

INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY

through Scientific Discovery and its Application Solving the World Health Problem



JULY



2021

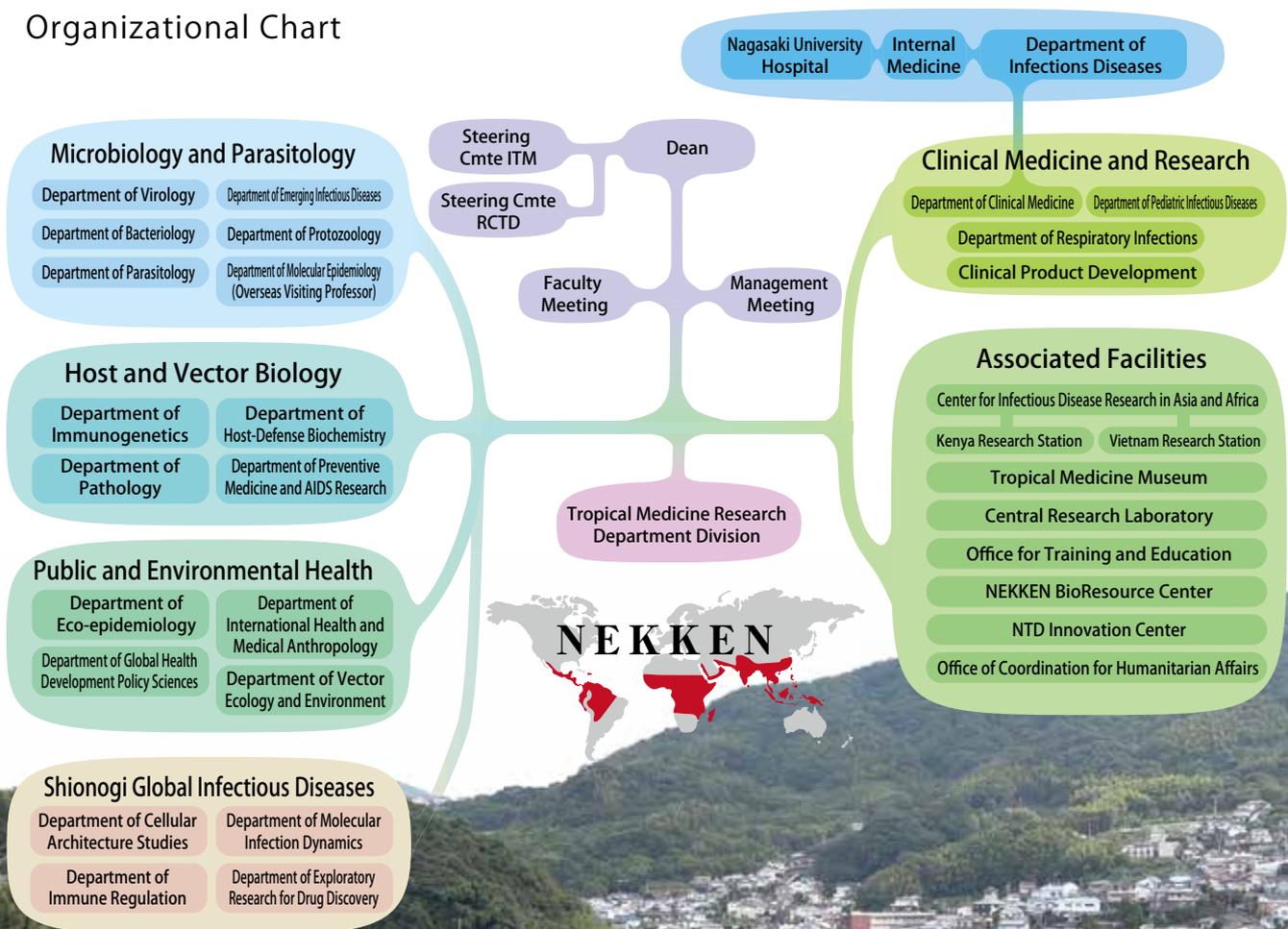
Mission Statement

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, we strive for excellence in the following areas:

1. Spear-head research in tropical medicine and international health
2. Global contributions through disease control and health promotion in the tropics by applying the fruits of our research
3. Cultivation of researchers and specialists in the above fields

Organizational Chart



Steering Committee for the Institute of Tropical Medicine (Committee Member outside the university)
 Shigeyuki Kano (National Center for Global Health and Medicine), Yasuhiko Suzuki (Hokkaido University),
 Shinichiro Kawazu (Obihiro University of Agriculture and Veterinary Medicine)

Towards Eradication of Tropical Infectious Diseases

Institute of Tropical Medicine (NEKKEN), Nagasaki University is a unique governmental institution for research on tropical medicine. The Ministry of Education, Culture, Sports, Science and Technology (MEXT) designated NEKKEN as a "Joint Usage / Research Center on Tropical Disease" in 2009. This recognition underlines the importance of NEKKEN as an open institute whose resources are freely available to the whole research community in Japan. Since 1993, the World Health Organization has designated NEKKEN as a WHO Collaborating Centre for Reference and Research on Tropical Viral Diseases. The current organization of the institute involves five major research fields (21 departments), two facilities, and one clinical unit at University hospital.

Many developing countries are located in the tropics, and are affected by a diverse group of tropical diseases, and emerging infectious diseases. As a consequence the remarkable advances made in the field of international transportation and communication in recent years, the industrialized countries of the temperate zones are also threatened by the same pathogens and it is imperative that they are addressed from a global perspective. Based on this paradigm, NEKKEN aims to overcome tropical and emerging infectious diseases, and the various related health problems in the tropics, in cooperation with related institutions, and to strive for excellence in the following areas:

1. Spear-head research in tropical medicine and global health
2. International contribution through disease control and health promotion in the tropics
3. Cultivation of researchers and specialists in the above fields

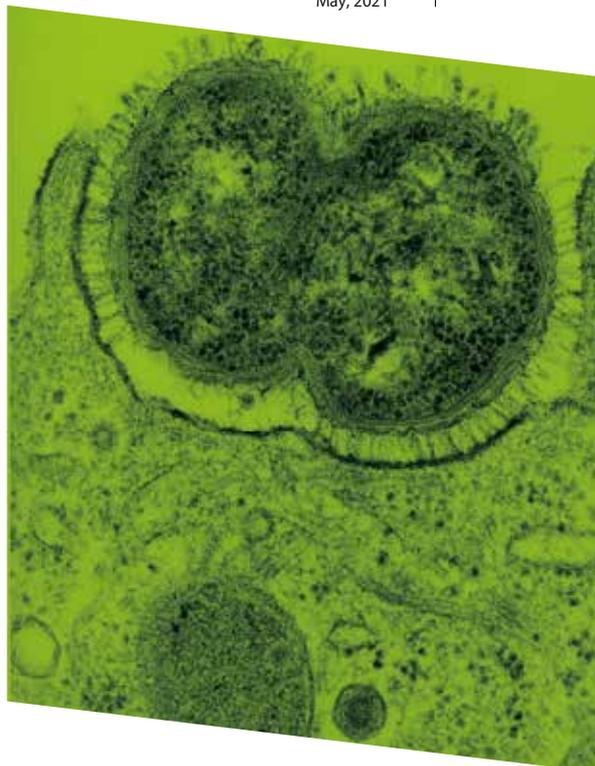
This pamphlet offers a brief, but hopefully intelligible explanation of our organization and its activities. As you will see, our research activities address major tropical diseases such as malaria, schistosomiasis, dengue fever, and yellow fever, and emerging and re-emerging infections such as HIV/AIDS, SARS, ebola and tuberculosis. We conduct basic medical sciences, epidemiology and clinical research for disease prevention and control. We also investigate entomology, ecology and social sciences. NEKKEN is also contributing to the education of students in PhD, and Masters as part of the Graduate School of Biomedical Sciences and the Graduate School of Tropical Medicine and Global Health of Nagasaki University. In addition, NEKKEN provides a three-month training course on tropical medicine. You will also find information about our research facilities in Kenya and Vietnam.

Hopefully you will be able to understand the intention of our research and education and will support us in the future.

Kouichi Morita
Dean and Professor
NEKKEN
May, 2021

History

- 1942.3 East Asia Institute of Endemics as Nagasaki Medical College affiliate
- 1946.4 Institute of Endemics, N.M.C
- 1949.5 Institute of Endemics, Nagasaki University, under postwar scheme
- 1967.6 Institute of Tropical Medicine, N.U.
- 1967.6 Added the Ward Tropical Internal Medicine, to University Hospital
- 1978.4 Diploma course, Kensyu-katei
- 1983.4 JICA Researcher Group-Course
- 1989.5 Certified as Joint Usage Research Center
- 1993.11 WHO Collaboration Center
- 1995.4 Certified as Center of Excellence, COE
- 1997.4 Tropical Infection Research Center
- 2003.4 COE program 21st Century Global Strategy against Tropical & Emerging Infection
- 2006.4 Tropical Medicine Master's Course
- 2008.4 Museum and Asia / Africa Facilities
- 2008.6 COE program Comprehensive Global Strategy against Tropical & Emerging Infection
- 2009.6 Certified as Tropical-medicine Joint Usage / Research Center
- 2011.4 Two clinical-field departments
- 2012.4 Global Leader Course for Tropical & Emerging Infection Intervention
- 2017.11 75th anniversary ceremony
- 2019.4 Shionogi Global Infectious Diseases Division



Joint Usage / Research Center on Tropical Disease

Our institute is the one and only public sector institute supported by MEXT (Ministry of Education, Culture, Sports, Science and Technology, Japan) that aims to conduct research on tropical diseases, and is identified as the Joint Usage / Research Center on Tropical Disease.

1. The Goal of the Center

Infectious diseases are caused by the collapse of symbiosis with other creatures, which cannot be avoided if we, human beings, live in nature. Although the ultimate aim of this center is to eradicate infectious diseases, it is needed rather to establish reciprocal relationships with other creatures than to eliminate them. Such establishment of reciprocal relationships requires collective knowledge, which can be achieved only by combining a broad aspect of disciplines.

Tropical infectious diseases have been spreading in tropical areas, which is a reflection of the environment and socio-economic situation existing there. It is considered to be a big challenge related to health. Emerging and re-emerging infectious diseases have been spreading globally with tropical areas at the epicenter. Tropical areas are not only the battle field where we, human beings, fight against them, but also the experimental ground where we newly create and develop our knowledge and technology in order to control infectious diseases.

Against the backdrop of past international activities and research facilities for infectious diseases in Asia and Africa, the Joint Usage / Research Center on Tropical Disease, together with researchers from diverse fields,

carries out joint research rooted in the local places where the infectious diseases are prevalent.

2. Outline of the Center's Activities

The Joint Usage / Research Center on Tropical Medicine supports collaborative research, which is either basic or applied research based upon an epidemiological, clinical or public health framework. It also supports research meetings, which promote and facilitate research into infectious diseases through exchanging information or technology where necessary. The Center serves as a bio-resource center to deliver such things as infectious agents, information, collected and stored here.

