

INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY

through Scientific Discovery and its Application Solving the World Health Problem



JULY



2022

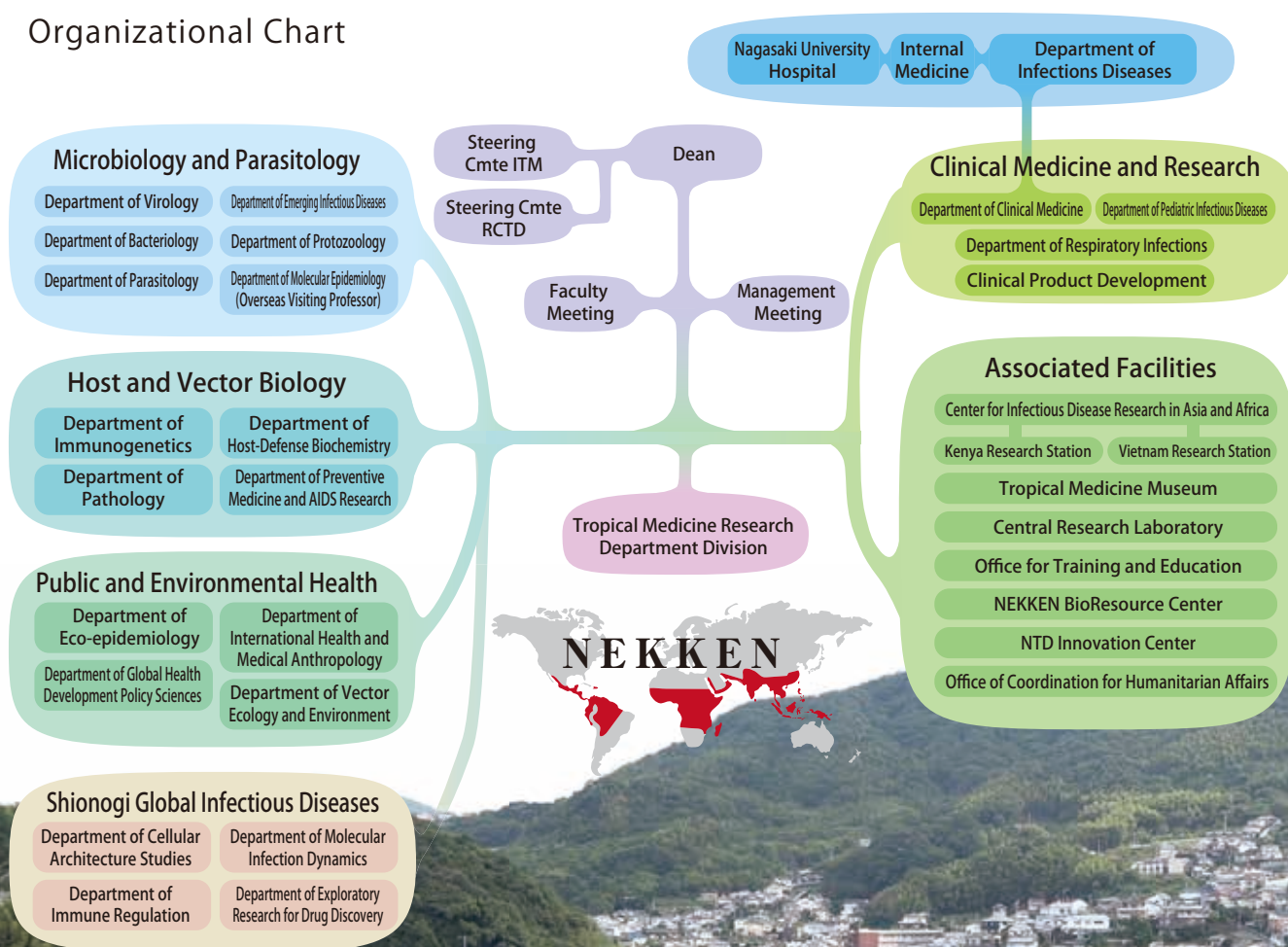
Mission Statement

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



Towards Overcoming Tropical Infectious Diseases

The Institute of Tropical Medicine (NEKKEN), Nagasaki University is the only public institution in Japan dedicated to research in tropical medicine. The Institute has been accredited by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) as a "Joint Usage / Research Center on Tropical Disease" and has contributed to the advancement and internationalization of tropical medical research in Japan as an institute open to the national as well as international research communities. The current organization consists of five major divisions (22 research departments), two affiliated facilities, and a department of medicine, with 60 faculty members (including fixed-term and concurrent post employees), 54 administrative staff members, and approximately 100 graduate students. Internationally, the Institute has been designated as a World Health Organization (WHO) Collaborating Center (for the collection and study of samples related to emerging and tropical viral diseases) since 1993.

In the tropics, there are many low-income countries with harsh natural and social environments, and they are exposed to serious health problems ranging from emerging infectious diseases to lifestyle-related diseases, in addition to classical tropical diseases. With the rapid development of international exchange today, the problems of these countries have a serious impact on the high-income countries located in the temperate zone, and as indicated in the Sustainable Development Goals (SDGs) of the United Nations, they are issues that must be solved from a global perspective. To overcome these issues, the Institute has set the following comprehensive goals.

