Three Published Patent Applications
About VLP Therapeutics – Publications

“Structural Studies of Chikungunya virus maturation”
Proceedings of National Academy of Sciences of the United States of America, December 2017

“Envelope-modified tetravalent dengue virus-like particle vaccine: implication for flavivirus vaccine design”
Journal of Virology, December 2017, Volume 91, Issue 23

“Development of a Novel Virus-Like Particle Vaccine Platform That Mimics the Immature Form of Alphavirus”
Clinical and Vaccine Immunology, July 2017, Volume 24, Issue 7

“Structural Studies of Chikungunya virus-Like Particles Complexed with Human Antibodies: Neutralization and Cell-to-Cell Transmission”
Journal of Virology, February 2016

“Cryo-EM structures elucidate neutralizing mechanisms of anti-chikungunya human monoclonal antibodies with therapeutic activity”
Proceedings of National Academy of Sciences of the United States of America, November 2015
About VLP Therapeutics - Non-dilutive Funding

**Dengue**

GHIT Fund
Global Health Innovative Technology Fund

$960K Grant
2016

**Malaria**

$2.4M Grant
2016

**Oncology**

National Cancer Institute

$300K SBIR Grant
2017

Life Science Grant 2015
Future GHIT Collaboration
Manufacturing and Clinical
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Thank You

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