3. Operational Organization of the Center

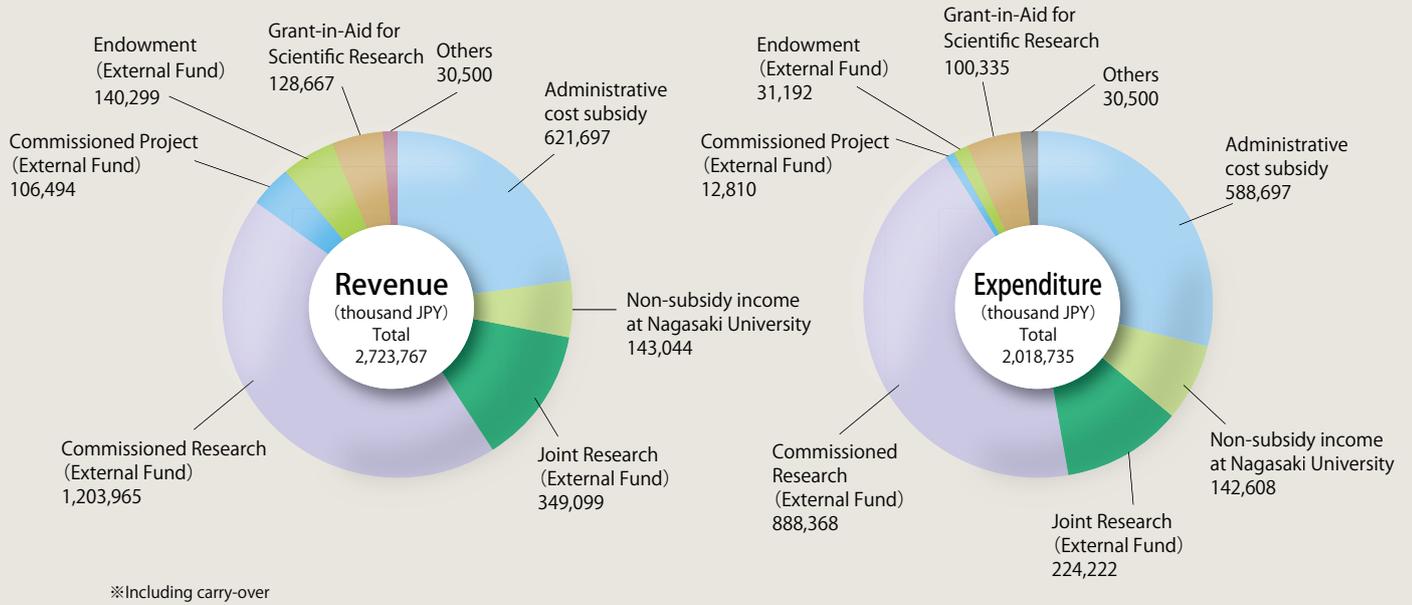
As for administration of this research center, the dean of the Institute of Tropical Medicine established the Steering Committee for the Center, which is composed of 11 members, out of whom more than half should be from outside the university concerned. The Steering Committee is responsible for the adoption of the applications, and monitoring and evaluation of the activities.

In order to support the above mentioned activities a specific administrative office supporting the Center is allocated in the institute and a professor is designated to be a section chief.

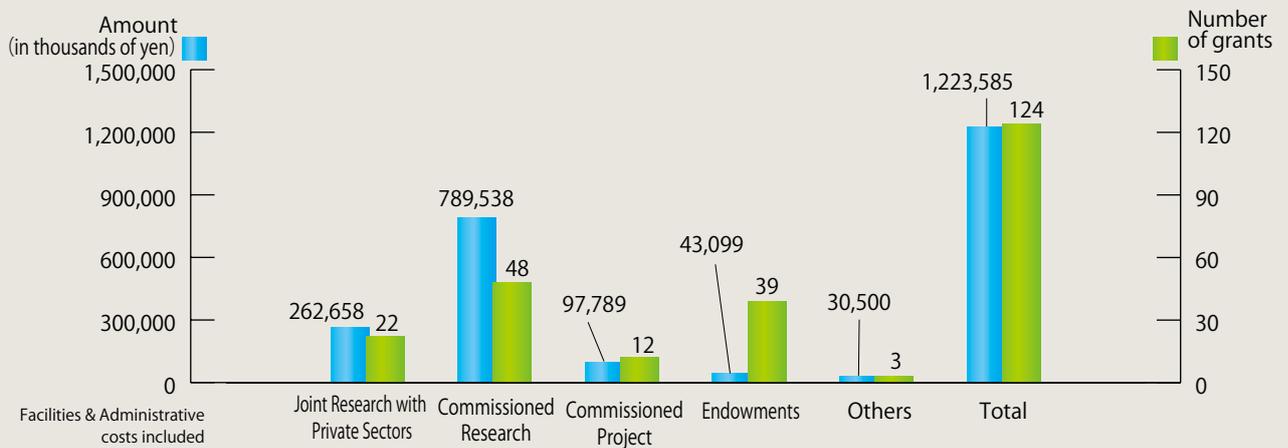


Steering Committee for the Joint Usage / Research Center on Tropical Disease (Committee Member outside the university)
 Manabu Ato (National Institute of Infectious Diseases),
 Shinichiro Kawazu (Obihiro University of Agriculture and Veterinary Medicine), Satoshi Sasaki (The University of Tokyo),
 Yukiko Higa (National Institute of Infectious Diseases), Sohkichi Matsumoto (Niigata University),
 Chizuru Misago (Tsuda University), Takayuki Miyazawa (Kyoto University)

Accounting (FY2020)



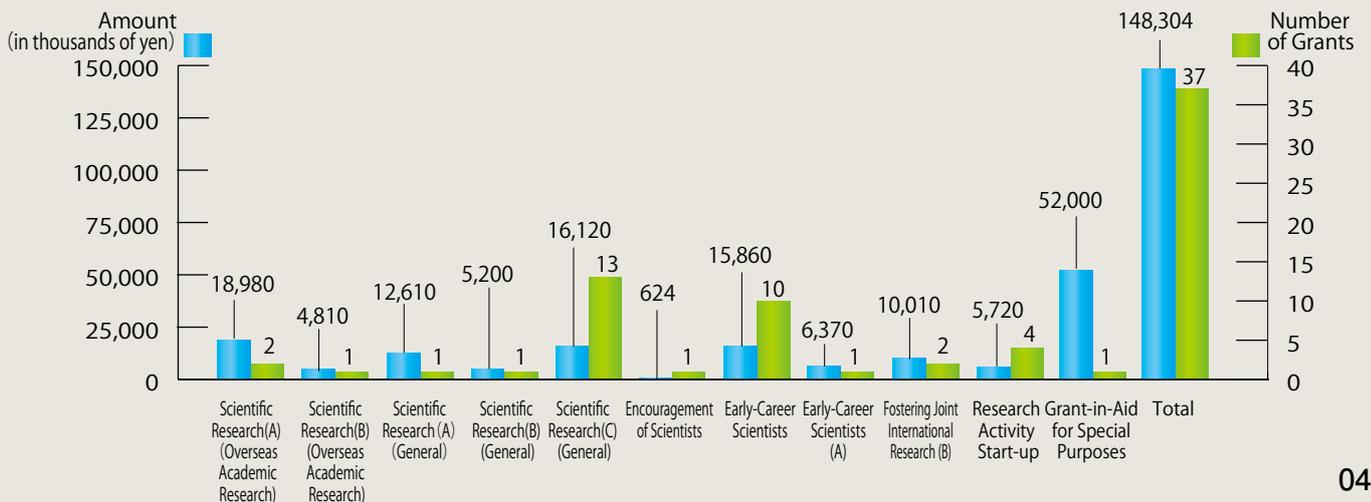
External Fund (FY2020)



Number of Staff (as of May 1, 2021)

Professor	Associate Professor	Senior Assistant Professor	Assistant Professor	Sub total	Others	Total
16	6	1	30	53	121	174

Grants-in-aid for Scientific Research (KAKENHI) (MEXT) (FY2020)



Microbiology and Parasitology Department of Virology



Professor and Head Kouichi Morita
Professor Moi Meng Ling
Assistant Professor Takeshi Nabeshima
Assistant Professor Mya Myat Ngwe Tun

This Department has been conducting basic and applied research on arthropod-borne viruses (arboviruses) such as Japanese encephalitis virus (JEV), dengue virus (DENV), Zika virus (ZIKV), Chikungunya virus (CHIKV), severe fever with thrombocytopenia syndrome virus (SFTSV) and COVID-19 virus (SARS-CoV-2)

Molecular epidemiology of arboviruses

We isolate DENV, JEV, CHIKV, ZIKV and SARS-CoV-2 in Asia and African regions and conduct molecular epidemiological analysis to determine international and inter-continental movement of these viruses. We also analyze unique genome sequences that are relevant to pathogenicity.

Research on vaccine development using reverse genetics

We have developed DENV infectious clones and identified viral determinants by modifying various parts of the genes. We are currently developing genetically engineered viruses as candidates for live attenuated DENV vaccines by financial support of GHIT.

Research on the pathogenicity of arboviruses and evaluation of therapeutic compounds using animal



model.

We elucidate the mechanism of pathogenicity and infectivity of arboviruses, such as DENV and SFTSV by using a mouse model.

Development of rapid diagnostic assay for infectious diseases

Various rapid diagnostics are being developed for arboviruses using PCR, LAMP, LC/MS and Immuno-chromatographic technologies for the detection of viral genome, protein and specific antibodies.

Activities as a WHO Collaborating Center

The department is designated as a WHO Collaborating Center for Reference and Research on Tropical Viral Diseases since 1993 and currently our department has been re-designated as a center for Tropical and Emerging Virus Diseases. The center has been collaborating with WHO in training WHO fellows from many developing countries and has deployed experts as WHO short-term consultants. From 2020 March, the laboratory is working as WHO Reference Centre for COVID-19.

1. Le et al. *Emerg Infect Dis* 2020; 26(7).
2. Wijesooriya et al. *Lancet Infect Dis* 2020; 20(2): 168-169.
3. Bastola et al. *Lancet Infect Dis* 2020; 20(3): 279-280.
4. Kyaw et al. *Am J Trop Med Hyg* 2019; 100: 643-646.
5. Yamane et al. *Nat Microbiol* 2019; 4(7): 1096-1104.

Microbiology and Parasitology Department of Bacteriology

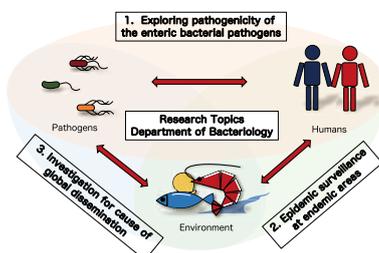


Professor Toshio Kodama
Associate Professor Hirotaka Hiyoshi
Associate Professor Hiroyuki Terashima

Our research focuses on the pathogenesis of enteric bacterial pathogens, including *Vibrio parahaemolyticus*, *Vibrio cholerae*, and *Salmonella enterica* spp. The emergence and spread of multidrug-resistant bacteria are big problems these days. It is predicted that drug-resistant bacterial infection will bring about 10 million annual deaths by 2050. We believe that understanding detailed mechanisms of bacterial pathogenicity gives us a clue to the development of effective vaccines and establishment of new treatment strategies without antibiotics. We will promote our study with various approaches, such as global epidemic surveillances, *in vivo* animal infection models, and *in vitro* molecular biological analyses, and make maximum efforts to produce talented researchers who can play on a global stage through study and experience.

● *V. parahaemolyticus* Pathogenesis

We have worked on *V. parahaemolyticus* for decades, and found that one set of Type III Secretion System (T3SS2) is necessary for induction of diarrhea in the patients infected with this pathogen. We have also identified and characterized effector proteins secreted from T3SS2, and revealed regulatory mechanisms of T3SS2-related genes. We recently demonstrated that an exotoxin, thermostable direct hemolysin (TDH), is secreted via T3SS2 in tandem with the Sec machinery, facilitates the distinct virulence traits. However, detailed mechanisms of how this pathogen colonizes the host intestine and induces diarrhea have remained unknown. We therefore try to understand a comprehensive mechanism of *V.*



parahaemolyticus infection by generating a new animal infection model, dissecting the expression mechanism of T3SS2-related genes, determining biological activities of T3SS2 effectors, analyzing the interaction of microbiota, and other multidimensional approaches.