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

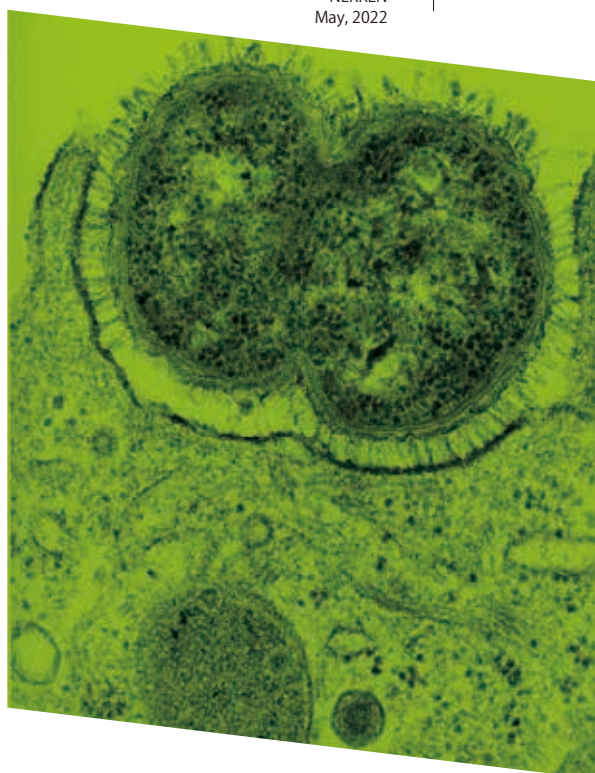
This pamphlet is intended to introduce the organization and activities of the Institute. Research in each field (including overseas teaching and research facilities in Kenya and Vietnam) covers a wide range of tropical infectious diseases such as malaria, diarrhea, schistosomiasis, dengue fever, and yellow fever, as well as emerging and re-emerging infectious diseases such as AIDS, COVID-19, and Ebola virus disease. Research is being conducted in a wide range of areas, including pathogens, pathophysiology, epidemiology, clinical and vector animal studies, as well as the natural and social environments in which these infectious diseases spread. We also introduce our social contribution activities at home and abroad, graduate education (doctoral and master's programs), and various educational and training courses.

We hope that you will understand the goals of the Institute and look forward to your continued support.

Osamu Kaneko
Dean and Professor
NEKKEN
May, 2022

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 the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in Japan that aims to conduct researches on tropical diseases, and is identified as the Joint Usage / Research Center on Tropical Disease since June, 2009.

1. The Goal of the Center

Infectious diseases are caused by the collapse of symbiosis with other living organisms, which is inevitable for humans to survive in the natural world. Although the ultimate goal of this center is to eliminate infectious diseases, it is needed rather to establish reciprocal relationships with other organisms 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 such as malaria have been major health problems in tropical and subtropical regions, which is a reflection of the environment and socio-economic situation existing there. In addition, emerging and re-emerging infectious diseases, such as newly emerging viral diseases, HIV and tuberculosis are also expanding globally, mainly in tropical and subtropical regions.

The Center plans and carries out collaborative research projects rooted in the endemic areas of infectious diseases with researchers from various fields, both domestic and international, based on our international activities and research infrastructure such as our Center for Infectious Diseases Research in Asia and

Africa. Furthermore, as a resource center for information and samples that contribute to research on infectious diseases that are prevalent on a global scale, the Center will organize research meetings and provide research support services. Through the above activities, the Center aims to maintain and activate a community of researchers who create knowledge and skills that contribute to the control of infectious diseases.

2. Outline of the Center's Activities

The Center supports basic and applied collaborative research projects on tropical diseases and the seeds of such researches. It also supports research meetings for the exchange of information on related research and the promotion of collaborative research, as well as training sessions for the dissemination of research techniques. The Center serves as a bio-resource center to acquires, stores, and delivers pathogens and their genetic information for research and educational purpose.

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 are from outside the University. The Steering Committee is responsible for the adoption of the applications, and monitoring and evaluation of the activities of accepted projects.

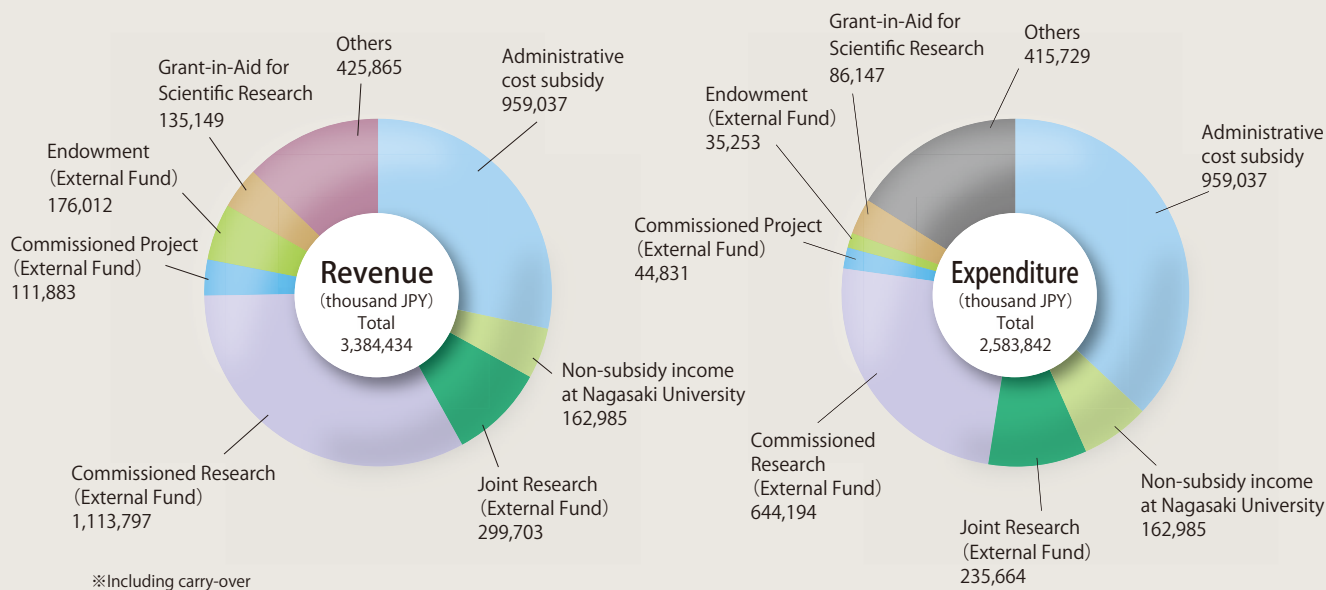
In order to support the above mentioned activities a specific administrative office has been allocated in the institute.

