Feb 2, 2022 (Wed)

GHIT Fund - Product Development Partnerships (PDPs)
Webinar Series Session 4 (FIND)
Advancing innovations through global partnerships
for neglected diseases during and beyond the COVID-19 pandemic

Global Partnerships to combat Neglected Tropical Diseases

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Introduction of the Speaker (Shinjiro HAMANO)

- 1987-1993 School of Medicine, Kumamoto University (M.D.)
- 1993-1997 Graduate School of Biomedical Sciences, Kyushu University (Ph.D.)
- 1997-2004 Assistant Professor, Kyushu University
  - ✓ Hamano S, et.al., Immunity. 2003;19(5):657-67., Yoshida H, Hamano S, et.al., Immunity. 2001;15(4):569-78.
- 2004-2006 Research Associate, Virginia State University (2 years)
- 2006-2009 Assistant Professor, Kyushu University
- 2009- Professor, Institute of Tropical Medicine (NEKKEN), Nagasaki University

- His research interests are tropical infectious diseases and host defense mechanisms to microbes, especially parasites. Besides the immunological approach, he conducts field studies on neglected tropical diseases, especially leishmaniasis and schistosomiasis. in Asia and Africa.
- Since 2020, he has been involved in a new international multidisciplinary collaboration to develop “A schistosomiasis rapid diagnostic test” with FIND, LUMC, Merck (MGHI) etc (G2020-104). In addition, he also dedicated himself to develop diagnostic tools targeting schistosomiasis with Lygature and LUMC (T2017-272, DTECT-Schisto) with the support by the GHIT.
- He has also contributed to developing live-attenuated prophylactic vaccines for leishmaniasis (G2015-115 and G2018-102) and trypanosomiasis (G2019-102) using CRISPR gene editing and leishmanin skin test for detection of *Leishmania* exposure and immunity (G2019-213).

Institute of Tropical Medicine, Nagasaki Univ.