● Endemic Stains of *Vibrio* spp.

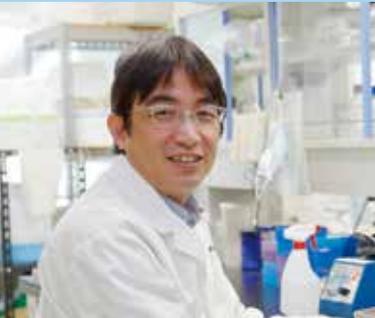
We are planning to isolate *Vibrio* spp. including *V. parahaemolyticus* and *V. cholerae* from patients, seafood and environmental samples in endemic areas to elucidate the genetic characteristics and dynamics of epidemic strains. We will also try to determine the factor(s) that contributes to global dissemination and characterize its role in infection.

● *Salmonella* Pathogenesis

We are interested in *Salmonella* pathogenesis. A big goal in this project is to understand how *S. enterica* spp. cause systemic infection in human for developing more effective vaccines and therapies without relying on antibiotics. Type III Secretion System (T3SS) coded on *Salmonella* Pathogenicity Island 2 (SPI-2) is well known as an essential virulence factor for establishing systemic infection and resisting the host innate immune defense system mediated by macrophage and neutrophil. To uncover the mechanism how *S. enterica* spp. cause systemic infection using T3SS, we have tried to dissect the functions of the T3SS for systemic infection and its effector proteins by various approaches, including *in vivo* mouse infection models, *in vitro* biological assays, epidemic surveillance, and *in silico* genetic comparisons among different *S. enterica* serovars (i.e., Typhimurium, Typhi, and Paratyphi A).

1. Yamazaki et al. *Virulence* 2020; 11(1): 840-848.
2. Kashimoto et al. *BMC Microbiol* 2020; 20(1): 69.
3. Matsuda et al. *Microbiol Immunol* 2020; 64(3): 167-181.
4. Okumura et al. *Mucosal Immunol* 2020; 13(1): 75-85.
5. Matsuda et al. *Nat Microbiol* 2019; 4(5): 781-788.

Microbiology
and Parasitology
Department of Emerging
Infectious Diseases



Professor and Head
Jiro Yasuda
Professor
Asuka Nanbo
Professor
Kentaro Yoshii
Associate Professor
Shuzo Urata
Associate Professor
Yohei Kurosaki
Assistant Professor
Haruka Abe
Assistant Professor
Yuri Ushijima
Assistant Professor
Yasuteru Sakurai
Assistant Professor
Wakako Furuyama
Assistant Professor
Misako Yajima
Assistant Professor
Rokusuke Yoshikawa

We are working on the basic and applied research to develop the countermeasures against emerging infectious diseases, especially viral hemorrhagic fevers and COVID-19.

**Research subjects:
Analyses of replication mechanisms of highly pathogenic viruses**

In infected cells, the viruses replicate using various cellular machinery and release a large number of progeny virions. Our interests are to clarify the molecular mechanisms of virus replication in host cells. We are currently analyzing the molecular interactions between viral proteins and cellular factors in infected cells. Especially, we are focusing on highly pathogenic viruses, such as Ebola virus, Marburg virus, Lassa virus and SARS-CoV-2.

Development of novel antiviral strategies

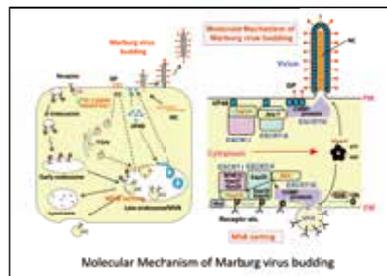
To establish novel antiviral strategies against viral hemorrhagic fevers and COVID-19, we are identifying the cellular factors which have antiviral activity and analyzing the molecular mechanisms of their antiviral action. We are also doing high-throughput screening of organic and chemical compound libraries for antiviral drug discovery against viral hemorrhagic fevers and COVID-19.

Development of detection methods for highly pathogenic viruses

In case of outbreak of emerging infectious diseases, rapid and accurate diagnoses are essential to control infection and to prevent further transmission. We have developed novel diagnostic assays for emerging viral diseases.

Research studies on viral diseases in Gabon republic

The followings are aims of this project; 1) to investigate prevalence of known and unidentified viral diseases in Gabon through genetical and serological assays, 2) to determine characteristics including genetic information and pathogenicity of viruses which are regarded as public health concern and those newly identified in Gabon, and 3) to develop rapid diagnostic methods for viral diseases of public health concern and those newly identified.



1. Ushijima et al. *Int J Infect Dis* 2021; 105: 452-459.
2. Sakurai et al. *BBRC* 2021; 545: 203-207.
3. Yoshikawa et al. *PLoS NTDs* 2020; 14(11): e0008855.
4. Abe et al. *J Viral Hepat* 2020; 27(11):1234-1242.
5. Zadeh et al. *J Gen Virol* 2020; 101(6): 573-586.

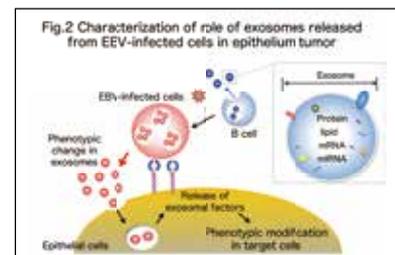
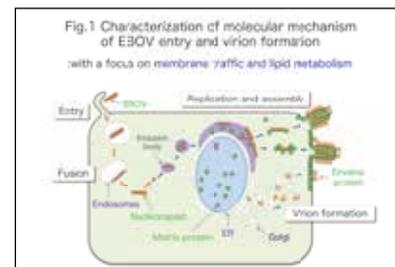
Ebolavirus and Epstein-Barr virus both cause major infectious diseases in humans, such as Ebolavirus disease and Epstein-Barr virus-associated malignancies, respectively. The long-term goal of our study is to provide insights into the molecular mechanisms of their pathogenesis, which shall lead to the development of rational therapies and diagnosis for them.

● Characterization of molecular mechanisms of EBOV entry and virus particle formation: toward the development of therapeutics for EBOV disease

Ebolavirus (EBOV), a member of the family *Filoviridae*, is an enveloped, single-stranded, negative-sense RNA virus that causes severe hemorrhagic fever with a high mortality rate, known as EBOV disease (EVD), in humans and nonhuman primates. Currently, no specific therapeutics has been approved for treatment and prevention of EVD. Because of the likelihood of future outbreaks and generation of mutant viruses, the development of a variety of EBOV therapeutics is urgent. Our goal is to elucidate the mechanism underlying virus entry and virion formation process with a focus on host membrane traffic dynamics and viral envelope's constituent phospholipids (Fig.1). We are also developing the therapeutics that specifically target the entry and virion formation process in multiple ways, which should lead to the significant contribution for prevention of EBOV infection in the future.

● Characterization of molecular mechanism of development of EBV-associated epithelium tumors

Epstein-Barr virus (EBV), a ubiquitous human γ -herpesvirus, establishes a persistent latent infection in B lymphocytes and epithelial cells in more than 90% of adults worldwide. Although this virus contributes causally to lymphomas and epithelial malignancies such as Burkitt's lymphoma, gastric carcinoma, and nasopharyngeal carcinoma, the molecular mechanism by which EBV cause these tumors remains fully elucidated. To update the understanding of the mechanisms for development of EBV-associated epithelial tumors, we are elucidating the physiological significance of exosomes, one type of extracellular vesicles, released from EBV-infected cells in tumor development. Moreover, we try to identify host and viral factors that are specifically and abundantly incorporated in exosomes, which shall lead to the development of potential biomarkers for EBV-associated tumors that contribute to the diagnosis of these tumors. An outline of this project is shown in Fig.2.



1. Nanbo, *Microorganism* 2020; 8: 729.
2. Furuyama et al. *PLoS Negl Trop Dis* 2020; 14(9): e0008602.
3. Isono et al. *Antivir Res* 2020; 183: 104932.
4. Zhao et al. *J Virol* 2020; 94(22): e01298-20.
5. Kheir et al. *Cancers* 2019; 11(6): E759.

Microbiology
and Parasitology
**Department of
Protozoology**



Professor
Osamu Kaneko
Assistant Professor
Kazuhide Yahata
Assistant Professor
Taeko Naruse

Malaria is responsible for a huge burden of death and disease in large areas of the tropical and sub-tropical world. Unfortunately, those countries hardest hit by the disease are often amongst the poorest. Despite continuing efforts, there is still no effective vaccine against the disease. In order to design and implement effective disease intervention strategies, we believe that one of the key priorities in malaria research should be the strengthening of our understanding of the basic biology of the parasite. We are currently investigating some

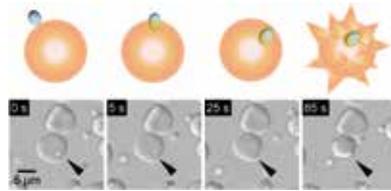


Fig.1 RBC invasion by *P. yoelii*. Merozoite-stage parasite (arrowhead) invades into RBC within 30 seconds (0 - 25 s) and deforms RBC to spike-like shape (85 s).

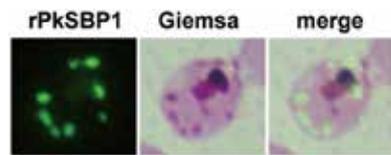


Fig.2 Colocalization of recombinant PkSBP1 protein (green) and Giemsa-stained 'Sinton and Mulligan' stipplings in monkey erythrocytes infected with PkSBP1-transgenic *P. knowlesi*.

fundamental aspects of the parasite's life cycle, such as the molecular interactions and signaling mechanisms behind red blood cell (RBC) invasion and the phenomenon of cytoadherence of parasite-infected RBCs. We utilize a variety of malaria parasites including human-infecting *Plasmodium falciparum*, the rodent malaria parasite *Plasmodium yoelii*, and *Plasmodium knowlesi* a causative agent of zoonotic human malaria. To expand a platform for basic and clinical malaria research, we are investigating the molecular epidemiology of malaria parasites in endemic countries, the biology of *Plasmodium vivax* hypnozoites, and the establishment of a novel malaria model using ungulate *Plasmodium*. In addition, we are also conducting research about the function and expression mechanism of trans-sialidase and the stage specific adaptation mechanisms of *Trypanosoma cruzi* that cause Chagas disease.

1. Hakimi et al. *PLoS Pathog* 2020; 16: e1008917.
2. Subudhi et al. *Nat Commun* 2020; 11: 2763.
3. Ishizaki et al. *Parasitol Int* 2020; 76: 102056.
4. Peng et al. *mBio* 2020; 11: e02995-19.
5. Thawnashom et al. *PLoS ONE* 2019; 14: e0226884.

Microbiology
and Parasitology
**Department of
Parasitology**



Professor
Shinjiro Hamano
Assistant Professor
Yoshinori Mitsui
Assistant Professor
Risa Nakamura
Technologist
Megumi Hamasaki

Various kinds of parasites infect humans for long periods of time without killing them, giving rise to tremendous afflictions, social and/or economic loss. We would like to develop deep insight into parasitic diseases and the surrounding factors from various points of view through both field and laboratory studies. Our goal is to contribute to new knowledge and to provide an enthusiastic environment for the training of the future generation of investigators.

We have been researching parasitic diseases in Mbita and Kwale, Kenya, in cooperation with Kenya Medical Research Institute (KEMRI) and Maseno University. In 2021, we started a new project on schistosomiasis with the support from MEXT Grant-in-Aid for Scientific Research (A). We also try developing ideal monitoring and diagnostic methods for schistosomiasis and



leishmaniasis with the support from Global Health Innovative Technology Fund (GHIT). In the laboratory, we maintain *Schistosoma mansoni*, its intermediate host snail, *Brugia malayi*, *B. pahangi* and *Aedes aegypti*.