The Institute of Tropical Medicine

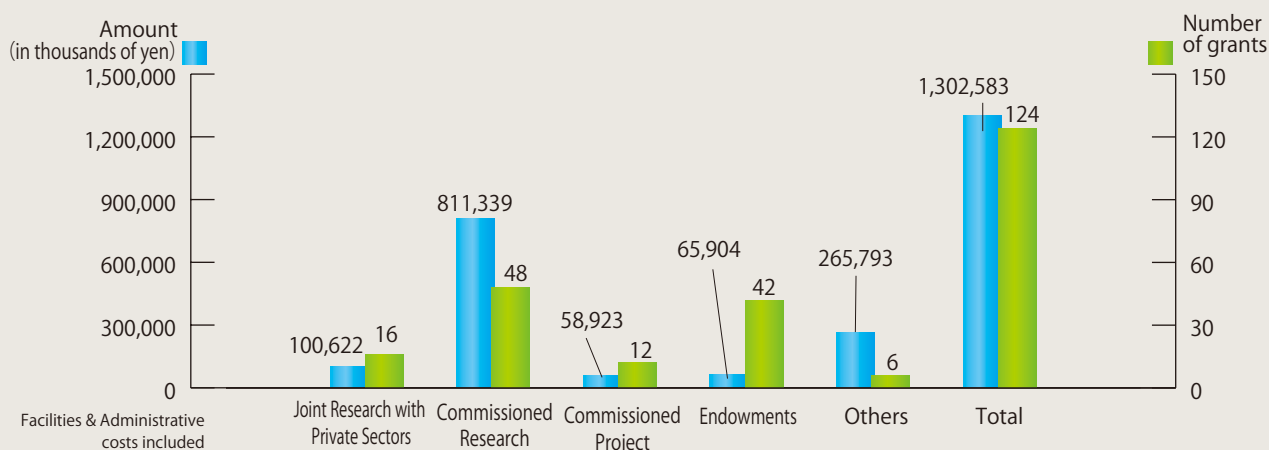


Steering Committee for the Joint Usage / Research Center on Tropical Disease (Committee Member outside the university)
Manabu Ato (National Institute of Infectious Diseases) ,
Shinichiro Kawazu (Obihiro University of Agriculture and Veterinary Medicine) , Satoshi Sasaki (The University of Tokyo) ,
Akira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

Accounting (FY2021)



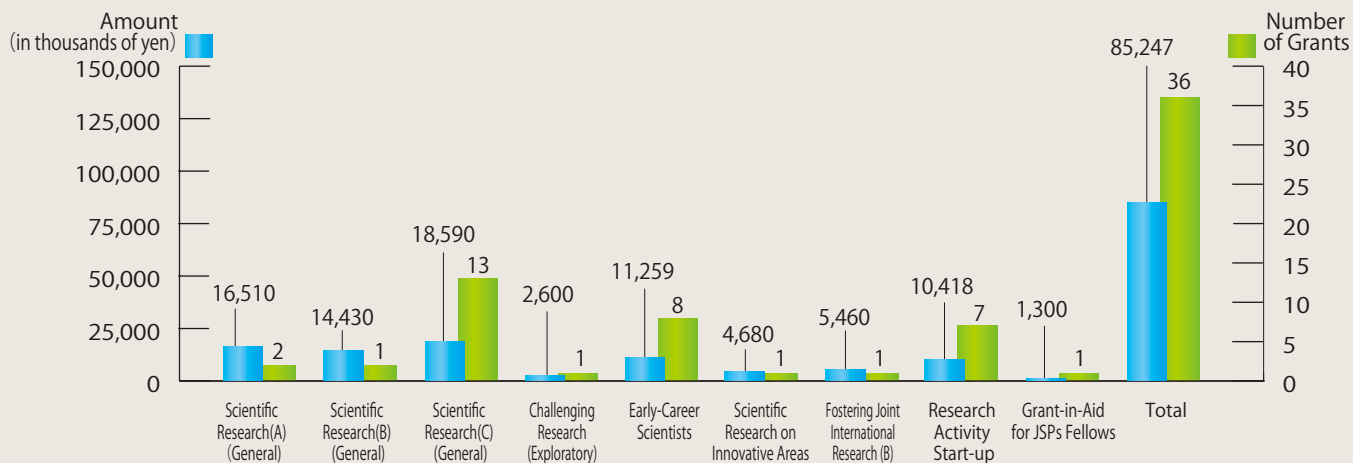
External Fund (FY2021)



Number of Staff (as of May 1, 2022)

Professor	Associate Professor	Senior Assistant Professor	Assistant Professor	Sub total	Others	Total
13	8	0	26	47	118	165

Grants-in-aid for Scientific Research (KAKENHI) (MEXT) (FY2021)



Microbiology and Parasitology Department of Virology



Professor
Kouichi Morita
Associate Professor
Yuki Takamatsu
Associate Professor (Vietnam Research Station)
Mya Myat Ngwe Tun

Nekken-Virology conducts basic and applied research on arthropod-borne (arbo) viruses; such as Japanese encephalitis virus, dengue virus, Zika virus, chikungunya virus, severe fever with thrombocytopenia syndrome (SFTS) virus, and highly pathogenic viruses; filoviruses and novel coronaviruses.

Intra-cellular dynamics analyses for highly pathogenic viruses

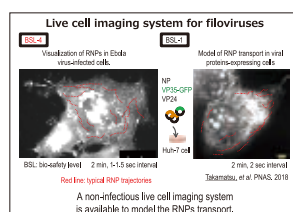
High-resolution microscopy (e.g. live cell imaging) is used to visualize the life cycle of viruses in infected cells and to elucidate the mechanisms of virus particle formation.

Molecular epidemiology of arboviruses

Molecular epidemiological analysis of dengue virus, Japanese encephalitis virus, chikungunya virus, novel coronaviruses and other viruses isolated in Asia and Africa to clarify virus migration and evolution to reveal viral factors related to the mechanism of disease severity and expansion.

Research on therapeutic drugs/vaccines development using reverse genetics

By using reverse genetics, recombinant



viruses are constructed to identify viral factors regulating viral proliferation in cells and viral pathogenicity in animals are comparatively analyzed to establish the basis for the development of new therapeutic agents and vaccines.

Development of rapid diagnostic assay for infectious diseases

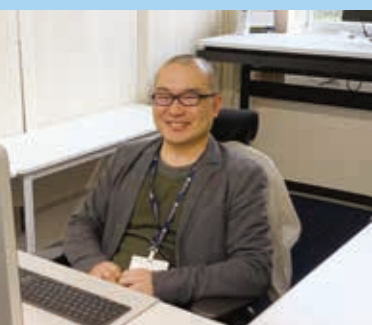
We also aim to contribute to the improvement of public health in Asia and Africa through the construction of novel diagnostic methods for viral infections, such as PCR, LAMP, immunochromatography and ELISA.

