INSTITUTE OF TROPICAL MEDICINE
NAGASAKI UNIVERSITY

through Scientific Discovery and its Application Solving the World Health Problem

JULY 2013
MISSION STATEMENT

Institute of Tropical Medicine (ITM), Nagasaki University

The tropics, the most ecologically diverse region on the Earth, presents an ongoing complexity of tropical diseases and other health problems. In view of the remarkable advances made in the field of international exchange in recent years, it is imperative that these problems be addressed from a global perspective.

Based on this understanding, the Institute of Tropical Medicine, Nagasaki University, aims to overcome tropical diseases, particularly infectious diseases, and the various health problems associated with them, in cooperation with related institutions, to strive for excellence in the following areas:

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

Coverpage Photo: Fieldwork in Uganda (by Mitsuru Toda, Kenya Station)
Nagasaki University Institute of Tropical Medicine (ITM) was established in 1942 as a unique government-assisted institution for research on tropical medicine, both in the basic and applied fields. The Ministry of Education, Culture, Sports, Science and Technology (MEXT) designated ITM as a “Collaborative Institute” and a “Center of Excellence” in 1982 and 1995 respectively. In 1993, the World Health Organization designated ITM a WHO Collaborating Centre for Reference and Research on Tropical Viral Diseases. Most recently, in 2009, ITM was authorized as a “Tropical Medicine Research Center of Joint Usage” supported by MEXT. This recognition underlines the importance of ITM as an open institute whose resources are freely available to the whole research community. The current organization of the institute involves four major research fields (15 departments, one domestic visiting department, one overseas visiting department), two centres, and one clinical unit.

Developing countries in the tropics, the most ecologically and culturally diverse regions of the world, are suffer from a complex of tropical diseases, new emerging infectious diseases and life-style diseases. In view of the remarkable advances made in the field of international exchange in recent years, the industrialized countries of the temperate zones are also affected by these problems and it is imperative that they are addressed from a global perspective. Based on this paradigm, ITM aims to overcome tropical and emerging infectious diseases, and the various related health problems in the tropics and the rest of the world, in cooperation with related institutions, and to strive for excellence in the following areas:

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

This pamphlet offers a brief but hopefully intelligible explanation of our organization and its activities in research, education and other related social activities. As you will see, our research activities address traditional tropical diseases such as malaria, schistosomiasis, dengue fever, yellow fever and acute respiratory infections, and emerging infections such as HIV/AIDS and SARS. We conduct basic, epidemiological and clinical research for disease prevention and control. We also investigate environmental factors including vectors, and natural and social environments. ITM educates students in PhD and Masters courses as part of the Graduate School of Biomedical Science and Graduate School of International Health Development of Nagasaki University. In addition, ITM provides a three-month training course on tropical medicine. You will also find information about our research bases in Kenya and Vietnam. Finally, the financial status of the institute is summarized.

Your suggestions, support and ideas for the further development of ITM are greatly appreciated.

July, 2013
Kouichi Morita
Dean and Professor
Institute of Tropical Medicine (ITM)
Nagasaki University
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Historical Review

The Institute of Tropical Medicine, Nagasaki University was originally founded in March 1942 as the East Asia Research Institute of Endemics, Nagasaki Medical College in order to perform basic and applied studies on endemic diseases in East Asia. At the beginning, most of its research activities were field studies conducted in mainland China by the Departments of Pathology, Bacteriology, Internal Medicine, and Dermatology of Nagasaki Medical College. August 9th, 1945, the atomic bomb was dropped in Nagasaki, and the Institute’s all the facilities and research materials were completely destroyed together with Medical School. Consequently, the development of the Institute and its research activities had lagged significantly behind.

In April, 1946, the Institute changed its name to the Research Institute of Endemics, Nagasaki Medical College, and moved to Isahaya City in May to resume research activities. Yet in accordance with the National School Establishment Law issued in May, 1949, the Institute once again changed its name to the Research Institute of Endemics, Nagasaki University. In 1957, the Institute was affected by another disaster of massive flooding, and its facilities, equipment, and research materials were severely damaged. Thus, construction of a new building started in Sakamoto, Nagasaki City in 1960, and the Institute moved to the building in April of the following year. The Institute’s Departments, which were only two at the time, Pathology and Clincics, increased its number every year after 1963, including Epidemiology, Parasitology, and Virology. The Sakamoto building finished its first expansion at the end of 1966.