We study host defense mechanisms against *Leishmania* spp and *Trypanosoma cruzi*, and in the process, have elucidated the function of the IL-12 cytokine family such as IL-27/WSX-1 during infection. We have been developing live attenuated vaccines to leishmaniasis and trypanosomiasis by editing genes using CRISPR-Cas9 system with the support from GHIT since 2015 and 2019, respectively. In addition, we developed animal models of intestinal amoebiasis together with Prof. Houpt at University of Virginia, and are devoting ourselves to the study on the molecular basis of pathogenicity of *E. histolytica* and host defense mechanisms to it.

1. Tanaka et al. *Parasitol Int* 2021; doi: 10.1016/j.parint.2021.102346
2. Mukendi JPK et al. *Parasit Vectors* 2021; 14(1): 70.
3. Zhang et al. *Nat Commun* 2020; 11(1): 3461.
4. Nakamura et al. *iScience* 2020; 23(9): 101544.
5. Sassa et al. *PLoS Negl Trop Dis* 2020; 14(8): e0008473.

Host and Vector Biology
Department of Immunogenetics



Professor
 Kenji Hirayama
 Professor
 Katsuyuki Yui
 Lecturer
 Mihoko Kikuchi

This department primarily focuses on the fundamental insights of the pathogenic genetic factors of the host and the pathogens of tropical infectious diseases such as Dengue fever, malaria and Chagas disease, through the application of immunology and genetics. With the understanding of the dynamic host-pathogen interactions, we are further concerned with the development of new tools to fight against these diseases including novel therapeutics (drugs) or vaccines.

We strive to build a highly interactive and collaborative network for sustainable research activities, and hence, we have various well-arranged collaborative projects with the following overseas and domestic facilities. 1) Research Institute for Tropical Medicine (RITM), Philippines. 2) UAGRM, Bolivia, 3) IICS University of Asuncion, Paraguay, 4) Pasteur Institute in Ho Chi Minh City, and National Institute of Hygiene and Epidemiology (NIHE), Vietnam, 5) Ahmadu Bello University, Nigeria, 6) Pasteur Paris, France, 7) London School of Hygiene and Tropical Medicine, UK, 8) National Institutes of Health (NIH), USA, 9) Tokyo Medical and Dental University, 10) Toyama University, 11) The National Institute of Advanced Industrial Science and Technology (AIST) 12) IS Global, Spain



Following research projects are going on.

1. Malaria

- 1) NGS analysis of host and malaria genome (KAKENHI)
- 2) Vaccine development (AMED)
- 3) Anti-malarial drug development (AMED, Toyama)

2. Chagas disease

- 1) Early bio-markers identification for chronic Chagas disease, namely, indeterminate, cardiac, and digestive forms in Bolivia (KAKENHI)
- 2) Anti-trypansomal drug development (Toyama, Nagasaki)

3. Dengue

- 1) Mechanism of cellular immunity on protection against Dengue virus (J-GRID).

1. Adamu et al. *Malar J* 2020; 19(1): 439-439.
2. Mochizuki et al. *Bioenergetics* 2020; 1861(11): 148283-148283.
3. Teklemichael et al. *Malar J* 2020; 19(1): 204-204.
4. Pare et al. *EBio Medicine* 2020; 51: 102584-102584.
5. Vásquez et al. *PLoS Negl Trop Dis* 2019; 13(9): e0007715.

Host and Vector Biology
Department of Host-Defense Biochemistry



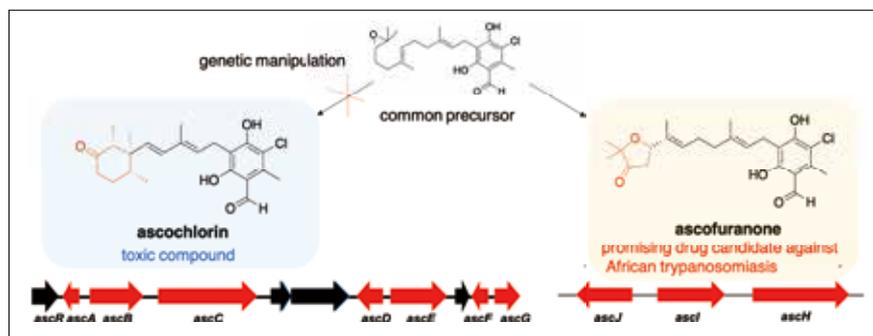
Professor
 Kiyoshi Kita

Education and research

Aim of our department is to contribute to global health and welfare from basic research. Main target of our research is energy metabolism, which is essential for the survival, continued growth and reproduction of living organisms. From the standpoint of biological adaptation, we have been studying on the molecular mechanism of energy transducing systems such as mitochondrial and bacterial

respiratory chain and drug discovery and development targeting them.

Our research has been focusing on human mitochondria, parasitic nematodes such as *Ascaris suum*, parasitic protozoa (*Plasmodium falciparum*, *Trypanosoma brucei*, *Trypanosoma cruzi*, *Cryptosporidium* etc.). In addition, by using research information obtained from these studies, we are trying to develop a new strategy to combat against other pathogens including SARS-CoV-2.



Bio-synthetic pathway of ascocofuranone. (from Araki et al., PNAS, 2019)

1. Enkai et al. *Eur J Clin Microbiol Infect Dis* 2021; in press.
2. Yamasaki et al. *Biochim Biophys Acta* 2021; 1862(4): 148356.
3. Nara et al. *PLoS ONE* 2021; 16(2): e0243855.
4. Sakurai et al. *Biochem Biophys Res Commun* 2021; 545: 203-207.
5. Mochizuki et al. *Biochim Biophys Acta* 2020; 1861 (11): 148283.

Host and Vector Biology
Department of Pathology
Nutrition and Infection Unit



Professor Sharon Cox

Department of Pathology, Nutrition and Infection (former Department of Pathology) was established in 2019 by Professor S. Cox (NU School of Tropical Medicine & Global Health (TMGH)) and is separate from the Department of Global Health Development Policy Sciences.

We are interested in how nutrition underpins human health and may mediate interactions between infections and non-communicable diseases such as diabetes. The research aims to provide an evidence base to support nutrition-based interventions to improve health outcomes and includes young children, adolescents, pregnant women and adults in low- and middle-income countries. Much of the current work is focused on Tuberculosis (TB), undernutrition and diabetes in TB patients in the Philippines, with research studies in both inpatient and outpatient populations. We collaborate with investigators from San Lazaro Hospital, Manila, the Nutrition Centre of the Philippines and the National TB programme. Professor Cox is the principle investigator of a large Filipino TB treatment cohort (the St-ATT cohort) (ISRCTN16347615), with active follow-up of patients until 2 years post-treatment. The cohort also includes 3 nested PhD student research projects with collaborators at the London School of Hygiene & Tropical Medicine (LSHTM). Professor Cox is also a co-investigator on a new, UK-funded, multi-country study investigating the role of the pancreas in long-term effects of malnutrition

occurring in child- and adulthood, with data collection in Philippines, India, Tanzania and Zambia, led by Prof Suzanne Filteau at LSHTM.



TB ward at San Lazaro Hospital, Manila

1. Edwards et al. *J Tuberc Lung Dis* 2020; 24(7): 712-719.
2. Miyazaki et al. *Trans R Soc Trop Med & Hyg* 2020; 114(6): 401-407.
3. White et al. *Sci Rep* 2020; 10(1): 4100.
4. Lee et al. *PLoS ONE* 2019; 14(6): e0218193.
5. White et al. *PLoS ONE* 2019; 14(5): e0215968.

Public and Environmental Health
Department of Eco-epidemiology



Professor Satoshi Kaneko
 Assistant Professor Kentaro Kato
 Assistant Professor Tomonori Hoshi

Our department is involved in various branches of public health research. With cutting-edge IT and biotechnology, we intend to create more accurate assessment methods in global health, improve responses to the public health needs on a local level, and open new directions in health sciences to future generations. Our activities include the following:

1) Research on the construction of a wide-area surveillance network for neglected tropical diseases (NTDs)

We are conducting research on the development of a monitoring network for NTDs using multiplex technology. We are also working with the University of Tokyo to automatically develop a system to identify houses using satellite data for regional sampling automatically.

2) Research on resident registration and population dynamics in developing countries

In order to conduct epidemiological and regional studies in developing countries with inadequate population registration, we have been operating a system to register all residents in the study area and periodically update information on births, deaths, migration. (Health and Demographic Surveillance system: HDSS) in Kenya. In addition, the introduction of cloud-based maternal and child registration and biometric system for identification at medical institutions



are ongoing.

3) Research contributing to public health measures for healthy growth of children in Africa

Epidemiological studies on stunting (short height compared to the norm for age in months) are being developed in rural Kenya. In addition, we are constructing a birth cohort on child development from pregnancy to birth and beyond, obtaining information on child care and feeding activities and on the environment to elucidate the epidemiological basis for determining factors related to child growth.

4) Research aimed at elucidating the molecular basis of parasitic diseases

We are conducting research on the molecular basis of parasitic diseases such as schistosomiasis, amebiasis, and leishmaniasis.

5) Development of mosquito vector survey tools and research on monkey malaria vectors

We are working with a research team from the University of Malaysia and the UK to develop a mosquito vector survey tool using 3D printing technology and its application to the survey of monkey malaria vectors.

1. Numair et al. *Int J Environ Res Public Health* 2021; 18: 6196.
2. Tanaka et al. *Parasitol Int* 2021; 83: 102346.
3. Fukuda et al. *BMC Oral Health* 2021; 21: 154.
4. Wanjihia et al. *Austin J Nutr Metab* 2021; 8: 1105.
5. Hitachi et al. *Int J Environ Res Public Health* 2020; 17(19): 7269.

Public and Environmental Health
Department of International Health and Medical Anthropology



Professor
Taro Yamamoto
Assistant Professor
Hiromu Ito
Assistant Professor
Hiroaki Arima

Department of International Health and Medical Anthropology has started its activities since 2008.

Our research was composed of four units; 1) research on infectious diseases in ecosystem, 2) research on the environment health, 3) research on biological evolution of microorganisms from the adaptation or fitness viewpoint and 4) research on the epidemiology from the historical viewpoint. The umbrella concept linking above four research units is to reconstruct infectious diseases "temporally" and "spatially" alike. Infection is the biological phenomenon as an interaction between hosts and microorganisms. In other words, host behavior, social structure as well as culture per se affect microorganisms in fitness and adaptation whereas microorganism



has impact on its hosts. Based on that perception, our department aims to get more detailed understanding and insight on infectious diseases. We would like to pursue the ways of analysis by various approaches such as molecular-evolutional technique, molecular epidemiology, detection of trace DNA, genomics based on bioinformatics, mathematical model, and computer science.

Another pillar of our department is a social responsibility. Now that even profit oriented organizations are required to have its corporate social responsibility, no need to say for academia or university. Out of the name of our department, it must be nothing but contribution to international health or people's health in resource-limited settings. What we think of important is to make solidarity in order to contribute to sustainable development. It is our department's goal.

1. Yazawa et al. *Am J Hum Biol* 2021; doi:10.1002/ajhb.2344.
2. Kunna et al. *Trans R Soc Trop Med Hyg* 2020; 115: 297-306.
3. Sabin et al. *J Physiol Anthropol* 2020; doi:org/10.1186/s40101-020-00239-5.
4. Akintije et al. *Acta Med Okayama* 2020; 74(6): 495-503.
5. Ito et al. *R. Soc. Open Sci* 2020; doi:10.1098/rsos.200891.