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. Fujita-Fujiharu et al. *Nat Commun* 2022; 13: 1191.
2. Kendra et al. *Antiviral Res* 2021; 192: 1-13.
3. Takamatsu et al. *J Virol* 2020; 94(9): 1-19.
4. Takamatsu et al. *mBio* 2020; 11(1): 1-17
5. Takamatsu et al. *Proc Natl Acad Sci U S A* 2018; 115(5): 1-19.

Microbiology and Parasitology Department of Bacteriology

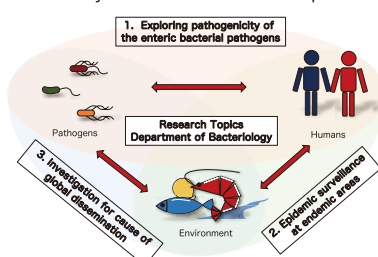


Professor
Toshio Kodama
Associate Professor
Hirotaka Hiyoshi
Assistant Professor
Hiroyuki Terashima

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.

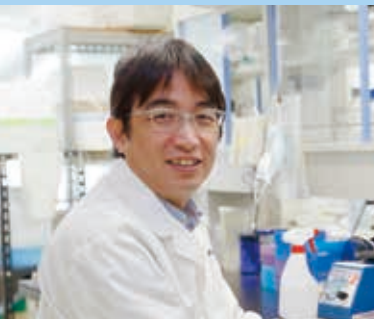
We are planning to isolate *Vibrio* spp. including *V. parahaemolyticus* and *V. cholerae* from patients, seafood and environmental samples in endemic areas to elucidate the genetic characteristics and dynamics of epidemic strains. We will also try to determine the factor(s) that contributes to global 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. Hiyoshi et al. *Cell Host Microbe* 2022; 30(2): 163-170.
2. Nishikino et al. *J Biochem* 2022; 171(4): 443-450.
3. Terashima et al. *Sci Rep* 2022; 12(1): 2979.
4. Al Kadi et al. *mSystems* 2021; 6(6): e0099621.
5. Prithvisagar et al. *Virulence* 2021; 12(1): 1936-1949.

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
Takaaki Kinoshita
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

Ebola virus (EBOV) and Epstein-Barr virus (EBV) both cause major infectious diseases in humans, such as Ebola virus disease (EVD) and EBV-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.

1.Characterization of molecular mechanisms of EBOV entry and virus particle formation: toward the development of novel therapeutics for EVD

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 EVD, in humans and nonhuman primates. Currently, only a few 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 viral particle formation processes with a focus on host membrane traffic dynamics and viral envelope's constituent phospholipids. We are also developing the therapeutics that specifically target the entry and viral particle formation process in multiple ways, which should lead to the significant contribution for prevention of EVD in the future.

2.Characterization of molecular mechanism of development of EBV-associated epithelium tumors

Flavivirus and Orthonairovirus include important pathogens which cause severe disease in human and animals, and many of them are transmitted by arthropod vectors in nature. We conduct research on the ecology of these viruses in hosts and environment to control infectious disease caused by these viruses.

•Research on mechanisms of virus infection and adaptation in hosts

Arthropod-borne viruses are maintained in the transmission cycle between arthropod (ticks and mosquitos) and vertebrate (mammals and birds) crossing species barrier. Although Each host has various anti-viral mechanisms, the viruses evolved to replicate in their hosts by adaptation to evade the mechanisms. We have studied the virus replication and adaptation mechanisms in terms of virus-host interactions.

•Research on virus epidemiology and development of diagnostics

High-containment biological laboratories are required to handle highly pathogenic viruses, such as

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.

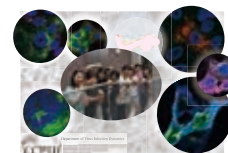
Research studies on viral diseases in Gabon republic

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. Abe et al. *Lancet Microbe*; in press.
2. Moni et al. *Viruses* 2022; 545: 14(1): 142.
3. Kinoshita et al. *Sci Rep* 2021; 11(11): 21259.
4. Wilkinson et al. *Science* 2021; 374(6566): 423-431.
5. Zoa-Assoumou et al. *Lancet Microbe* 2021; 2(8): e349.

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 including microRNAs 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.



1. Dochi et al. *Cancer Sci*, in press.
2. Nanbo et al. *Front Microbiol* 2021; 12: 679210.
3. Becnel et al. *Viruses* 2021; 13(5): 877.
4. Avilala et al. *Front Microbiol* 2021; 12: 657036.
5. Nanbo, *Microorganism* 2020; 8: 729.

tick-borne encephalitis virus, West Nile virus and Crimean-Congo hemorrhagic fever virus. It causes difficulties for the research institute to conduct research on these viruses. We have developed safe substitute such as virus-like particle system for live viruses by molecular technology and applied them to new and safe diagnostics. By using these diagnostics, we have constructed frameworks and have conducted surveys to reveal the virus epidemiology inside and outside Japan.



1. Hirano et al. *Antiviral Res* 2022; 200: 105276.
2. Takahashi et al. *Ticks Tick Borne Dis* 2022; 13: 101900.
3. Kodama et al. *Nat Commun* 2022; 12: 5539.
4. Maezono et al. *Sci Rep* 2022; 11: 9213.
5. Haviernik et al. *Antiviral Res* 2021; 185: 104968.

Microbiology and Parasitology Department of Protozoology



Professor
Osamu Kaneko
Assistant Professor
Taeko Naruse
Assistant Professor
Minami Baba
Assistant Professor
Nattawat Chaiyawong

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

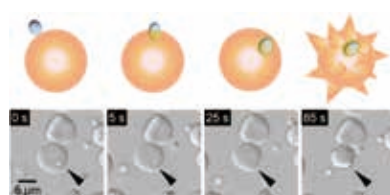


Fig.1 RBC invasion by *P. yoelii*. Merozoite-stage parasite (arrowhead) invades into RBC within 30 seconds (0 - 25 s) and deforms RBC to spike-like shape (85 s).

