

JSPS Core – to – Core Program
Establishment of South – South and Triangular Cooperation Core for Elimination of Asian
Zoonotic Schistosomiasis

October 24 – 27, 2023 (PK Hall, NRCPD, Obihiro, Japan)

DAY 1 SYNTHESIS

The JSPS Core-to-Core Kick-off Meeting began with an opening message from Dr. Shin-ichiro Kawazu, the Director General of the National Research Center for Protozoan Diseases (NRCPD) at Obihiro University of Agriculture and Veterinary Medicine. He welcomed all the participants to the center and introduced the JSPS Core-to-Core Program. Dr. Kawazu emphasized in his message that schistosomiasis, as a Neglected Tropical Disease and a national public health concern, was the focus of the activity. The goal was to establish an alliance among participants and their respective institutions through mutual collaborations to combat schistosomiasis in the five endemic countries in Asia. This alliance would enable all participating countries to share their experiences in addressing the challenges of controlling and eliminating schistosomiasis. Workshops on epidemiology and the development of novel diagnostic techniques would aid in improving the monitoring and surveillance of the disease. Furthermore, Dr. Kawazu highlighted the opportunities that this meeting may provide to young scientists in building networks and establishing strong research collaborations for further schistosomiasis research.

Dr. Pilarita Rivera of the University of the Philippines Manila discussed the situation of schistosomiasis in the Philippines. She presented the trend of the schistosomiasis cases in the country, she mentioned that there has been a decline in cases in the past years. Dr. Rivera mentioned the current control measures in the Philippines through the implementation of Mass Drug Administration using praziquantel. Furthermore, she discussed the current problem with the use of Kato-katz in the diagnosis of *S. japonicum*. The said technique has low sensitivity and might not be able to detect cases with low infection rate especially if there is intermittent shedding of parasite eggs. The Philippines being an agricultural land with farming as one of the most common livelihoods of Filipinos is critical in the perpetuation of schistosomiasis. Water buffaloes, one of the main resources used in farming is the main reservoir host identified for *S. japonicum* in the country. It is in this regard that, surveillance of animal reservoir hosts must also be included in the control strategies in the country.

On the other hand, Dr. Aya Yajima, Technical Officer for Neglected Tropical Diseases at the World Health Organization South-East Asia Regional Office, provided an overview of the status of schistosomiasis in the five endemic countries in Asia: the Philippines, Indonesia, Thailand, Lao PDR, and Cambodia. Similarly, she reported a decline in cases over the last ten years, however, there are several challenges which hinder the goal of achieving the disease's elimination status. These challenges include Mass Drug Administration (MDA) coverage and inadequate diagnostic and treatment services. Consequently, the current WHO framework aims to control the disease, eliminate it as a public health concern, and finally interrupt its transmission. According to Dr. Yajima, the current WHO activities and assessments to achieve the target of elimination include (1) Effective intervention by expanding MDA coverage, (2) Strengthening elimination surveillance

by developing and introducing highly sensitive and validated serological tests, (3) Developing cross-sectoral programs within countries to strengthen the management of domestic animals and livestock, and (4) Intensifying targeted snail control activities. Based on the above-mentioned activities, this emphasizes the importance of an intersectoral and multidisciplinary approach in the elimination of schistosomiasis through (1) Collaboration, (2) Communication, (3) Coordination, and (4) Capacity building. Dr. Yajima in her message encouraged all participating countries, to establish future collaborations to promote sharing of experiences and resources such to ensure that the target to eliminate schistosomiasis which will be achieved soon.

All these target priorities will not become a reality without research. Dr. Jose Ma. M. Angeles of the University of the Philippines Manila presented several research projects on schistosomiasis in the Philippines. Most of these projects involve both humans and animals. By including animals in these studies, researchers will be able to determine the extent to which animal reservoirs play a role in the continuous transmission of the disease.

In the afternoon, Dr. Yuma Ohari of the International Institute for Zoonosis Control at Hokkaido University highlighted the use of population genetics to understand the dynamics of target organisms. He stated that population genetics is nowadays relevant as it helps us understand the complex epidemiology of different infectious diseases. Furthermore, he discussed how this allows scientists to observe variations within species over time. In fact, in his current study, he was able to conclude that cross-infection occurs between hosts, specifically in the case of reemerging fasciolosis.

Following Dr. Ohari's presentation, Dr. Claro Mingala introduced the Philippine Carabao Center (PCC-DA), an attached agency of the Department of Agriculture. He presented PCC-DA's vision to become a premier research and development institution. In detail, the Research and Development Division of PCC-DA prioritizes the Research for Development (R4D) program on animal health. Among the institution's research objectives are vaccine development and the development of novel diagnostic techniques. Dr. Mingala also presented one of his studies on schistosomiasis. The results concluded that water buffalo play an important role in spreading the infection.