Public and Environmental Health
Department of Vector Ecology and Environment



Professor
Noboru Minakawa
Associate Professor
Hitoshi Kawada
Assistant Professor
Toshihiko Sunahara
Assistant Professor
Kyoko Futami

Our research interests include anything from ecology to molecular biology of medically important arthropods, particularly mosquitoes that transmit pathogens such as malaria parasites and dengue virus in Africa and Southeast Asia. We are also interested in their relationships with environmental variables and development of environmentally friendly vector control tools.

For dengue virus vectors, we revealed the geographical distributions of two subspecies of *Aedes aegypti* in East and South African regions. Our study also found that the genetic structures of *Ae.aegypti* populations in the endemic areas of Africa are similar to those of



Southeastern populations. The results suggest that the African mosquito populations were introduced from the overseas. To test the hypothesis further, we are currently conducting various studies, including a study on virus susceptibility.

For reducing malaria risk, we are evaluating the effectiveness of new insecticides and insecticide treated mosquito nets (ITNs) in Kenya and Malawi. We are also developing a malaria early warning system in Africa.

1. Morimoto et al. *Parasites Vectors* 2021; 14: 151.
2. Kawada et al. *Parasites Vectors* 2020; 13: 213.
3. Itokawa et al. *PLoS ONE* 2020; 15(4): e0232192.
4. Tamari et al. *Malaria Journal* 2020; 19: 373.
5. Hashimoto et al. *Microorganisms* 2020; 8(11): 1769.



Professor
Kazuhiko Moji
Professor
Yasuhiko Kamiya
Professor
Hirotsugu Aiga

Department of International Health Development and Policy (former Department of Social Environment) was re-established in 2018 by inviting three concurrent professors from the School of Tropical Medicine and Global Health (TMGH). The three professors have expertise of health system strengthening (H. Aiga), child health and emergency assistance (Y. Kamiya), and human ecology and ecohealth (K. Moji). The department promotes policy researches in various global health fields for making critical evaluation and constructive proposal for health policy.

Health Policy based on Human Ecology

Social determinants of health disparities have been revealed through studies of social epidemiology since the late 20th Century. Health impacts of global climate change as well as global (and local) environmental changes have been revealed almost



A research field in Laos

simultaneously. To integrate all the factors related to our health, human ecological system thinking, or "ecohealth" thinking is indispensable. For global health (or international health development) policy, not only improvement of medical services but also health promotion and disease prevention by means of better hygiene and safer and healthier lifestyle and non-medical care and social supports should be collectively implemented. Health policy is beyond the narrow medical policy. This department will promote researches on evaluation of health policy on population health for better policy proposal.

1. Sato et al. *One Health* 2020; 11: 100191.
2. Latio et al. *PLoS ONE* 2020; 15(9): e0238643.
3. Hsai et al. *Patient Prefer Adherence* 2020; 14: 2489-2499.
4. Miyazaki et al. *Glob Health Med* 2020; 2(4): 247-254.
5. Tomokawa et al. *Health Promot Int* 2020; doi:10.1093/heapro/daaa100.

Implementation Science in Health and Disability

My support and study is focused on redressing health disparity in low- and middle-income countries. Notwithstanding global evidence-based aid and national policy, health disparity has been widening with know-do gap and mismatch (coexistence of excess and deficiency) in health service delivery due to organizational path dependency, lack of coordination, vertical silo of programs and aid fragmentation. Just attributing health disparity to lack of access to, and low supply of health care can mislead and delay its fundamental problems. Through Implementation Science applying to international cooperation for maternal and child health, support for disabled children and non-communicable diseases, and emergency humanitarian assistance, my assistance and research facilitate local staff and people identify bottlenecks and barrier to

strengthen health systems and governance based on bottom-up problem-solving.



Training for Community Health Workers in Honduras

1. Takeuchi, et al. *Pediatr Int* 2021; 14729.
2. Hsai et al. *Patient Preference Adherence* 2020, 14: 2489-2499.
3. Kimitsuki et al. *PLoS NTDs* 2020; 14(11): e0008844.
4. Tomokawa et al. *Glob Health Promot* 2020.
5. Akiyama et al. *Health Promot Int* 2020; daaa005.

Health System Strengthening

In the absence of appropriately functioning systems for health service delivery, new medical technologies and drugs that are clinically effective would end up not reaching the populations in need. Key elements of health systems (e.g. health workforce, health information and health financing) particularly in the context of LMICs are one of my research topics. Needless to say, while recognizing the importance of optimization and adaptation of global standards for health systems to local settings, their critical verification and examination in view of field realities are equally important.



An experienced nurse managing a rural health center in Brundi

1. Aiga et al. *BMJ Nutr Prev Health* 2020; 3(2): 320-338.
2. Kawakatsu et al. *Health Policy Open* 2020; 1: 100019.
3. Kawakatsu et al. *Vaccine* 2020; 38(42): 6600-6608.
4. Balogun et al. *Trials* 2020; 21: 737.
5. Aiga, *Lancet* 2020; 395(10217): 27.

Clinical Medicine and Research

Department of Clinical Medicine



Professor
Koya Ariyoshi
Professor
Chris Smith
Associate Professor
Yoshinao Kubo
Assistant Professor
Momoto Yamauchi

This is the only clinical department in NEKKEN, which does clinical practices in Nagasaki University Hospital. We conduct a wide range of multi-disciplinary studies bridging our strength of clinical epidemiology to laboratory-based microbiology and immunology both in- and outside Japan. Our main research interests are respiratory infectious diseases, acute undifferentiated febrile illness, tuberculosis (TB) and HIV/AIDS. Specific research topics are as described below:

- Respiratory Infections Diseases, including Tuberculosis

We apply our in-house multiplex-PCR assays to identify 19 different viral and bacterial respiratory pathogens and a novel nano-fluidic real-time PCR-based assay to determine 50 pneumococcus serotypes for studies in- and outside Japan. We also conduct TB research with a special interest in



Bed-side clinical training course in San Lazaro Hospital

TB-specific cellular immune responses protective to the disease progression. In response to SARS-CoV-2 pandemic, we started to conduct clinical epidemiology research on COVID-19 in the Philippines in early 2020.

- Fever management in the tropical countries

It's challenging to diagnose and manage non-malarial fever without localizing sign such as leptospirosis, rickettsiosis, dengue fever, which are common in the tropical countries. We are investigating acute undifferentiated febrile illness in the Department of Infectious Diseases, Bac Mai Hospital, Hanoi, Vietnam and the National Infectious Disease Hospital (San Lazaro Hospital), the Philippines, by applying various new diagnostic tests.

- HIV/AIDS Studies and others

In collaboration with National Institute of Health, Thailand, we have conducted a natural history cohort of HIV infection. New research is still on-going based on the data and clinical samples derived from the cohort. Furthermore, we investigate molecular mechanisms of pathogenesis caused by retroviruses and other microbials.

1. Saito et al. *Clin Infect Dis* 2021; 72: 61-68.
2. Yanagisawa et al. *PLoS ONE* 2020; 15: e0242438.
3. Yamashita et al. *Front Immunol* 2019; 10: Article 2807.
4. Katoh et al. *PLoS Negl Trop Dis* 2019; 13: e0007928.
5. Saito et al. *Clin Infect Dis* 2018; 67: 897-904.

Clinical Medicine and Research

Department of Respiratory Infections



Professor
Konosuke Morimoto
Associate Professor
Bhim Gopal Dhouhadel

We are conducting epidemiological studies of respiratory infectious diseases caused by both bacteria and viruses, mainly *Streptococcus pneumoniae*, mainly in the domestic field. Our research activities are as follows.

- In the clinical epidemiological study of pneumococcal pneumonia, we are conducting surveillance of adult pneumococcal pneumonia in 27 city hospitals in Japan. The purpose of this study is to clarify the serotype distribution of pneumococcal pneumonia and the epidemiological characteristics of each serotype, and to recommend optimal vaccine policies in the older people.
- Using the latest serotype distribution obtained from the pneumococcal pneumonia surveillance, we are conducting a cost-effectiveness analysis of pneumococcal vaccines in the older people in collaboration with Yokohama City University. We are also conducting research to evaluate the quality of life and burden of care,

which is one issue in the study of cost-effectiveness of vaccines for the elderly.

- We are conducting a research on upper respiratory tract carriage of *Streptococcus pneumoniae* in the older people, both at home and in nursing homes. For this study, we are also developing methodology that are appropriate for studies of older people with low bacterial load and carriage rates.
- Under the COVID-19 pandemic, we are trying to clarify the epidemiological characteristics of COVID-19 through cluster analysis. Currently, we are conducting a cluster analysis of long-term care facilities in Nagasaki City.

1. Miyahara et al. *Emerging Infect Dis* 2021; 27(3): 915-918.
2. Sando et al. *J Travel Med* 2021; 28(2): taaa163.
3. Furuse et al. *Emerging Infect Dis* 2020; 26(9): 2176-2179.
4. Yasuda et al. *Vaccine* 2020; 38(21): 3752-3758.

Clinical Medicine and Research

Department of Pediatric Infectious Diseases



Professor
Lay-Myint Yoshida
Associate Professor
Michiko Toizumi
Assistant Professor
Mohammad Shah
Assistant Professor
Lina Madaniyazi
Assistant Professor
Hirono Otomaru

Clinical Epidemiological Studies on Pediatric Infectious Diseases

The Department of Pediatric Infectious Diseases conducts research on a wide range of infectious diseases with special attention on severe pediatric infectious diseases including pneumonia, diarrhea, and dengue which are the major causes of under 5 mortality. We also investigate congenital infections and its impact on child development. The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) outbreak occurred in Wuhan, China in December 2019 which then spread globally and became pandemic in March 2020. Thus, we expanded our research activities to COVID-19. We have setup a field research laboratory and a population cohort study site in Nha Trang, Vietnam. Environmental epidemiology is another area of our interest, focusing on the health impacts of atmospheric environmental changes including climate variability, global climate change and air pollution.

The current research topics,

1. Cohort studies on Pediatric Infectious Diseases in Vietnam: We receive funding from the Japan Initiative for Global Research Network on Infectious Diseases (JGRID), Japan Agency for Medical Research and Development (AMED) to conduct a large population-based cohort study on Pediatric Infectious Diseases in Nha Trang, central Vietnam since 2006.
2. Pediatric ARI surveillance: A population based hospitalized Pediatric acute respiratory infection (ARI) surveillance at Khanh Hoa General Hospital, Nha Trang, Vietnam was established to determine incidence, etiology and risk factors for pediatric ARI/pneumonia since 2007. We also investigate the emergence of new viruses and its molecular and clinical importance. In addition, we also investigate the impact or potential of various vaccine introduction on pneumonia and dengue in a population level.
3. Birth cohort study: We have conducted a birth cohort study on 2000 new born babies in Nha Trang, Vietnam since 2009. This study is to study congenital infection and host genetic factors on physical-neurological development of the child and development of severe pediatric infectious diseases. We also set up a new birth cohort study in 2017-2018 to investigate congenital infection including rubella, cytomegalo, and zika

virus and the effect on the child development.

4. Pneumococcal conjugate vaccine (PCV) reduced dosing trial: We received a multimillion dollar grant from Bill and Melinda Gates Foundation to conduct a PCV reduce dosing trial in Vietnam. We believe that the study outcome will change global PCV vaccination strategy to improve the availability of PCV and other vaccines in developing countries.
5. Dengue intra-family transmission in the community: In collaboration with London School of Hygiene and Tropical Medicine, we are conducting a dengue intra-family transmission study in the community in Nha Trang.
6. COVID-19 related research: We are currently conducting clinical epidemiological characterization and long-term complication and immunological responses of COVID-19 in Vietnamese population. We are also investigating the vaccine response among medical, non-medical and previous COVID-19 cases in Vietnam and Japan.
7. Environmental epidemiology: We are conducting several studies on health impact of climate change and air pollution on the local and global scale.