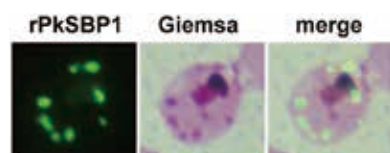


Fig.2 Colocalization of recombinant PkSBP1 protein (green) and Giemsa-stained 'Sinton and Mulligan' stipplings in monkey erythrocytes infected with PkSBP1-transgenic *P. knowlesi*.

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. Nugraheni et al. *Sci Rep* 2022; 12: 5747.
2. Yahata et al. *Proc Natl Acad Sci USA* 2021; 118: e2114442118.
3. Chaiyawong et al. *Parasitol Int* 2021; 86: 102479.
4. Moraes Barros et al. *Malar J* 2021; 20(1): 247.
5. Miyazaki et al. *Parasitol Int* 2021; 83: 102358.

Microbiology and Parasitology Department of Parasitology



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

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

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



Technology Fund (GHIT) support. In the laboratory, we maintain *Schistosoma mansoni*, its intermediate host snails, *Brugia malayi*, *B. pahangi* and *Aedes aegypti*.

We have studied host defense mechanisms against *Leishmania spp* and *Trypanosoma cruzi* and, in the process, elucidated the function of the IL-12 cytokine family, such as IL-27/WSX-1, during the infections. Furthermore, we have developed live attenuated vaccines for leishmaniasis and trypanosomiasis by editing genes using the CRISPR-Cas9 system. In addition, we have developed animal models of intestinal amoebiasis and devoted ourselves to studying the molecular basis of the pathogenicity of *E. histolytica* and host defense mechanisms to it.

1. Tanaka et al. *Parasitol Int* 2021; 83: 102346.
2. Talaam et al. *Antimicrob Agents Chemother* 2021; AAC0041821.
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

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 (SATREPS)

2. Chagas disease

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

3. Dengue

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



1. Hung et al. *Int J Infect Dis* 2022; 120: 217-227.
2. Mohammed et al. *PLoS Negl Trop Dis* 2022; 16(3): e0010309.
3. Mizoguchi et al. *ALTEX* 2022; doi: 10.14573/altex.2111181.
4. Thach et al. *PLoS Negl Trop Dis* 2022; 16(1): e0010164.
5. Ngwe Tun et al. *J Nat Med* 2022; 76(2): 402-409.

Host and Vector Biology

Department of Host-Defense Biochemistry



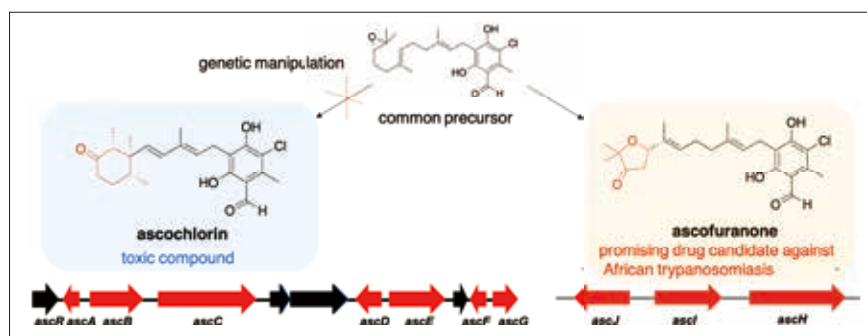
Professor
Kiyoshi Kita

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 such as 5-aminolevulinic acid to combat against other pathogens including SARS-CoV-2.



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

1. Ngwe Tun et al. *Trop Med Health* 2022; 50: 6.
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. Enkai et al. *Eur J Clin Microbiol Infect Dis* 2021; 749153.

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. Hyuga et al. *Travel Med Infect Dis* 2022; 7: 2.
- Yoneoka et al. *Lancet Reg Health West Pac* 2022; 18: 100330.
- Hashizume et al. *PLoS Negl Trop Dis* 2022; 16: e0010274.
- Larson et al. *Trop Med Health* 2021; 49: 54.
- Kato et al. *Molecules* 2021; 26: 5504.

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

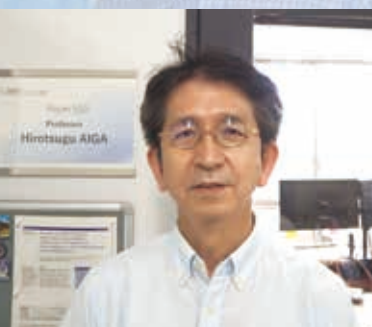


has impact on its hosts. Based on that perception, our department aims to get more detailed understanding and insight on infectious diseases. We would like to pursue the ways of analysis by various approaches such as molecular-evolutional technique, molecular epidemiology, detection of trace DNA, genomics 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. Ito et al. *Theor Biol Medical Model* 2022; 18: 18.
- Sabin et al. *Malar J* 2022; 20: 389.
- Kunna et al. *Acta Med Okayama* 2021; 75(4): 487-493.
- Arima et al. *Trop Med Health* 2022; 49: 2.
- Takahashi et al. *Psychiatry Res* 2021; 295: 113565.

Public and
Environmental Health
Department of International Health
Development and Policy



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.

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. Kamiya. *Pediatr Int* 2021; 63: 1277-1281.
2. Theingi et al. *Trop Med Int Health* 2021; 26: 1117-1126.
3. Mananggit et al. *PLoS NTDs* 2021; 15(12): e0009891
4. Yamada et al. *Microbiol and Immunol* 2021; 65: 438-448.
5. Mananggit et al. *Trop Med Health* 2021; 49(1): 49-59.

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. Kawakatsu et al. *Prim Health Care Res Dev*. 2022; 23: e 20.
2. Horii et al. *PLoS One*. 2021; 16(7): e0254238.
3. Aiga et al. *BMJ Nutr Prev Health*. 2021; 4(1) 18-29.
4. Aiga et al. *BMJ Nutr Prev Health*. 2020; 3(2): 320-338.
5. Aiga, *Lancet*. 2020; 395(10217): 27.

Public and Environmental Health Department of Vector Ecology and Environment



Professor
Noboru Minakawa
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 Asia. We are also interested in their relationships with environmental variables and development of environmentally friendly vector control tools.