In June, 1967, with the partial alteration of the National School Establishment Law, the name of the Institute was changed for the third time to carry out basic and applied studies on tropical medicine. Around the same time, the Department of Internal Medicine, Institute of Tropical Medicine, equipped with 20 beds, was opened in the University Hospital. In 1974, the Department of Bacteriology and the Reference Center were attached, and in 1978, the Department of Preventive Medicine, consisting mainly of visiting professors, associate professors, and researchers, and the Tropical Medicine Training Course were launched. In the ensuing year, the Infectious Animals Deprivation Experiment Laboratory was promoted to become the Animal research Center for Tropical Infections, and the second building expansion was concluded in March, 1980. In September, 1983, a JICA-sponsored group training program Tropical Medicine Research Course was opened, the Department of Protozoology was established a year after, and the third building extension was finished in July the year after that. Two years later, the Department of Medical Entomology was created and the Institute was reorganized into the collaborative institute in another two years. In 1991, the Department of Biochemistry was added, and the fourth building expansion was ended in March, 1994. In April, 1994, the Institute was divided into three big Divisions, Tropical Microbiology, Pathogenesis and Clinical Sciences, and Environmental Medicine, with the establishment of two new research Departments, Thermal Adaptation and Social Environment, which have expanded to 12 Departments at present. The Institute was designated as Center of Excellence in the forefront of scientific research in 1995, and a new research Department, Molecular Epidemiology, was established under the Research Field of Microbiology in 1996 to invite overseas visiting professors. In 1997, the Reference Room for the Tropical Medicine was replaced by the Tropical Disease Information and Reference Center, and it was again succeeded by the Research Center for Tropical Infectious Disease in 2001. In March, 2003, when the Sakamoto building finalized its fifth expansion, its extension work of almost 40 years came to an end. In March, 2006, the main building’s repair work was completed. In April, 2008, the Research Center for Tropical Infectious Disease for the Tropical Medicine was replaced by the Center for Infectious Disease Research in Asia and Africa and Tropical Medicine Museum. In June, 2009, the institute was authorized as the Collaborative Research Center on Tropical Disease by the Ministry of Education. More recently, two additional departments on clinical medicine, i.e., pediatric infectious diseases and clinical pharmaceutical science, were admitted for installation.

In June, 2013, the Animal Research Center for Tropical Infections was closed.
Successive Deans of the Institute

(East Asian Research Institute of Endemics)

Susumu Tsunoo  May. 4, 1942 - Aug. 22, 1945
Kiyoshi Takase  Jan. 24, 1948 - Aug. 31, 1948
Noboru Tokura  Sept. 1, 1948 - May. 30, 1949

(Research Institute of Endemics)

Noboru Tokura  May. 31, 1949 - Aug. 31, 1958
Nanzaburo Omori  Sept. 1, 1958 - Nov. 30, 1963

(Institute of Tropical Medicine)

Daisuke Katamine  Dec. 1, 1969 - Nov. 30, 1973
Kaoru Hayashi  Dec. 1, 1973 - Nov. 30, 1977
Daisuke Katamine  Dec. 1, 1979 - Apr. 01, 1981
Keizo Matsumoto  Apr. 2, 1981 - Apr. 01, 1991
Hideyo Itakura  Apr. 2, 1991 - Apr. 01, 1993
Mitsuo Kosaka  Apr. 2, 1993 - Apr. 01, 1997
Akira Igarashi  Apr. 2, 1997 - May. 31, 2001
Yoshiki Aoki  Apr. 1, 2001 - May. 31, 2007
Kenji Hirayama  Apr. 1, 2007 - May. 31, 2011
Tsutomu Takeuchi  Apr. 1, 2011 - May. 31, 2013
Kouichi Morita  Apr. 1, 2013 - Up to the present
Research Center on Tropical Diseases

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

1. The Goal of the Center

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

The Tropical Infectious Diseases have been spreading in the tropical area, which is the reflection of environment and socio-economic situation existed there. It is considered to be a big challenge related to health. As a matter of fact, emerging and re-emerging infectious diseases including newly emerging infectious diseases, HIV and tuberculosis have been spreading globally with tropical area being its epicenter. The tropical area is not only the battle field where we, human being, fight against them but also the experimental ground where we newly create and develop our knowledge and technology alike in order to control infectious diseases.