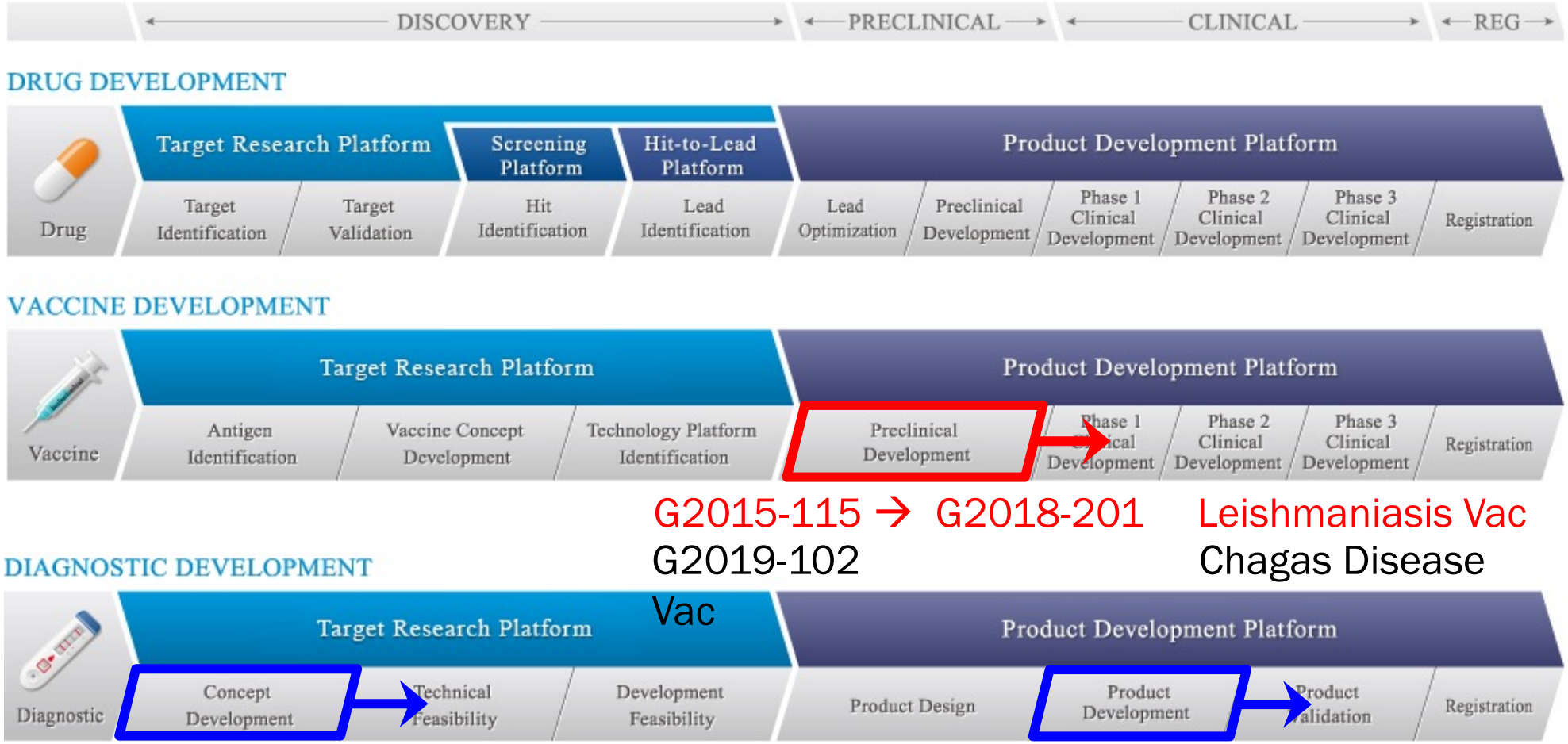
MISSION STATEMENT

The tropics, the most ecologically diverse region on the Earth, presents an ongoing complexity of tropical diseases and other health problems. In view of the remarkable advances made in the field of international exchange in recent years, it is imperative that these problems be addressed from a global perspective. Based on this understanding, the Institute of Tropical Medicine, Nagasaki University, aims to overcome tropical diseases, particularly infectious diseases, and the various health problems associated with them, in cooperation with related institutions, to strive for excellence in the following areas:

1. **Leading research in tropical medicine and international health**
2. **Global contribution to disease control and health promotion in the tropics by applying the fruits of the research**
3. **Cultivation of the researchers and specialists in the fields mentioned above**

The GHIT facilitate international partnerships that bring Japanese innovation, investment, and leadership to the global fight against infectious diseases and poverty in the developing world

GHIT Fund
Global Health Innovative Technology Fund



G2015-115 → G2018-201 Leishmaniasis Vac — OSU, McGill Univ., US FDA, NIAID/NIH, Gennova Biopharmaceuticals

G2019-102 Chagas Disease Vac — OSU, CIDR-Ecuador

T2017-272 Schistosomiasis DTECT-Schisto (Ab detection) — Lygature, LUMC

G2019-213 Skin test for Leishmaniasis

G2020-104 Schistosomiasis CAA-RDT — FIND, LUMC, Merck, Mologic, KEMRI & UERM

A list of specific questions for the GHIT fund - PDPs webinar series session 4 (FIND)

1. How did we first learn about PDPs and the PDPs of our session (FIND)?
2. Present about the project(s) working with PDPs/FIND (on-going and past), preferably a GHIT-related project.

   (e.g. how the partnership/project started, the PDP's and your organization's role in the project, its merits/impact to your organization)
3. Lessons learned and challenges from the partnership and share how these lessons can be implemented in future projects with PDPs and/or our organization's R&D activities.