In his second presentation, Dr. Jose Ma. M. Angeles discussed the use of recombinant antigens – specific proteins in parasites produced through DNA recombinant technology. Specifically, the SjTPX1 recombinant antigen, first developed at NRCPD for ELISA, has been assessed to have higher sensitivity and specificity in detecting the presence of *Schistosoma* antibodies in humans and animals. The technique is currently being utilized in several research studies to evaluate its performance in a field setting. The development of this technique paved the way for proving the value of serologic techniques in the diagnosis, monitoring, and surveillance of schistosomiasis.

Lastly, Dr. Wanlop Acharaphan of the Institute of Tropical Medicine (NEKKEN) at Nagasaki University, along with Ms. Sirin Kunluang, presented the prevalence of schistosomiasis among animal hosts. They elaborated on the previous discussion by Dr. Ohari regarding population genetics. They explained that population genetics enables the detection of different hosts' genetic

diversity using multi-locus genotyping analysis with microsatellite markers. This contributes to the understanding of the transmission dynamics of *S. japonicum* between human hosts and animal reservoirs. They also discussed the miracidium hatching technique (MHT) used to prepare single genome DNA samples from the parasites. Although successful hatching was achieved with experimental egg samples, they observed variations in the conditions and properties of egg samples collected from the field. Since miracidium hatching is unsuccessful in egg samples from the field, they are currently optimizing the extraction of genomic DNA from the parasite's eggs. Ms. Kunluang's recent research proposal aims to determine the genetic variations and genetic structure of *Schistosoma japonicum* and to identify the extent to which each animal host affects the transmission.

DAY 2 SYNTHESIS

On the second day of the JSPS Core-to-Core Meeting, Dr. Masashi Kirinoki from the Laboratory of Tropical Medicine and Parasitology at Dokkyo Medical University presented on *Schistosoma mekongi* in Cambodia. He discussed the similarities and differences between *S. mekongi* and *S. japonicum*, including aspects like egg morphology, snail hosts, snail breeding sites, the risk of seasonal transmission, and their respective reservoir hosts. Dr. Kirinoki also presented his research team's 2016 survey on the elimination status in Cambodia, using various diagnostic techniques. The study compared the serologic test, SMEK ELISA, with the conventional Kato-katz technique. According to Dr. Kirinoki, the SMEK ELISA showed promising results in *S. mekongi* diagnosis, exhibiting high sensitivity and specificity without false positives or cross-reactions.

Subsequently, Dr. Virak Khieu from the National Center for Parasitology, Entomology, and Malaria Control in Cambodia, and Dr. Somphou Sayasone from the Lao Tropical and Public Health Institute, provided updates on the status of *S. mekongi* in Cambodia and Laos, respectively. They emphasized that geographic areas and ecological factors create niches for parasite transmission, as all identified *S. mekongi* endemic areas are near the border or situated within the Mekong River. They highlighted the role of Mass Drug Administration (MDA) in reducing schistosomiasis prevalence to below a 2% positivity rate, but they noted that discontinuing MDA often leads to an increase in schistosomiasis cases. Reemergence is associated with poor hygiene and sanitation practices in endemic areas. Collaboration between Laos and Cambodia has been crucial in sharing control and elimination strategies, including ONE HEALTH intervention packages and community involvement through education, sanitation, and hygiene programs.

Hokudo, a comprehensive company in life sciences, presented the potential for commercializing SjTPX1 ELISA, upscaling it into an ELISA KIT, or developing recombinant SjTPX1 into immunochromatography. Such advancements could lead to more sensitive diagnostic tests for monitoring and surveillance, especially in regions close to elimination like Cambodia and Laos.

In the first afternoon session, Dr. Triwibowo Ambar Garjito from the National Research and Innovation Agency in Indonesia gave an overview of the history and status of schistosomiasis in Indonesia. Control projects started in the early 1990s, leading to a significant reduction in cases. However, as in Cambodia and Laos, the cessation of control measures often results in an increase in cases. Dr. Garjito presented detailed epidemiological data from 2008 and introduced community-based schistosomiasis control programs mobilizing community resources and collaborations with institutions like the University of the Philippines Manila.

Dr. Yanin Limpanont from Mahidol University, Faculty of Tropical Medicine, discussed Opisthorchiasis in Thailand, another public health concern in Southeast Asia. She covered the history of the disease, the parasite's life cycle, and prevalence rates over the years. She also noted the success of the 2009-2022 national strategy program for liver fluke prevention and control. Dr. Poom Adisakwattana from the same university presented current research on Opisthorchiasis, emphasizing the need for advanced research due to its high prevalence. His team is working on

the development of a POCT (Point of Care Test) using RPA-Crispr/cas12 for the detection of Opisthorchis, a promising, reliable, cost-efficient, and rapid diagnostic tool.

Finally, Mr. Derek Lee presented what SD Biosensor can offer to aid research in diagnostic tool development. He provided data on the different rapid diagnostic tests manufactured by SD Biosensor and the various facilities and diagnostic tools available from the company.