Currently, we are analyzing the population genetic structures of *Aedes aegypti* in Africa. This study has already revealed that the genetic structures of mosquito populations in dengue fever endemic areas are distinct. We are also working on the genetic structure of the



Aedes albopictus population that was introduced in Mozambique in the recent years. This study will reveal its origin and introduction pathway.

For reducing malaria risk, we are evaluating the effectiveness of new insecticides and tools in Kenya and Malawi. We are also developing malaria parasite transmission models and COVID-19 transmission models.

1. Huynh et al. *PLoS Negl Trop Dis* 2022; 16(1): e0010119.
2. Kawada et al. *Jpn J Environ Entomol Zool* 2021; 32(3): 99-103.
3. Yang et al. *PLoS Negl Trop Dis* 2021; 15(10): e0009827.
4. Kawada et al. *Jpn J Infect Dis* 2021; doi: 10.7883/yoken.JJID.2021.584.
5. Minakawa et al. *Am J Trop Med Hyg* 2021; 105(2): 461-471.

Clinical Medicine and Research Department of Clinical Medicine



Professor
Koya Ariyoshi
Professor
Chris Smith
Associate Professor
Yoshinao Kubo
Assistant Professor
Momoko 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 microbes.

1. Saito et al. *Clin Infect Dis* 2021; 72: 61-68.
2. Mukadi et al. *PLoS Negl Trop Dis* 2021; 15: e0009670.
3. Domai et al. *Lancet Reg Health West Pac* 2021; 19: 100334.
4. Yanagisawa et al. *PLoS ONE* 2020; 15: e0242438.
5. Katoh et al. *PLoS Negl Trop Dis* 2019; 13: e0007928.

Clinical Medicine and Research

Department of Respiratory Infections



Professor
Kosuke Morimoto
Associate Professor
Bhim Gopal Dhouhadel
Project Researcher
Haruka Maeda

We conduct epidemiological studies of infectious diseases caused by respiratory pathogens including novel coronaviruses (COVID-19), mainly in Japan.

- We conducted a clinical epidemiological study of adult pneumococcal pneumonia in 27 community hospitals in Japan. The purpose of this study is to determine the serotype distribution of pneumococcal pneumonia and epidemiological characteristics of each serotype, and to recommend vaccine policies of pneumococcal vaccine for older people. Using the latest serotype distribution obtained from 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 a study to evaluate quality of life and burden of care, which is one of the issues in the study of cost-effectiveness of vaccines for older people.
- Studies of upper respiratory tract carriage of *Streptococcus pneumoniae* in

the elderly are being conducted among community dwelling older people and residents of long-term care facilities. We are also developing updated suitable multi-plex PCR for carriage study of elderly patients with low bacterial load and carriage rates.

- We have conducted mainly two types of study on the COVID-19. First, epidemiological characteristics were clarified through cluster analysis, and a cluster analysis of nursing homes for the older people in Nagasaki City was conducted. Regarding the COVID-19 vaccines, we have been investigating the vaccine effectiveness in preventing symptomatic disease since July 2021, and have reported the results of the analyses four times, providing them as reference data for the Ministry of Health, Labour and Welfare.

1. Sando et al. *J Travel Med* 2021; 28: taal163.
2. Maeda et al. *Emerg Infect Dis* 2021; 27: 2251-2260.
3. Sando et al. *Ann Am Thorac Soc* 2021; 18: 1475-1481.

Clinical Medicine and Research

Department of Pediatric Infectious Diseases



Professor
Lay-Myint Yoshida
Associate Professor
Michiko Toizumi
Assistant Professor
Shah Mohammad Monir
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.

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, cytomegalovirus, 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. Kitamura et al. *Int J Infect Dis* 2022; 116: 273-280.
2. Althouse et al. *Sci Rep* 2021; 11(1): 5163.
3. Mohamed et al. *Sci Rep* 2021; 11(1): 337.
4. Wang et al. *Lancet Glob Health* 2021; 9(8): e1077-1087.
5. Satoh et al. *Vaccine* 2021; 39(19): 2613-2619.

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

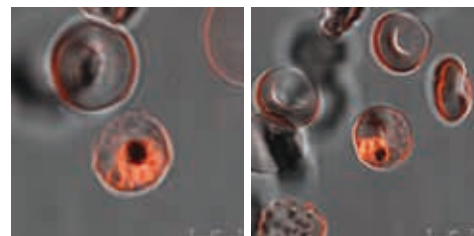
1. Shionogi Global Infectious Diseases Division

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 server 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. Iso-o et al. *Front Cell Dev Biol* 2021; 9: 749153.
2. Tokumasu et al. *Parasitol Int* 2021; 83: 102369.
3. Tanaka et al. *Biol Open* 2019; 8: bio042259.
4. Shindou et al. *J Biol Chem* 2017; 292: 12054-12064.
5. Tokumasu et al. *Biol Open* 2014; 3(6): 529-541.

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.

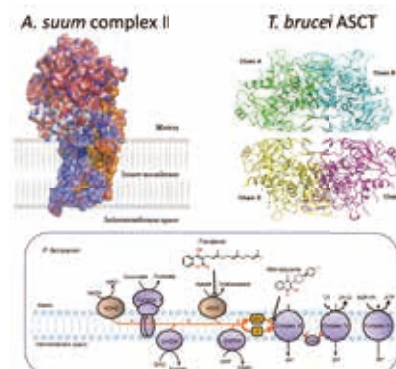
We utilize multidisciplinary approaches, consisted by biochemistry, molecular biology, biophysics, structural biology and chemical biology, to conduct our basic and applied research.

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.

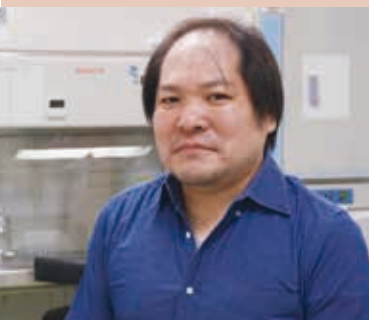
Our activities are supported by research grants acquired from KAKENHI (MEXT), AMED, GHIT and Private Companies.