The Research Center on Tropical Diseases is to accomplish with the members in the diverse scientific communities collaborative researches rooted upon the field where infectious diseases are prevailing, making use of the facilities like Asia and Africa Research Stations internationally recognized. It also serves as a resource center for information and biological samples related to infectious diseases speeding globally.

2. Outline of the Collaborative Research

The Research Center on Tropical Medicine appeals to the public for the collaborative research, which is either basic or applied research based upon epidemiological, clinical or public health framework. The Research Center on Tropical Medicine appeals to the public for the research meeting, which promotes and facilitates the research of infectious diseases through exchanging information or technologies necessary. The Research Center on Tropical Medicine is also to deliver bio-resources including infectious agents, information, and etc. collected and stored here, and thus serves as a resource center on Tropical Medicine.

3. Organizational Chart of the Center

As for administration of this research center, the dean of the Institute of Tropical Medicine established the Steering Committee for the Collaborative Research Center on Tropical Medicine, which was composed of 11 members, out of whom more than half should be outside the university concerned. The Steering Committee for the Collaborative Research Center on Tropical Medicine is responsible for adoption of the applications and monitoring and evaluation of the activities in question. In order to support activities above mentioned, the specific section supporting the Research Center on Tropical Medicine was newly formed and a professor was designated to be a section chief.

4. Applications for Collaborative Researches

There were 29 applications for collaborative researches, out of which 23 were adopted. There were 4 applications for research meeting, out of which 4 were adopted. There were 3 applications for collaborative researches specified research area, out of which 3 were adopted.
Concept Diagram

The Institute of Tropical Medicine

Dean

Advice / Report

The Tropical Medicine Research Center Committee

Discuss important matters on its management

Expert advisors

Discuss specialized matters that are inquired

The Tropical Medicine Research Center Office

Support for its management and follow the intention of the committee

Researchers’ Communities

Send a delegate/delegates as a member of the committee to address opinions from communities

Research Grants

A collaborative Research Topic

A collaborative Research Topic

A collaborative Research Topic
The Steering Committee for the Collaborative Research Center on Tropical Medicine

Committee Member outside the university

National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine

Professor Ikuo Igarashi

Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

Director Nobukatsu Ishikawa

Center for Integrated Area Studies, Kyoto University

Professor Fumiko Oshikawa

Department of Tropical Medicine and Malaria Research Institute National Center for Global Health and Medicine

Director Shigeyuki Kano

National Institute of Infectious Diseases

Deputy Director-General Ichiro Kurane

RIKEN Center of Research Network for Infectious Diseases

Director Yoshiyuki Nagai

Committee Member outside the institute

Graduate School of Biomedical Sciences

Professor Noriyuki Nishida

Graduate School of Biomedical Sciences

Professor Noboru Takamura

Committee Member inside the institute

Institute of Tropical Medicine

Professor Toshiya Hiyayama

Institute of Tropical Medicine

Professor Koya Ariyoshi

Institute of Tropical Medicine

Professor Taro Yamamoto

© : Chairman
The prevalence of tropical diseases depends on the geographic, social and economic factors. Therefore the institute has established the special research system which helps forward the multidisciplinary studies on tropical diseases.

Graduate Courses

In April 2002, the structure of doctoral course in Nagasaki University was re-organized by integrating the three graduate schools from the Schools of Medical Science, Dental Science and Pharmacology into the Graduate School of Biomedical Sciences. The school now offers four doctoral courses. All the departments in the Institute of Tropical Medicine (ITM) are involved in teaching the Course on Infection Research. In April 2013, the “Program for Nurturing Global Leaders in Tropical and Emerging Communicable Diseases” was incorporated in this course. Limited to 15 students per year, the new program is one of the several programs adopted by the Program for Leading Program supported by the Ministry of Education, Culture, Sports, Science and Technology. It focuses on controlling tropical and emerging infectious communicable diseases and on leadership. One of its unique features is that students will be given practical trainings in a cross-field curriculum, which includes hands-on training at overseas Nagasaki University Research Stations in Kenya and Vietnam and other international organizations. In addition, 23 staff of ITM composed of professors, associate professors and assistant professors participate in this program. They play an important role in giving lectures related to tropical and emerging communicable diseases and in helping students to write their dissertations.