We learnt about PDPs through the GHIT project to develop live attenuated prophylactic vaccines for leishmaniasis

A Multidisciplinary Team With Complementary Expertise

G2015-115 → G2018-201

Innovative approach and achievements

- Using CRISPR-Cas, generated marker free *centrin* gene deficient *L. major* (*LmCen*$^{-/-}$).
- Demonstrated safety of *LmCen*$^{-/-}$ in immunodeficient host, their failure to survive in sand fly vector and inability to revert to virulence after multiple animal passages.
- Demonstrated efficacy of *LmCen*$^{-/-}$ parasites in preventing sand fly-transmitted cutaneous (CL) as well as visceral leishmaniasis (VL) in mice and hamsters.
- Showed that *LmCen*$^{-/-}$ parasites induce protective immune response and parasite-specific effector memory T cells.
- Using CRISPR-Cas, generated marker free *centrin* gene deficient *L. mexicana* (*LmexCen*$^{-/-}$).

Publications

1. Zhang, W.W., Karmakar, S., Gannavaram, S., Dey, R., et.al.: A second generation leishmanization vaccine with a markerless attenuated *Leishmania major* strain using CRISPR gene editing. **Nat. Commun.**, 2020; 11(1): 3461.
2. Karmakar, S., Ismail, N., et.al.: Preclinical validation of a live attenuated dermotropic *Leishmania* vaccine against vector transmitted fatal visceral leishmaniasis. **Commun. Biol. (Nature)** , 2021; 4(1): 929.
3. Volpedo, G., et.al.: *Centrin*-deficient *Leishmania mexicana* confers protection against new world cutaneous leishmaniasis. **npj Vaccines (Nature)**, 2022; in press

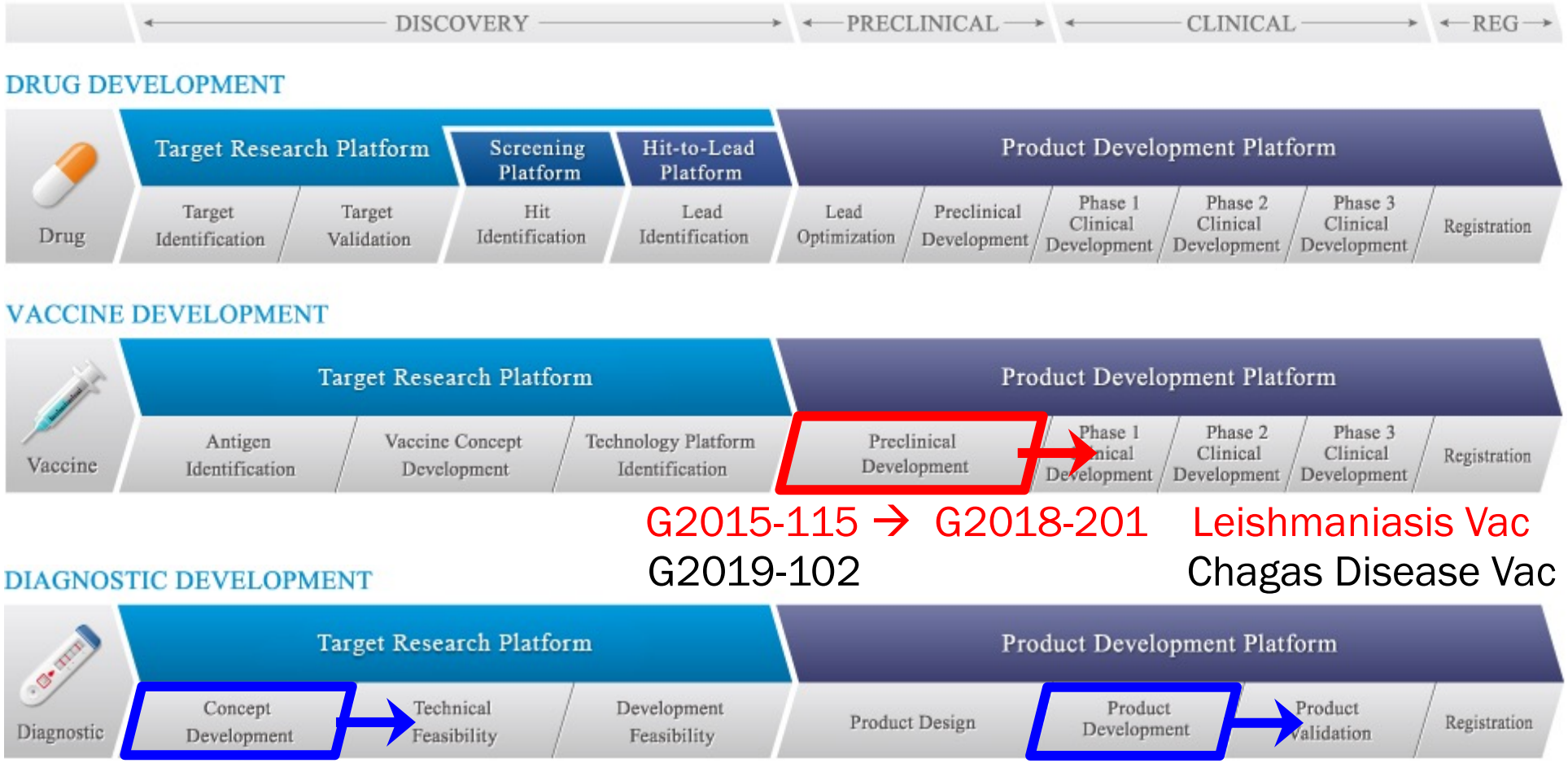
https://www.ghitfund.org/investment/portfoliodetail/detail/135/en