1. Komatsuya et al. Pharmaceuticals (Basel) 2022; 15(7): 903.
2. Acharjee et al. Int J Mol Sci 2021; 22(15): 7830.
3. Talaam et al. Antimicrob Agents Chemother 2021; 65(10): e0041821.
4. Villafraz et al. mBio 2021; 12(3): e0037521.
5. Nurkanto et al. Front Cell Infect Microbiol 2021; 11: 639065.

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 untavorable side effects are available, and thus, vaccine and novel antimalarial drug development are still and 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 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. Mizoguchi et al. ALTEX 2022 doi: 10.14573/altex.2111181.
2. Raini et al. Antiviral Res 2022; 199: 105245.
3. Ngwe et al. J Nat Med 2022; 76(2): 402-409.
4. Hashim et al. J Nat Med 2022; 76(1): 281-290.
5. Hashim et al. J Nat Med 2021; 75(4): 915-925.

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. Unoh et al. *J Med Chem* 2022, 65, 6499-6512.

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 Kenya Research Station



Professor
Satoshi Kaneko
(Chief Representative)



Professor
Shingo Inoue
Associate Professor
Raita Tamaki
Assistant Professor
Takeshi Nabeshima

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 30 staff from NU and a further 36 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 related to COVID-19, flavivirus and HIV were conducted 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. The Vietnam Research Station has been conducting educational support as an early exposure



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

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. The Vietnam project has been conducting research that contributes to prevention, diagnosis and treatment for the control of infectious diseases such as dengue fever, influenza and COVID-19 for many years, and also training of human resources in Vietnam. As a result of this, August 20, 2021, the project was awarded the group category of the Foreign Minister's Commendations for FY 2021 in Japan.



Bat survey in Lang Son province. (2020.11.19)

1. Fukuta et al. *Int J Environ Res Public Health* 2021; 18(18): 9845.
2. Mao et al. *Pathogens* 2021; 10(12): 1558.
3. Ngo et al. *Trop Med Health* 2021; 49(1): 42.
4. Yasuda et al. *Viruses* 2021; 13(4): 665.
5. Morales Vargas et al. *Infect Genet Evol* 2021; 90: 104764.

Associated Facility Tropical Medicine Museum



Professor
Taro Yamamoto
Technologist
Kazuo Araki

The museum exhibits and preserves a wide range of items, including overview panels on tropical diseases, specimens of parasites, bacteria, viruses, pathogenic insects and dangerous animals, visual materials, books and other valuable documents from the history of medicine. In the audiovisual section, visitors can watch videos of mosquitoes sucking blood and a variety of other genres on an 80-inch large screen. A new section has also been set up where visitors can classify mosquitoes and separate male and female mosquitoes, with the aim of increasing interest in and understanding of tropical infectious diseases among many people.

In FY2021, the number of visitors to the museum remained considerably lower (about 600, about half of the pre-coronavirus number), affected by the outbreak of new coronavirus infection (COVID-19), as in the previous year. The museum's main activities under these circumstances were as follows.

● Museum management: approximately 100 overview panels on diseases that frequently occur in the tropics, microscopic images, pathological films, specimens and models of pathogen vectors, a model of a high-safety laboratory (BSL-4) facility and BSL-4 protective clothing are displayed and explained to domestic and international visitors. Languages available are Japanese, English and Chinese.

In addition to the regular museum operations, the following activities were also undertaken.

- 1) From the perspective of infection control measures



against COVID-19, an online seminar mainly for junior and senior high school students was organized as "Nekken Summer School 2021", instead of the conventional Nekken Summer School for visitors, as in the previous year. The theme was 'Fighting against various infectious diseases' and four young researchers gave presentations. The seminar was well received by the more than 100 participants and the speakers facilitated a smooth Q&A session.

- 2) The Japan-Korea joint project 'Japan-Korea collaboration on the control of lymphatic filariasis' was organized in collaboration with the Meguro Parasite Museum and the Parasite Museum in Seoul, South Korea, at the invitation of the Archives of Infectious Diseases (AIDH). The museum exhibited photos and documents related to the control of filariasis in Nagasaki during 17-31 August. A new main panel on the history of filariasis control in Japan and South Korea was also established and made available online during the period, together with a video explaining filariasis. These exhibited materials and the main panel will continue to be on permanent display after the exhibition is over.

● IT (Information Technology) the IT environment is enhanced with the updating of servers and network equipment, and efforts are made to maintain a high level of security. At the same time, maintenance and management of the Institute's website, including updating of information, is carried out. In addition, the Institute is working to improve the environment, including a system for lending IT equipment to meet the diverse needs of researchers and others at the Institute of Tropical Medicine.

1. Kounnavong et al. *Int Health* 2021; 14(3): 319-328.
2. Okumura et al. *Trop Med Health* 2021; 49: 38.
3. Canara et al. *BMC Public Health* 2020; 20(1): e1298.
4. Okumura et al. *J Int Health* 2019; 34(1): 35-43.
5. Delamou et al. *Lancet Glob Health* 2017; 5(4): e448-e457.

Associated Facility Central Research Laboratory



Head and Professor
Fumika Mi-ichi
Assistant Professor
Miako Sakaguchi

Central Laboratory in NEKKEN maintains state-of-the-art machines and helps all the researchers in this institute facilitating their projects. This Laboratory is also approved by the Minister of Education in Japan as Joint Usage/Research Center for Tropical Medicine and is open for the researchers who proceed the collaborative project with NEKKEN.

○Molecular & Cellular Biology Unit

At the Molecular & Cellular Biology Unit in Central Laboratory in NEKKEN, the state-of-the-art research equipment is provided including 8 and 16 Capillary DNA sequencers, High-throughput sequencers, Real time PCR systems, Flow cytometers, Multiplex assay systems, Chemiluminescence imaging systems, and Multimode plate readers. Additionally, as the commonly used research equipment, MilliQ system, Ultracentrifuge machines, Vacuum Concentrators, Freeze dryers, Darkroom, and Laboratory cold room are also provided. Molecular & Cellular Biology Unit members (as of April 1, 2022, Fumika Mi-ichi and Akemi Ura) are in charge of maintaining these research facilities.