PCV vaccination field work in Nha Trang

1. Wang et al. *Lancet Glob Health* 2021; 9(1): e33-e43.
2. Mohamed et al. *Sci Rep* 2021; 11(1): 337.
3. Biggs et al. *BMC Med* 2020; 18(1): 364.
4. Ngwe et al. *Am J Trop Med Hyg* 2020; 103(5): 2059-2064.
5. Madaniyazi et al. *Environ Int* 2020; 140: 105610.

Shionogi Global Infectious Diseases

Alliance Coordinator



Professor
Tsuyoshi Kihara

Nagasaki University has entered into a comprehensive cooperation agreement with Shionogi & Co., Ltd. (Head Office: Osaka, Japan) in the field of infectious diseases focused on malaria on February 28, 2019. Through this agreement, Nagasaki University and Shionogi intended to establish Shionogi Global Infectious Disease Division (SHINE) as a collaborative research division at Institute of Tropical Medicine. The aim of the establishment is to accelerate and facilitate the drug discovery research for malaria. This division will concentrate on studies to understand the life cycle of malaria parasites and the host defense mechanism, which are essential for the diagnosis and treatment of malaria. And final goals are to create an innovative novel drug and vaccine to meet Target Product Profile based on the findings from the studies.

Malaria is one of the top 3 infectious diseases worldwide along with AIDS and tuberculosis, and mainly occurs in epidemics in tropical regions and subtropical regions. The efficacy of existing preventive vaccine is insufficient and also a number of parasites have been developing resistance to existing medicines. Therefore, malaria has been a serious threat to human globally.

Our division consists an Alliance Management and 4 departments, Cellular Architecture Studies, Molecular Infection Dynamics, Immune Regulation and Exploratory Research for Drug Discovery.

Through the collaboration, Nagasaki University and Shionogi will become a key part of the new open innovation based on the industry-academia collaboration both domestic and overseas, and will establish a platform aiming at eradication of malaria. We will strive to contribute to the health of people around the world through ongoing provision of the best preventive and therapeutics of malaria.



Shionogi Press Release, Feb28, 2019, Shionogi enters into Comprehensive Cooperation Agreement in the Field of Infectious Disease Focused on Malaria with Nagasaki University

Shionogi Global
Infectious Diseases
Department of Cellular
Architecture Studies



Professor
Fuyuki Tokumasu
Assistant Professor
Shinya Miyazaki

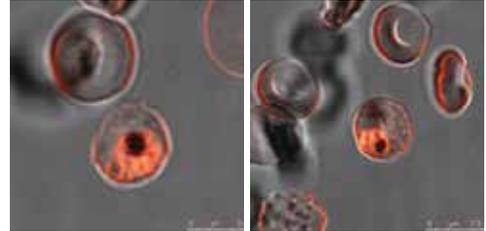
1. Shionogi Global Infectious Diseases Division

Shionogi Global Infectious Diseases Division was established in April 2019, through the collaboration agreement between Shionogi & Co., LTD. and Nagasaki University to tackle malaria. Four laboratories, Departments of Cellular Architecture Studies, Molecular Infection Dynamics, Immune Regulation, and Exploratory Research for Drug Discovery. We share same laboratory space and team up for our mission to find new drug and vaccine candidates by taking advantages of expertise from each department. This is the unique but powerful collaboration that expands our scientific potential and flexibility.

2. Research Activity

Blood stage of malaria parasite invades human erythrocytes and proliferates by creating its own cellular environment. This process includes formations of complex membrane structures inside erythrocyte cytoplasm and transportations of parasite proteins to erythrocyte membrane. Studying this host cell modifications is essential in *Plasmodium falciparum* research, that often induces severe forms of malaria. We believe that unveiling the molecular mechanisms of structural and chemical balance of parasitized erythrocytes allows us to find important information to

discover a new drug target. We search molecular factors that are involved in 'intelligent interior design' by parasites, and aim to find new antimalarial drug targets and compounds which prevents transition to severe malaria. Our research has been merging advantages of classical biochemistry/cellular biology and biophysical approaches. High-resolution imaging, lipidomics, protein chemistry, high-throughput screening for inhibitor compounds have been actively used to achieve our goal. We share our data and collaborate with other three laboratories for advanced experiments for fortifying our scientific competence.



Complex membrane structures that appear in parasitized human erythrocytes soon after the infection with a variety of size and shape.

1. Tokumasu et al. *Parasitol Int* 2021; 83: 102369.
2. Tanaka et al. *Biol Open* 2019; 8: bio042259.
3. Hayakawa et al. *Exp Parasitol* 2015; 153: 174-9.
4. Tokumasu et al. *Biol Open* 2014; 3: 529-541.
5. Tokumasu et al. *Exp Parasitol* 2012; 131: 245-251.

Shionogi Global
Infectious Diseases
Department of Molecular
Infection Dynamics



Associate Professor
Daniel Ken Inaoka
Assistant Professor
Takaya Sakura

The Department of Molecular Infection Dynamics, in cooperation with Department of Exploratory Research for Drug Discovery aim to identify drug target molecules and to establish screening systems in order to find lead compounds with potential use for treatment, prophylaxis and transmission blocking against malaria.

This Department conduct research on microaerophilic metabolism conserved in several pathogens such as parasites (protozoa and helminth) and bacteria, in order to understand the molecular mechanism of parasitism phenomena.

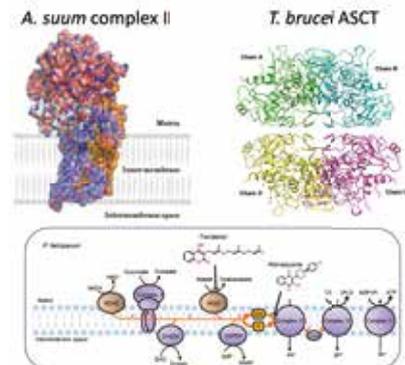
We utilize multidisciplinary approaches, consisted by biochemistry, molecular biology, biophysics, structural biology and chemical biology, to conduct our basic and applied research.

Our target infectious diseases include protozoan parasites such as *Plasmodium* spp., *Theileria* spp., *Trypanosoma cruzi*, *T. brucei* and *Leishmania* spp.; helminthes such as *Ascaris suum*, *Anisakis* spp., *Haemonchus contortus* and *Fasciola* spp., and bacterial pathogens such as *Mycobacterium* spp., *Campylobacter jejuni* and

Helicobacter pylori.

We also conduct research on cancer. Intestinal parasites have evolved sophisticated machinery to adapt and survive in hypoxic and nutrient deprived environment (microenvironment). Certain type of cancer cells also possess similar machinery to survive under tumor microenvironment.

Our activities are supported by research grants acquired from KAKENHI (MEXT), AMED, GHIT and Private Companies.



1. Endah et al. *Int J Mol Sci* 2021; in press.
2. Villafraz et al. *mBio* 2021; in press.
3. Nurkanto et al. *Front Cell Infect Microbiol* 2021; 11: 639065.
4. Sato et al. *Genes* 2020; 11(12): 1468.
5. Mochizuki et al. *BBA Bioenergetics* 2020; 1861(11): 148283.

Shionogi Global
Infectious Diseases
Department of
Immune Regulation



Associate Professor
Shusaku Mizukami

Our scope is the human immune response against malaria, and malaria vaccine development.

Malaria parasite life cycle is divided into liver (pre-erythrocytic) stage and erythrocytic stage in human. Even with urgent appearance of drug resistant strain, many antimalarial drugs are available for erythrocytic stage. However, in liver stage, only a few drugs with side effects are available, and thus, vaccine and novel antimalarial drug development are still an urgent issue for liver stage.

Considering the immunity against malaria pathogen in liver stage, cytotoxic T lymphocytes in cellular immunity is essential. However, current vaccine development is biased in inducing neutralizing antibody.

To archive the goal, our vaccine development focuses on cellular immunity during malaria liver stage. We put effort in examining and optimizing (a) vaccine antigen, (b) antigen delivery system, (c) vaccine adjuvant, and (d) route of administration.

Our study started with mouse malaria model, and eventually, we aim to apply our understanding

into vaccine development to against *Plasmodium falciparum*, one of the malaria parasites affected human most.

1. Tran et al. *Acta Trop* 2021; 105:823.
2. Manh et al. *Front Immunol* 2020; 11: 1980.
3. Iglesias Rodriguez et al. *BMJ Open* 2020; 10(9):e032546.
4. Teklemichael et al. *Malar J* 2020; 19(1):204.
5. Manh et al. *J Gen Viol* 2018; 99(9): 1239-1247.

Shionogi Global
Infectious Diseases
Department of Exploratory
Research for Drug Discovery



Visiting Associate Professor
Teruhisa Kato
(Director, Head of Infectious Diseases
3 Group, SHIONOGI & CO., LTD.)

Malaria is one of the three largest infectious diseases in the world, which aligns with HIV and tuberculosis. More than 200 million people are infected with malaria and more than 400,000 people died annually. There has been still no effective vaccine, and resistant malaria to existing therapeutic drugs have been reported, and the development of new drugs is urgently necessary.

In this department, a Shionogi's researcher is in charge of principal investigator, and together with the three departments in SHINE division. We will take on the role of hubs that connect research assets such as know-how and global network of malaria research, which are the strengths of Nagasaki University, and screening drug discovery utilizing the small molecule SAR (structure-activity relationship) engine, which is the strengths of Shionogi, to promote the discovery research of new therapeutic drugs by taking advantage of each strengths. Especially, the purpose is to create a therapeutic drug with strong antimalarial activity and high safety with the department of Molecular Infection Dynamics.

Research activities are as follows:

- Promotion of drug discovery research on screening-based drug discovery
- Implementation of Hit to Lead Structure-Activity Relationship (SAR) approach, and optimization of lead scaffolds
- Strengthening external collaboration for clinical development and identifying new targets

- Optimization of drug metabolism, safety, and physical parameters of candidate compounds within Shionogi
- Conducting target discovery and basic research for antimalarial drugs

1. Ryckmans et al. *Bioorg Med Chem Lett* 2011; 21: 4857-4859.
2. Mori et al. *J Pharmacol Exp Ther* 2009; 328: 671-679.

Associated Facility
Center for Infectious Disease Research in Asia and Africa

Kenya Research Station



Professor
Satoshi Kaneko
(Chief Representative)

Professor
Shingo Inoue

Nagasaki University Institute of Tropical Medicine and Kenya Medical Research Institute (NUITM-KEMRI) Project was launched by signing the Memorandum of Understanding between the President of NUITM and the Director of KEMRI in 2005. The project's objective was to enhance research and develop capacity building in tropical medicine at the laboratory and field levels. In January 2006, Kenya Research Station was established and set up biosafety Level 2 and 3 laboratories and Health and Demographic Surveillance System (HDSS) in Mbita near Lake Victoria and Kwale on the coast side of Kenya, which has registered about 120,000 people. Additionally, Mosquito Surveillance System (MSS) has been functional for research on malarial mosquitos in Mbita.