〈Master of Tropical Medicine (MTM)〉

In 2006, Nagasaki University Graduate School of Biomedical Sciences opened the Master of Tropical Medicine (MTM) course, which accommodates 12 students from various countries. This one-year course starts from October with one month of lectures/practice on conducting research, followed by research period leading to Master thesis writing supervised by respective professors. From April to June, they have intensive lectures and practices on Clinical Tropical Medicine and Tropical Public Health. Degree of Master of Tropical Medicine is awarded to successful students. The applicant should have more than two years of clinical experience as a medical doctor, and should have sufficient communication skill in English.

〈Master of Public Health (MPH)〉

In April, 2008, the Graduate School of International Health Development was founded at Nagasaki University. The main aim is to cultivate specialists who contribute to the promotion of good health in developing countries. A Master of Public Health (MPH) degree is awarded to students who successfully complete this two-year course. Since tropical medicine plays a pivotal role in promoting good health internationally, four professors from ITM serve as a full-time faculty member in the program. The applicants are required to have sufficient command of Japanese language.

The information on these courses including application form is available through our homepage. http://www.tm.nagasaki-u.ac.jp/nekken/english/index.html
This is a short-course of tropical medicine. 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, directing disease control programs and conducting medical research in tropical and developing countries. The course began in 1978. Fifteen participants are accepted to attend the course in each year. As of the 36th course in 2013, 455 participants in total (including 185 medical doctors, and 270 co-medical such as nurses, community health nurses, midwives, pharmacists) 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 (ITM).

The full-time staff members of the ITM and a substantial number of visiting professors and lecturers provide the 13 weeks (April to June, in 2013) of lectures, laboratory practicals 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.

Our official publications are as follows;
1. Bulletin of Nagasaki University Institute of Tropical Medicine (in Japanese, yearly since 1964, PDF files are available at our Web page.)
2. English Brochure: INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY (this copy. Yearly since 1977, PDF files are available at our Web page.)
3. Japanese Brochure (in Japanese yearly since 1977, PDF files are available at our Web page.)
4. Report of Nation-wide Cooperative Research Projects (Information of research activities and achievements as a nation-wide cooperative research center for tropical medicine is compiled.)

Lectures and film shows for citizens are held occasionally. Every year, several groups of high school students with teachers visit our museum, attending lectures and film shows. In 2012, we had 4 open lectures at Nagasaki City Library. To accumulate know-how of risk communication on tropical infectious diseases in our institute, we are planning to have open lectures where we have frank communication with citizens on the present state and future prospects of research on tropical medicine.
This Department has been conducting basic and applied research on mosquito-borne viruses such as Japanese encephalitis (JE) virus, dengue virus and West Nile virus, as well as emerging infectious viruses such as SARS virus and Nipah virus.

**Molecular epidemiology of Japanese encephalitis and Dengue viruses**

We isolate JE and dengue viruses in Asia and African regions and conduct molecular epidemiological analysis to clarify international and inter-continental movement of those viruses. We also analyze unique genome sequences that are relevant to pathogenicity.

**Research on animal and organ specificity of Flavivirus**

JE virus infects more efficiently in swine, whereas dengue virus multiplies well in humans. We are identifying the molecular basis for such host-specific infection of flaviviruses.

**Research on viral gene functions and vaccine development using reverse genetics**

We have developed infectious clones for JE and dengue viruses and identify gene functions by modifying various parts of the genes or constructing chimeric viruses between the two viruses. In addition, we are developing genetically engineered viruses as candidates for live attenuated vaccines.

**Development of rapid diagnosis**

Various tools for rapid diagnoses are being developed for flaviviruses and other emerging viruses using PCR, LAMP and nLC/MS technologies. Also, genetically engineered antigens are being developed to provide affordable serological tests for developing countries.

**Research on emerging viral infectious diseases**

Epidemiological studies on SARS virus, Nipah virus and H5N1 avian influenza virus are being conducted in Viet Nam, Malaysia and other countries in the South East Asia.