Further Achievements

- Developing Master Cell Bank and Working Cell Bank for *LmCen*$^{-/-}$ parasites at ATCC, USA for manufacturing of cGMP product in an endemic country.
- Validating the assays for final characterization of cGMP *LmCen*$^{-/-}$ product.
- Preparing regulatory dossier for Phase 1 study with regulatory authorities in the US.
- Initiated discussions with our Indian vaccine manufacturer for Phase 1 studies in the India.
- Developed GLP material for *L donovani* antigens for Skin Test for leishmaniasis as a surrogate marker for immunity. (G2019-213).

We learnt about the PDP with FIND through GHIT-related project

GHIT Fund
Global Health Innovative Technology Fund



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with Lygature, LUMC

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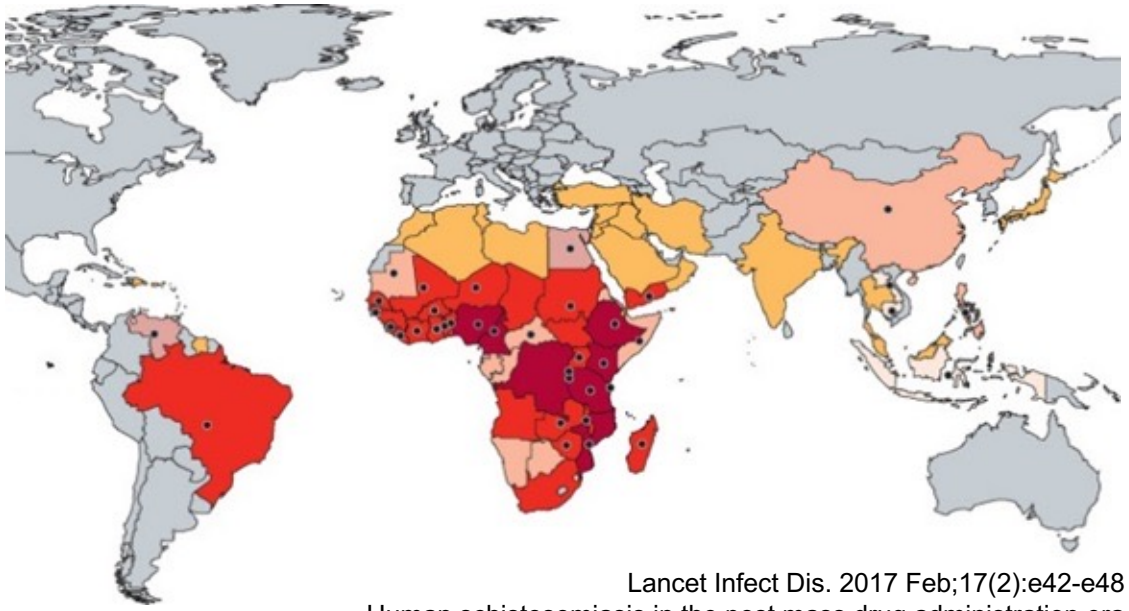
with FIND, LUMC, Merck, Mologic, KEMRI & UERM