1. Research activities:

Primary research teams are organized according to the external research grants or funds. The SATREPS Project for rapid diagnostics and establishing an alert system for the outbreak of Yellow Fever and Rift Valley Fever were achieved and completed in 2017. AMED-funded project for serological surveillance on neglected tropical diseases (NTDs) is completed in 2020. We have start research activities toward the formation of IoT



academic centers that contribute to the improvement and improvement of global health as an Asia-Africa Science Platforms of Core-to-Core Program supported by the JSPS. There are 13 research activities conducted at Kenya Research Station funded by the JSPS (KAKEN). In addition, research projects supported by pharmaceutical companies for Rotavirus research and by funding agencies such as the Grand Challenge Canada had been organized to develop the mother and child registration system.

2. Education and training activities:

The station accepts Master's and Ph.D. students from the Graduate School of Tropical Medicine and Global Health and the Graduate School of Biomedical Sciences at Nagasaki University. The station is also providing research opportunities for young researchers and students from Kenyan institutions.

3. Social contribution activities:

We kicked off a JICA Grass-root project focusing on Jigger control in Mbita in 2020 to give feedback to the communities.

1. Fukuda et al. *BMC Oral Health* 2021; 21: 154.
2. Wanjihia et al. *Austin J Nutr Metab* 2021; 8.
3. Tanaka et al. *Parasitol int* 2021; 83: 102346.
4. Tomokawa et al. *Glob Health Promot* 2020; 27: 78-87.
5. Inziani et al. *Int J Infect Dis* 2020; 91.

Associated Facility
Center for Infectious Disease Research in Asia and Africa

Vietnam Research Station



Chief Representative, Professor
Futoshi Hasebe
Assistant Professor
Taichiro Takemura

Since 2015, the Japan Initiative for Global Research Network on Infectious Disease (J-GRID) project has been taken over to the newly established Japan Agency for Medical Research and Development (AMED) and J-GRID project, a new five-year project, "Study on Emerging and Re-emerging Infectious Diseases in Vietnam." has been started from 2020. The Vietnam Research Station in the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi is currently manned by 3 staffs from NU, and the Nha Trang sub-station by a permanent staff, in addition to which 21 staff from NU and a further 32 researchers from other research institutions participate in the activities of the Station and conduct research. The main research topics are dengue fever, infectious diarrhea, influenza, and drug-resistant bacteria, severe childhood pneumonia, zoonotic diseases (bat-derived infectious diseases) and new coronavirus infection (COVID-19) are included to study to contribute to prevention of infectious diseases collaboration with National Center for Global Health and Medicine. In addition, six joint research projects were adopted as research for utilizing the Vietnam Research Station collaboration with the National Institute of Infectious Diseases, Osaka University, Kyoto University, Hokkaido University, Tokai University, and Kumamoto University. An outbreak of COVID-19 occurred in Vietnam in late January 2020, we cooperated with NIHE to conduct a rapid diagnostic method by SARS-CoV-2 specific real time



NIHE-Nagasaki University Scientific Symposium in Hanoi. (2020.09.30)

RT-PCR, virus isolation, viral gene analysis, and developed an ELISA system using the N protein of SARS-CoV-2 for COVID-19 serodiagnosis. It was used in sero-epidemiological survey of COVID-19 in Vietnam. On September 30, 2020, a joint web symposium "Research on Infectious diseases in Vietnam and development of application in diagnosis, prevention and treatment" was held between NIHE and Nekken at The ANN Hotel in Hanoi. The Vietnam Research Station has been conducting educational support as an early exposure facility in the Program for Nurturing Global Leaders in Tropical and Emerging Communicable Diseases, and also utilized as an on-the-job-training facility for other researchers from NU and other universities. However, due to the pandemic of COVID-19 in 2020, all overseas training program utilizing the Vietnam Research station and outreach activity such as NU Hanoi public lecture were cancelled.



Bat survey in Lang Son province. (2020.11.19)

1. Buerano et al. *Emerg Infect Dis* 2020; 26(9): 2300-2301.
2. Inagaki et al. *J Virol* 2020; JVI00673-20.
3. Nguyen et al. *BMC Infect Dis* 2020; 20(1): 332.
4. Nguyen et al. *J Glob Antimicrob Resist* 2020; pii: S2213-7165(20)30125-9.
5. Maeda et al. *J Virol* 2020; pii: JVI00193-20.

Associated Facility Tropical Medicine Museum



Professor
Junko Okumura
Technologist
Kazuo Araki

The Museum of Tropical Medicine has functions as a resource center on Tropical Medicine. There are sections providing information on tropical diseases, parasites, bacteria, virus, insects (vectors), specimen of dangerous animals, audio-visual materials and historically valuable documents on tropical medicine. The audio-visual section demonstrates interesting scientific movies with 80-inch screen. We have newly established a booth to identify mosquitoes by observation to arouse interest and understanding on tropical infectious diseases for wider age group.

In the fiscal year of 2020, the Coronavirus Disease (COVID-19) influenced on our activities. Particularly, the State of Emergency declared by the government made us temporarily close the museum from April 17 through May 22 2020. Also, various events were hold online. Due to these above mentioned, number of visitors to the museum have been drastically decreased. Under the situation, main activities of the museum in 2020 are as indicated below.

● **MUSEUM MANAGEMENT & OPERATION:** The museum provides information on tropical infectious diseases by using approximately 100 panels, microscopic images, movies, specimens, educational models of Bio-safety level-4 (BSL-4), and Personal Protective Equipment (PPE) for BSL-4. Although main visitors are Japanese, quite a few people visit from overseas. Therefore, we provide information in English and Chinese (mandarin) for non-Japanese speakers.

In addition to the museum routine tasks, we actively worked the following event and issues. Regarding the



education material development for primary school pupils to provide life-skills in a Post-COVID-19 society, it will be carried on to the next year.

- 1) Considering the COVID-19 endemic, we organize and operate 'NEKKEN Natsu-juku 2020' which was implemented as an online seminar. Besides taking a role of management for the seminar, Prof. Okumura worked as a chairperson and promoted discussions during the event.
- 2) COVID-19 related stigma is one of the great concerns in Japan as well as the world. In collaboration with faculties of Education and Technology, Nagasaki University, Prof. Okumura developed a teaching material (tentative version) for primary school pupils. This work will be carried on to the year of 2021.

● **IT (INFORMATION TECHNOLOGY) INFRASTRUCTURE MAINTENANCE:** Network tools and servers are updated with technological innovation and maintaining its security. It provides safe and secure IT environment to researchers, students and staff members who work at NEKKEN. In addition, we update and maintain the contents and the system for the NEKKEN homepage.

With IT innovations, the requests from the NEKKEN members are getting wider and more variety ones. To respond to them we obtain new software and devices as much as possible.

● **RESEARCH:** Prof. Okumura conducts research in Lao PDR and Republic of Guinea. She collects epidemiological data on infectious diseases, health seeking behavior, nutrition etc. in order to identify risk factors affect people's health. Also, she collects various kinds of information on BSL-4 laboratories in the world to establish much secure environment of the National Research Center for the Control and Prevention of Infectious Diseases, Nagasaki University.

1. Canara et al. *BMC Public Health* ; 2020; 20(1) : e1298.
2. Okumura et al. *J Intl Health* 2019; 34(1): 35-43.
3. Delamou et al. *Lancet Glob Health* 2017; 5(4): e448-e457.
4. Camara et al. *Trans R Soc Trop Med Hyg* 2017; 111: 22-29.
5. Delamou et al. *BMJ Global Health* 2017; 2: e000202.

Associated Facility Central Research Laboratory



Head and Professor
Shinjiro Hamano
Senior Assistant Professor
Mihoko Kikuchi
Assistant Professor
Miako Sakaguchi

The aim of the Central Research Laboratory is to efficiently operate and manage common equipments and to support general laboratory activities in the institute. In addition, this laboratory also supports research activities conducted in the institute by extramural investigators.

○Molecular & Cellular Biology Unit

Molecular & Cellular Biology Unit is responsible to maintain and operate following equipments located in the Central Research Laboratory; 16- and 48-capillary sequencers, GS junior genome sequencer and Mass Spectrometry-based Genotyping system for genome analysis; Flow Cytometer for cell function analysis; luminescence imager for visualization analysis; and Luminex Bead-array system and Fluorescence- Luminescence Multilabel Counter for multipurpose analysis. In addition, this unit is also responsible for maintaining the equipments/facilities to support general laboratory activities; such as Pure Water Supply, Ultracentrifuge, Lyophilizer, Speed-Vac, French Press, Bioruptor, Bead Crusher, sample storage in liquid nitrogen, Autoclave, dark room and cold room.

○Light Microscope Unit

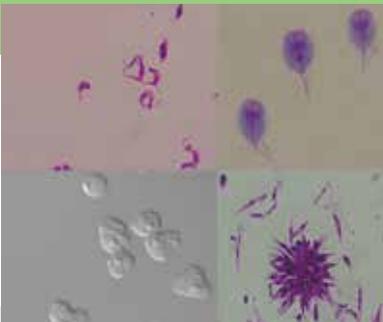
Light Microscope Unit provides optical

instruments to perform basic, translational, and clinical research on the imaging features of infectious disease. We operate Nikon Infectious Disease Imaging Core laboratory established in April 2015. The laboratory has equipped laser scanning confocal/fluorescence microscope (NIKON), Imaging Flow Cytometer (Luminex), laser scanning confocal/super-resolution microscope (ZEISS), and a Virtual Slide Scanner (Nanozoomer 2.0-RS, Hamamatsu Photonics).

○Electron Microscope Unit

Electron Microscope Unit supports ultrastructural characterization of microbial pathogens and the structural change of the pathogen-infected cells. This unit offers high quality imaging services by state-of-art techniques such as conventional and immuno-electron microscopy and 3D tomography, and also provides training on sample preparation and equipment usage. This unit is responsible for Transmission and Scanning Electron Microscopes (JEOL), Ultra-Microtomes (LEICA and REICHERT), vacuum coater, Hydrophilic Treatment Device, and Osmium Plasma Coater in addition to general laboratory facilities for a wide range application of electron microscopy.

Associated Facility
**NEKKEN Bio-Resource
 Center**



Project Representative, Professor
Osamu Kaneko
 Service Manager, Assistant Professor
Makoto Kazama

NEKKEN Bio-Resource Center (NBRC) was established in 2015 to take charge of National BioResource Project (NBRP) mission in Institute of Tropical Medicine (NEKKEN). NBRP constructs the framework for systematic collection, preservation, and distribution of bio-resources with a focus on those that required strategic development by the National Government. To promote life sciences it is important for researchers to share the various bio-resources necessary for pursuing researches and developments. NEKKEN has participated to NBRP services since 2002 when it was initiated by the Ministry of Education, Culture, Sports, Science and Technology (MEXT). NBRP has been maintained by Japan Agency for Medical Research and Development (AMED) during 2015-2020 and by MEXT from 2021 again. We have been serving as Division of Protozoa in "Pathogenic Eukaryotic Microorganisms of a Core Facility Upgrading Program" under Medical Mycology Research Center (MMRC), Chiba University.

NBRC supports the research and education on pathogenic protozoa by providing following services; (1) web-based database of pathogenic protozoa maintained

in Japan, including NBRC, with their owner and strain information (2) acceptance of pathogenic protozoa for deposit, (3) preservation of protozoan strains, (4) distribution of a variety of protozoan strains, and (5) distribution of their microscopic specimens for education in academic organizations. To facilitate the collection, preservation, and provision of bio-resources, NBRC also implements the development of related technologies. Approximately 900 strains of pathogenic protozoa are preserved in NBRC, and approximately half of them are available to supply. Last year NBRC provided 47 protozoan strains to researchers. NBRC is currently preparing deposit and supply of genetically modified protozoan parasites. Your cooperation and support to the project would be highly appreciated. Pathogenic protozoan resources available from NBRC are listed in the following website.