○Light Microscope Unit

Light Microscope Unit provides optical instruments to perform basic, translational, and

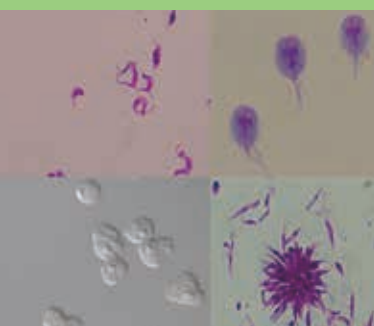
clinical research on the imaging features of infectious disease. We operate Nikon Infectious Disease Imaging Core laboratory established in April 2015. The laboratory has equipped laser scanning confocal/fluorescence microscope (NIKON), Imaging Flow Cytometer (Luminex), laser scanning confocal/super-resolution 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 also provides sample preparation for EM observation. 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.

1. Hiyoshi et al. *Cell Host Microbe* 2022; 30(2): 163-170.
2. Mi-ichi et al. *Microbiol Spectr* 2021; 9(1): e0051121.
3. Hakimi et al. *PLoS Pathog* 2020; 16(10): e1008917.
4. Mousa et al. *Parasitol* 2020; 147(12): 1305-1312.
5. Zadeh et al. *J Gen Virol* 2020; 101(6): 573-586

Associated Facility NEKKEN Bio-Resource Center



Project Representative, Professor
Fumika Mi-ichi
Service Manager, Assistant Professor
Makoto Kazama

NEKKEN Bio-Resource Center (NEKKEN BRC) 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.

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

in Japan, including NEKKEN BRC, with their owner and strain information (2) acceptance of pathogenic protozoa and their genetically modified organisms 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, NEKKEN BRC also implements the development of related technologies. Approximately 900 strains of pathogenic protozoa are preserved in NEKKEN BRC, and approximately half of them are available to supply. Last year NEKKEN BRC provided 29 protozoan strains to researchers. NEKKEN BRC 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 NEKKEN BRC are listed in the following website.

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

The Neglected Tropical Diseases Innovation Center (NTDi Center) was established within the Institute of Tropical Medicine in 2016 to stimulate research and development in tropical medicine, including neglected tropical diseases (NTDs), utilize the research resources of the Institute, promote collaboration between industry, government, and the private sector, and build domestic and international networks. So far, the institute has supported the acquisition of sizeable external research funds and managed the Japan Alliance on Global NTDs (JAGntd) project (established in 2018), a domestic network related to NTDs. The Center has also added the function of the secretariat for the NTD Subcommittee (to be launched in 2022) of the Nikkei-FT Communicable Diseases Conference, which brings together all stakeholders in the industry, government, and academia, including administrative agencies, organizations, and academic societies related to infectious disease control from Japan and abroad.



※ JAGntd is a network that connects organizations, companies, and individuals involved with NTDs in Japan and abroad to promote their participation in Japan's efforts to control Neglected Tropical Diseases (NTDs) and to exchange information with each other. The secretariat is located at the Institute of Tropical Medicine, Nagasaki University.

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 tropical countries, 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, 583 participants in total (including 207 medical doctors, and 376 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
Hirotomo 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 general internal medicine ward (16 beds) and 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. We regularly organize a clinical case conference in English Staff and resident doctors are often dispatched to hospitals in the tropics of Asia and Africa. That helps us to accumulate our knowledge and experience with clinical tropical medicine.



Group photo of staff members

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.)



1



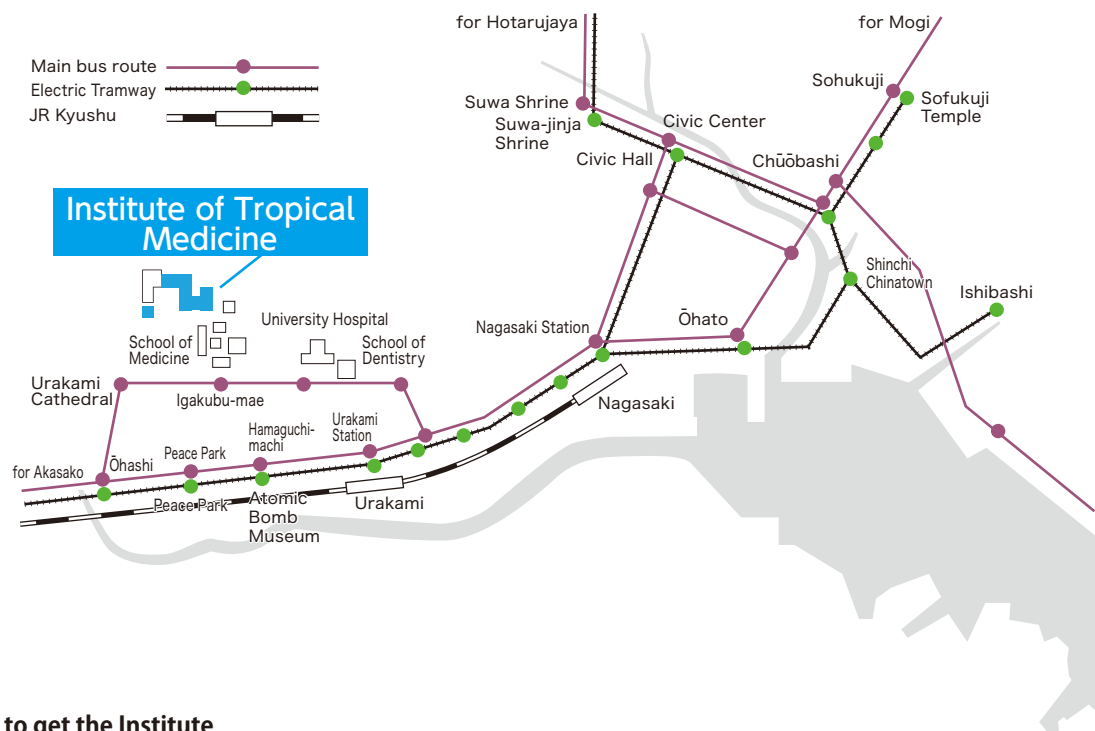
2

2. INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY
(This copy, published yearly since 1977; PDF files are available at our web page.)

3. Report of Research activities and achievements as the Joint Usage / Research Center on Tropical Disease (PDF files are available at our web page.)



3



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 "Shimookashi" 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/>