Globally prevalent schistosomiasis (230 million people are infected)

Global Health Problem

- ✓ Schistosomiasis affects 230 million people worldwide, including many children <14yrs of age
- ✓ Control programs largely based on Mass Drug Administration (MDA) with praziquantel (PZQ)
- ✓ Efforts move from control towards elimination of schistosomiasis (WHO Roadmap)



Lancet Infect Dis. 2017 Feb;17(2):e42-e48
Human schistosomiasis in the post mass drug administration era

Unmet Need

✓New diagnostic or monitoring tools are urgently needed to support, monitor and sustain schistosomiasis control and elimination programs.

Current diagnostic methods have limitations:

- ✓ Insensitive for low-intensity infections & not suitable for post-MDA application AND/OR
- ✓ Not able to discriminate between current and past infection AND/OR
- ✓ Not able to detect infection with different *Schistosoma* species AND/OR
- ✓ Not in rapid test or field-applicable format (invasive, based on blood collection)

Schistosomiasis control toward elimination

Control
MDA with PZQ + Other actions

Transmission

Prevalence Intensity

Tools with higher sensitivity

Monitoring & Surveillance

Detection of antigen by RDT
(G2020-104)

Detection of eggs

Detection of antibody
(T2017-272)

How can we monitor and survey (re)transmission of schistosomiasis in pre- and post elimination settings ?

Partners DTECT-Schisto (T2017-272)

Development of defined antigens for detection of *schistosoma* infection-specific antibodies in blood and urine