**Activities as a WHO Collaborating Center**

Dr. S. T. Han, then Regional Director of WHO Western Pacific Region (WPR), designated the Department of Virology as 'a WHO Collaborating Center for Reference and Research on Tropical and Emerging Virus Diseases' on 23 Nov. 1993. In 2003, the department was re-designated as 'a WHO Collaborating Center for Reference and Research on Tropical and Emerging Virus Diseases' by Dr. Shigeru Omi, former Regional Director of WHO/WPR. The Department has been collaborating with WHO in training for WHO fellows from many developing countries and deployment of experts as WHO short-term consultants. In addition, Dr. Kouichi Morita was dispatched to WHO/WPRO as Regional Adviser on Communicable Diseases from 16 May 1995 to 15 May 1998. Dr. Futoshi Hasebe was also dispatched for a long term to collaborate in the global emerging infectious disease control program from March 2004 to March 2006. The Department initiated and held the First GOARN/WHO National Training Course in Nagasaki from 25 to 29 February 2008 in collaboration with WHO/WPRO.
Emerging infectious diseases are infectious diseases whose incidence in humans have increased in the past 20 years and threaten to increase in the near future. We are working on the basic research to develop and produce countermeasures against emerging infectious diseases, especially viral hemorrhagic fevers and influenza.

**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 virus infected cells. Especially, we are focusing on highly pathogenic viruses, such as Ebola, Marburg, Lassa and Influenza viruses.

**Development of novel antiviral strategies**

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

**Development of detection methods for highly pathogenic viruses**

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

**Studies on Lassa fever in Nigeria**

Lassa fever is a viral hemorrhagic fever and now endemic in West African countries. Annually 300,000-500,000 peoples are infected with Lassa virus and 5,000 patients have died in Lassa fever every year. We are carrying on the epidemiological studies, the development of novel diagnostic methods and the pathological studies on Lassa fever in collaboration with a Nigerian group.

**Studies on endogenous retroviruses**

Recently, it has been reported that a portion of live attenuated vaccines for pets, which were produced using mammalian cell lines, were contaminated with infectious endogenous retrovirus. Furthermore, in therapeutic use of animal cells, tissues, and organs derived from pigs as donors for xenotransplants, a major international concern is the possibility of cross-species transmission of infectious porcine endogenous retrovirus from animal donor to immunosuppressed human transplant patients. To reduce the risk induced by endogenous retroviruses in vaccine preparation and xenotransplantation, we are developing the strategies to regulate the production of endogenous retroviruses from cells.

**Collaboration research work in the South Africa BSL-4 facility**

Molecular Mechanism of Marburg virus budding
Our major research interest is to elucidate the etiologic agents isolated from pathogenic bacteria related to the worldwide emerging and reemerging diseases and to know the virulence mechanisms of bacterial pathogens.

*Helicobacter pylori* is a bacterial pathogen found in the stomach mucosa of more than 50% of the world population and more common (over 80%) in developing and tropical countries. Infection with *H. pylori* plays a major role in the development of chronic gastritis and peptic ulcer, and is a risk factor for gastric cancer. Pathogenic strains of *H. pylori* secrete a potent protein toxin, a vacuolating cytotoxin, termed VacA, which causes progressive vacuolation of epithelial cells and gastric injury. We found that VacA induces multiple effects on epithelial cells, including mitochondrial damage [1] and apoptosis [2]. These actions of VacA appear to result from activation of cellular pathways, independent of those leading to vacuolation. Similarly, VacA-induced phosphorylation of G protein-coupled receptor kinase-interactor 1 (Git 1), which may be responsible for epithelial cell detachment caused by VacA, leading to peptic ulceration [3], and VacA-induced activation of p38/ATF-2 mediated signal pathway [4] are independent of VacA effects on cellular vacuolation.

Analysis of VacA receptors provided new insights into the molecular basis of VacA function. We reported that two VacA proteins, termed m1 VacA and m2 VacA, which were defined by sequence differences in the middle of the molecules, interacted with target cells by binding to two types of receptor-like protein tyrosine phosphatases (RPTPs), i.e., RPTPα and RPTPβ, resulting in toxin internalization and vacuolation of the human gastric adenocarcinoma cell lines AZ-521 and G 401 [5, 6, 7]. By analysis of the pathological responses of wild type and RPTPβ-deficient mice to oral administration of VacA, we found that RPTPβ functions as a receptor for VacA and produces the disease associated with VacA toxicity including gastritis and gastric ulcer [3].