DAY 3 SYNTHESIS

Session 5 commenced with a presentation by Dr. Shinjiro Hamano of the Institute of Tropical Medicine (NEKKEN) at Nagasaki University. He discussed their 5-year project for integrated Research and Development toward Control and Elimination of Schistosomiasis in Kenya. Notably, the project is a collaboration among several research institutions with a common goal: to control or, ideally, eliminate schistosomiasis in Kenya. Remarkably, the project is being implemented through integrated research and aims to develop novel control measures for schistosomiasis along with other Neglected Tropical Diseases (NTDs). Dr. Hamano emphasized that improving and strengthening control programs can lead to behavior modification among at-risk populations, ultimately interrupting the transmission of schistosomiasis. Post-elimination status, he stressed the importance of having a more sensitive method for monitoring and surveillance to reduce the risk of re-emergence. Furthermore, he mentioned that the development of a new drug capable of killing larvae with a low risk of drug resistance is essential in control and elimination efforts.

The next presenter was Moritoshi Iwagami of the National Center for Global Health and Medicine. Dr. Iwagami provided a comprehensive overview of the current situation and challenges related to schistosomiasis elimination in Lao PDR. The country aims to eliminate the transmission of schistosomiasis by 2025. Data he presented showed that cases of schistosomiasis increased due to fewer control programs and challenges in implementing prevalence surveys because of the COVID-19 pandemic. He further added that factors such as age, educational status, and the presence of latrines are associated with the presence of infection. Prevalence surveys were conducted using various diagnostic methods such as LAMP, FECT, and Kato-Katz in both humans and animals. Although the animal positivity rate is low in Lao, Dr. Iwagami recommended continued monitoring of animals. He also discussed the use of environmental DNA from water samples for the detection of *S. mekongi* in Lao. In addition to his presentation, he discussed the status of *Opisthorchis viverrini* in Lao.

Dr. Sung Hye Kim of Hanyang University College of Medicine presented on partnerships and networking for Neglected Tropical Diseases (NTDs). She emphasized the important role of research in disease elimination and the critical role of research advancement in solving public health challenges. Dr. Kim presented development platforms to connect researchers with donors who can support studies from conceptualization to commercialization. She also introduced the role of GAELF in filariasis elimination and current diagnostic tools for its diagnosis. Finally, she stressed the importance of commitment, partnerships, and intersectoral collaborations in addressing NTD challenges, particularly Asian schistosomiasis, through networks and platforms.

On the same day, Dr. Kawazu presented the future plan of the JSPS Core to Core Program, including the proposed activities in the next two years. Specifically, he presented the plan of having workshops in Lao PDR and/or Cambodia in 2024; and a Steering meeting for future collaboration in Philippines, Manila in 2025. At the same time, Dr. Kawazu, led the symbolic signing of the Cooperation Core's Pledge of Commitment. The signing signifies the commitment of each institution to supporting the establishment of South-South Triangular Cooperation Core for the elimination of Asian zoonotic schistosomiasis.

The final two sessions were presented by Ms. Katrina Theresa M. Balboa with the assistance of the NRCPD team. She demonstrated in detail the procedures of the SjTPX-1 ELISA test. The serological diagnostic tests provide a more sensitive tool for the detection of schistosomiasis, especially for infections with low intensity. Additionally, the technique has been proven to detect active infection, as indicated by non-reactive results when testing serum samples from individuals who took praziquantel a year prior to blood collection. In conclusion, this test responds to the need for sensitive diagnostic surveillance in the pre-elimination, elimination, and post-elimination stages of control. The use of a more sensitive and specific recombinant antigen ELISA will strengthen the surveillance needed to ensure the elimination of this parasitic disease.

PLEDGE OF COMMITMENT

We commit ourselves to supporting the establishment of South-South Triangular Cooperation Core for the elimination of Asian zoonotic schistosomiasis initiated by the JSPS Core to Core Program. We see this cause as an opportunity to have a strong and dynamic partnership with the involved institutions towards the achievement of eliminating this parasitic disease.

This pledge is legally non-binding and has no legal consequences. It only serves as a symbol of our intent to collaborate towards a common goal.

Signed on the 26th day of October 2023 at the National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Hokkaido, Japan,

河津信一郎
Signature over printed name

NRCPD, Obihiro Univ.
Affiliation

Chhoun Kirik
Signature over printed name

ENM, MOH
Cambodia
Affiliation

Tri Wibowo
Signature over printed name

Vector-borne & zoonotic dis.
RCPHN, Nat. res. in. agency-Indonesia
Affiliation

Sung Hye Kim
Signature over printed name

Hanyang Univ
College of Med
Affiliation

NCGM
Signature over printed name

M. Imai
Signature over printed name

尾針由真
Affiliation
IIZC, Hokkaido Univ.

[Signature]
Signature over printed name

COLLEGE OF PUBLIC HEALTH
UNIVERSITY OF THE PHILIPPINES MANILA
Affiliation

[Signature]
Signature over printed name

Leo Tropical and public health institute
Affiliation

[Signature]
Signature over printed name

Faculty of Tropical Medicine
Mahidol University, THAILAND
Affiliation

M. Kiminaka
Signature over printed name

Dokkyo Medical
University
Affiliation

Signature over printed name

清野真三郎
NEKKEN Nagasaki Univ.
Affiliation

後藤 厚之
Affiliation
The University of Tokyo