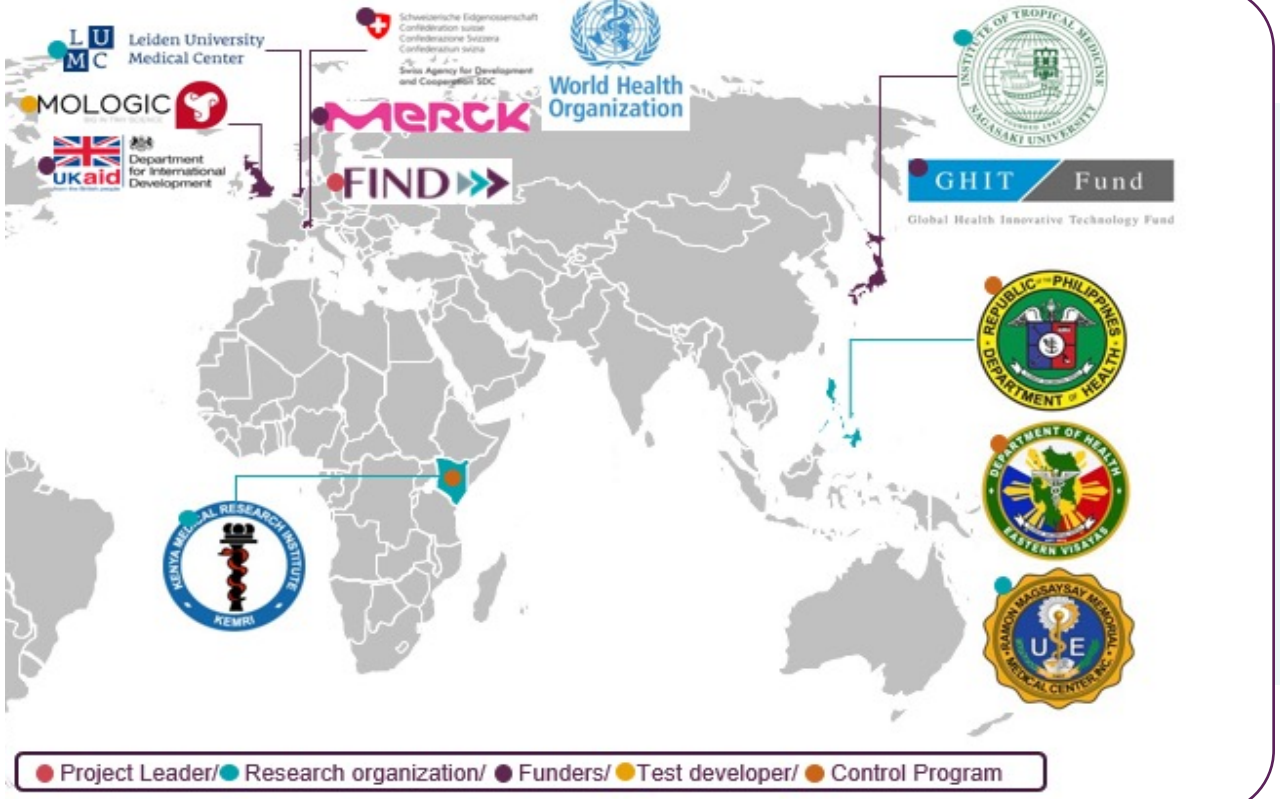
NAGASAKI UNIVERSITY	LUMC	LYGATURE	FIND
			
• Experts with protein antigens of NTDs • Experts in detecting antibodies in urine • Access to samples from *Schistosoma*-endemic areas	• Schistosomiasis expert • Expert in anti-glycan antibody detection technology applications • Access to controlled human infection model • Access to biobanked samples from *Schistosoma*-endemic areas	• Independent “broker” • Experts in managing multi-stakeholder consortia in health R&D and access (>100 partnerships since 2007) • Current Global Health portfolio includes 5 projects	• Bridge between technology development, policy and clinical care • Experts in overseeing the development of diagnostic tests for NTDs

1. Diagnostic Ab response profiles and protein/glycan targets have been identified.
2. Data analysis to identify and validate specific targets and use cases is ongoing.

SPOTLIGHT ON SCHISTOSOMIASIS

RAPID TESTS TO SUPPORT DISEASE CONTROL & ELIMINATION

SUPPORTING NATIONAL PROGRAMMES TO MONITOR THE IMPACT OF MASS DRUG ADMINISTRATION CAMPAIGNS AND PRECISION MAPPING EFFORTS



GHIT grant approved July 2020

Consortium of 8 partners

In 2021, first field evaluations of prototype in Kenya and the Philippines (led by NUITM) yielded very encouraging results

Further development of the CAA RDT is required to meet the sensitivity targets, with a final field evaluation required prior to design-lock and transfer to manufacturing – planned for Q2/3 2022

FIND in collaboration with GHIT and the Merck Global Health Institute are developing an access strategy for the SCH CAA RDT

NUITM is monitoring the field studies of the prototype in the Philippines and will manage the clinical trials with the support from FIND.

Lessons learned and challenges from the partnership

- Lessons learned:
  - Making international multidisciplinary team with complementary expertise is critical, which can bring the projects forward from academic research to the product development with overcoming scientific, technical, and regulatory hurdles.
  - Managing multi-stakeholder consortia with leadership and coordination is essential and crucial.
- Challenges:
  - Establishing strong relationships in the absence of in-person meetings. The SCH CAA RDT project got funded in July 2020, in the first year of COVID-19. To this day, we have not had the chance to meet the FIND team nor any of other partners in person. Yet, we've successfully completed the first field evaluations with very promising results.
  - COVID-19: having to monitor field-based studies outside of Japan with new partners. We had to find innovative ways to work around this, by developing new tools, and hiring a clinical research associate to be present at the field site, instead of us.

How can these lessons be implemented in future projects with PDPs and/or our organization's R&D activities?

- In future projects with PDPs
  - We will try having an independent "broker" with expertise in managing multi-stakeholder consortia in health R&D and access.
  - We need to be more familiar with the regulatory processes in FDA, EMA, WHO or other national authorities for the development of new vaccines, drugs and diagnoses.
- Our organization's R&D activities
  - Our organization will promote and strengthen public-private partnership (PPP) for sustainable, efficient, and fruitful development of R&D activities.