<http://www.tm.nagasaki-u.ac.jp/nbrc/>
 E-mail: protozoa@tm.nagasaki-u.ac.jp

Associated Facility
**Neglected Tropical Diseases
 Innovation Center
 (NTDi Center)**



**Neglected
 Tropical
 Diseases
 Innovation
 Center**

Professor (Director)
Satoshi Kaneko
 Professor (Deputy Director)
Tsuyoshi Kihara
 Assistant Professor
Kota Yoshioka
 Assistant Professor
Taeko Moriyasu

The Center for Neglected Tropical Diseases Innovation (NTDi Center) was established in 2016 to stimulate research and development in the field of tropical medicine, including neglected tropical diseases (NTDs) at the Institute of Tropical Medicine (NEKKEN), utilize NEKKEN's research resources, promote collaboration between industry, government, and the private sectors, and build domestic and international networks. To date, it has provided support for the acquisition of large-scale external research grants and established the Japan Alliance on Global NTDs (JAGntd) project in 2018, a domestic network related to NTDs. Currently, the center is under reconstruction for strengthening an intelligence function of NEKKEN for the 4th mid-term goal of the University.

The mission, vision, and values of the NTDi Center were established this year as follows.

Mission: The role of the NTDi Center

The NTDi Center will support the revitalization

of research and development activities of the Institute of Tropical Medicine.

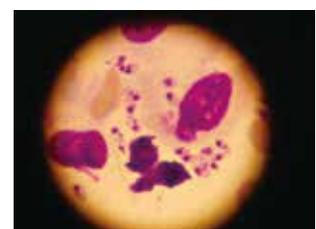
Vision: What the NTDi Center aims to achieve

To function as an intelligence organization that supports the strategic development of NEKKEN.

Value: Guidelines for NTDi Center activities

The NTDi Center will operate according to the following policies;

1. Strategic utilization of NERC's research resources (including overseas sites)
2. Cooperation with inside and outside the University
3. Strengthening of related networks
4. Acquisition of large scale grants for research
5. Identifying talented young researchers for tropical medicine



Associated Facility
Office of Coordination
for Humanitarian Affairs



Section Chief, Professor
Taro Yamamoto

(Introduction)

In 2016, the Office of Coordination for Humanitarian Affairs was set up in our institute. Prof. Taro Yamamoto, who also heads the Department of International Health and Medical Anthropology, was nominated as the first chief of this section. One year has passed since its inception during which time we have dispatched missions to natural disaster affected areas and yellow fever epidemic areas.

(Aims)

The aims of this office are to provide support to both natural and manmade disaster areas. In order to undertake these missions, this office shall develop more human resources, do research, and become the center of an international humanitarian network.

(Organization)

1. Office of Coordination for Humanitarian Affairs was set up in NEKKEN
2. Appoint one section chief (professor)

(Past, Present and Future)

NEKKEN has dispatched missions to disaster afflicted areas such as Haiti in 2010,

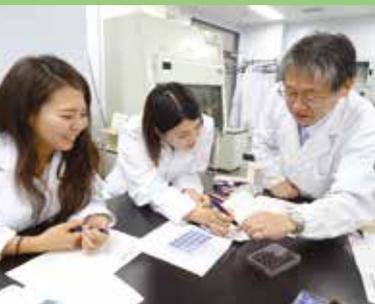
Tohoku region in 2011 just after the East Japan Great Earthquake, West Africa in 2014 and Nepal 2015. These activities make NEKKEN one of the leading organizations in Japan in terms of disaster relief activities.

Further, the infectious diseases team for Japanese Disaster Relief was decided in a cabinet meeting in October, 2015 based upon the fact that Ebola broke out in West Africa in 2014 and there was an international call for cooperation to help deal with it. NEKKEN is expected to serve as one of the main stakeholders in this field and was asked to participate on that team.

Because of all these events, setting up the Office of Coordination for Humanitarian Affairs was proposed.



Associated Facility
Office for Training
and Education



Head and Professor
Koya Ariyoshi
Assistant Professor
Momoko Yamauchi

The main role of our office is to run a short-course of tropical medicine, Training Course of Tropical Medicine (TTM). This course aims to support medical and co-medical personnel who plan to work in the tropics, by providing opportunities to learn a broad range of skills and knowledge relevant to practicing medicine, implementing disease control programs and conducting medical research in tropical and developing countries. The course began in 1978 and since 2016, it opens to the researchers who pursue technology for global health. Over 15 participants are accepted to attend the course in each year. As of the 44th course in 2021, 603 participants in total (including 210 medical doctors, and 393 co-medical such as veterinarian, nurses, community health nurses, midwives, pharmacists and others) from all over Japan have

completed the course. The course is run by the steering committee, which consists of members from both inside and outside the Institute of Tropical Medicine (NEKKEN).

During the thirteen weeks (April to June), the full-time staff members of NEKKEN and a substantial number of visiting professors and lecturers provide lectures, laboratory practical and field work, in the fields of virology, bacteriology, protozoology, parasitology, medical entomology, pathology, immunogenetics, epidemiology, human ecology, social medicine, clinical medicine and also geography and culture in tropics. Participants who successfully completed the course are awarded the Diploma in Tropical Medicine.



Completion ceremony in 2021

The University Hospital Infectious Disease Ward

Professor
Koya Ariyoshi
Professor
Chris Smith
Professor
Konosuke Morimoto
Professor
Akitsugu Furumoto
Lecturer
Hiroto Yamanashi
Assistant Professor
Kensuke Takahashi
Assistant Professor
Kosuke Matsui
Assistant Professor
Momoko Yamauchi
Assistant Professor
Mai Izumida
Assistant Professor
Takashi Sugimoto
Assistant Professor
Shogo Akabame
Assistant Professor
Masumi Shimizu

The clinical department of the Institute of Tropical Medicine (NEKKEN) is the only department in NEKKEN, which has clinical duties in the Nagasaki University Hospital. It was originally established in 1967 and since, it has been locally known as "NEKKEN-NAIKA".

Currently the department runs an out-patient clinic and provides in-patients care in a general internal medicine ward (16 beds) and a TB ward (6 beds), closely collaborating with the department of general medicine. We are mainly responsible for treating patients with complicated infectious diseases, such as sepsis, unknown febrile illness, HIV/AIDS, tuberculosis, rickettsiosis, SFTS, tropical infectious diseases. In addition, we receive over 600 consultation cases per year,

referred by almost all the other departments, suspected with infectious diseases. We also run a travel clinic for international travelers.

We take a major role of training and education on infectious diseases for undergraduate students and bed-side training programs for resident physicians and infectious disease fellows. One of our missions is to support medical doctors who aim to work abroad as a clinician volunteer or a clinical researcher. Therefore, we regularly organize a clinical case conference in English, occasionally linking with oversea. Staff and resident doctors are dispatched to hospitals in the tropics of Asia and Africa. That helps us to accumulate our knowledge and experience with clinical tropical medicine.



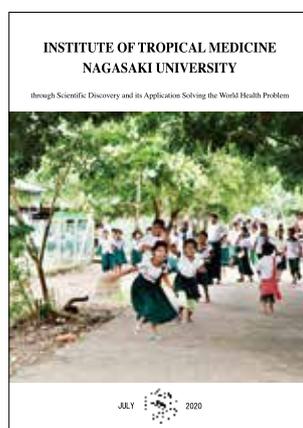
Publications

Our official publications are as follows;

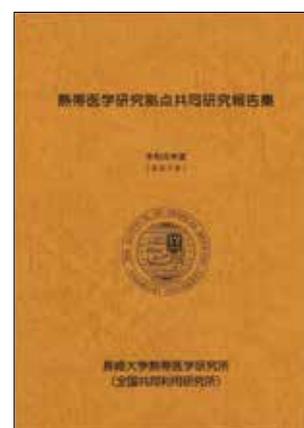
1. Bulletin of Nagasaki University Institute of Tropical Medicine (In Japanese, published yearly since 1964; PDF files are available at our web page.)
2. INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY (This copy, published yearly since 1977; PDF files are available at our web page.)
3. Report of Nation-wide Cooperative Research Projects (Information on research activities and achievements as a nation-wide cooperative research center for tropical medicine is compiled.)



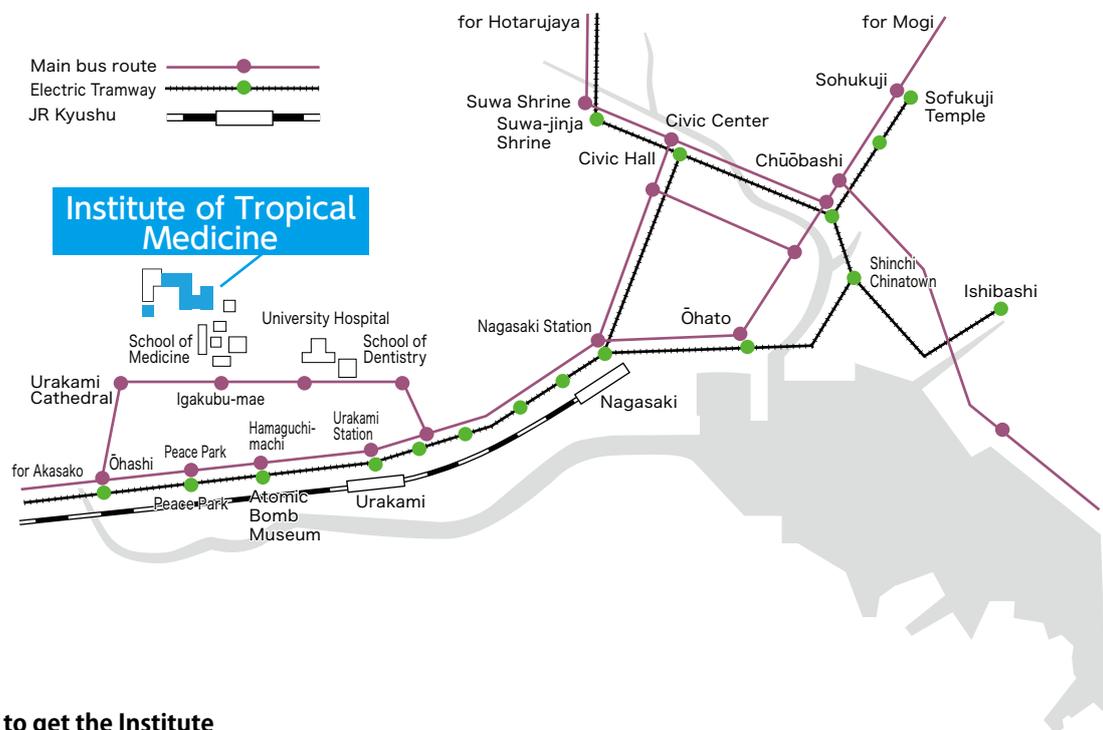
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How to get the Institute

- From JR Nagasaki Station
 - ▶ Electric Tramway "Nagasaki Station" (bound for "Akasako") → "Atomic Bomb Museum" → about 10-minute walk
 - ▶ Nagasaki Bus "Nagasaki Station" (No.8 bound for "Shimoohashi" via "School of Medicine") → "School of Medicine"
- From JR Urakami Station
 - ▶ Electric Tramway "Urakami Station" (bound for "Akasako") → "Atomic Bomb Museum" → about 10-minute walk
- From Nagasaki Airport
 - ▶ Kenei Bus "Nagasaki Airport No.4" Bus Stop (For "Nagasaki Sta." (via "Showa-machi" / via "Showa-machi • Sumiyoshi")) → "Hamaguchi-machi" → about 10-minute walk



Nagasaki University

Institute of Tropical Medicine

Location 1-12-4 Sakamoto Nagasaki 852-8523

URL <http://www.tm.nagasaki-u.ac.jp/nekken/>