More recently, we purified from AZ-521 cells, a human gastric epithelial cell line, a surface membrane protein, p500, which binds VacA, and identified it as low-density lipoprotein receptor-related protein-1 (LRP1). LRP1 binding of VacA was shown to be specifically responsible for VacA-induced autophagy and apoptosis, but not activation of the Wnt/β-catenin signaling pathway. Similar to RPTPα and RPTPβ, LRP1 mediates VacA internalization in AZ-521 cells, but in contrast to RPTPβ and RPTPα, LRP1 targeted downstream pathways leading to autophagy and apoptosis. VacA-induced autophagy via LRP1 binding precedes apoptosis suggesting that an excessive autophagic activity can also lead to cell death. This is the first study to provide evidence that LRP1 mediates autophagy [8]. Surprisingly, CagA, which is an oncogenic protein injected by its type IV secretion system into host cells, was degraded by autophagy induced by m1 VacA, but not m2 VacA, whereas CagA in CD44v9-expressing cancer stem-like cells escaped this autophagy system, resulting in accumulation of CagA in cells [9].


**Professor**

**Senior Assistant Professor**

**Assistant professor**

**Assistant**

Toshiya Hirayama

Akihiro Wada

Masayuki Nakano

Kayo Maeda
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 fundamental aspects of the parasite's life cycle, such as the mechanisms behind erythrocyte invasion and the phenomenon of cytoadherence of parasite-infected erythrocytes. In addition, we are also conducting research aimed at elucidating the intracellular survival strategy of *Trypanosma cruzi* that cause Chagas disease and a molecular epidemiology of *Leishmania donovani* that cause visceral leishmaniasis.

We are actively pursuing the following lines of investigation:

1. **Malaria**
   1) The molecular basis of host cell invasion by parasites
   2) The molecular basis of cytoadherence of parasite-infected erythrocytes
   3) Transcriptional control in malaria parasites
   4) How different malaria parasite species interact in the host
   5) Recrudescence of malaria parasites
   6) Molecular epidemiology of *P. falciparum* malaria in endemic countries
   7) Transmission dynamics of *P. knowlesi*, a zoonotic monkey malaria parasite

2. **Trypanosoma**
   1) The function and expression mechanism of trans-sialidase
   2) Stage specific adaptation mechanisms employed by different *Trypanosoma* species

3. **Leishmania**
   1) Molecular epidemiology of *Leishmania donovani*

Professor Osamu Kaneko
Senior Assistant Professor Haruki Uemura
Assistant Professor Shusuke Nakazawa
Assistant Professor Kazuhide Yahata
Assistant Professor Masahito Asada
Research Fellow Shinya Miyazaki
Research Fellow Phonepadith Xangsayarath
Visiting Researcher Pedro Eduardo Mendes Ferreira
Visiting Researcher Kishor Pandey
Visiting Researcher Miho Goto
Visiting Researcher Tomoko Komagata
Visiting Researcher Wataru Kagaya
Assistant Miki Kinoshita
Assistant Yoshihiko Matsuo
Assistant Momoko Ogoshi
Graduate Student Joe Kimanthi Mutungi
Graduate Student Amuza Byaruhanga Lucky

![Schematic of the malaria merozoite and its invasion-related molecules](image1)

Newly identified malaria proteins were localized to the apical end of the merozoite. Blue is parasite nucleus, green and red indicate the location of the identified proteins. Upper panels are DIC images of the malaria parasite.

![Amastigotes (left) and trypomastigotes (right) of Trypanosoma cruzi](image2)
Infectious diseases are still a huge menace to human health and continue unabated in tropical areas under the conditions of poverty and the unique natural and social environments. Various kinds of parasites infect humans for long periods of time without killing them, giving rise to tremendous 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.

Target diseases of our studies

We have been carrying out both field and laboratory studies on several of the most important helminthic diseases, including schistosomiasis, filariasis and intestinal helminthiasis and on important but neglected protozoan diseases such as amoebiasis, leishmaniasis and trypanosomiasis.

1. Schistosomiasis and Filariasis

Since 1981, the research project on Schistosoma haematobium has been carried out in Kwale, Kenya, in cooperation with Kenya Medical Research Institute (KEMRI). In 2011, we started a new research project on parasitic diseases in Mbita and Kwale, Kenya. In the laboratory, we have been maintained Schistosoma mansoni and intermediate snails and are trying to elucidate immune responses as well as to develop sensitive and specific diagnostic methods through the study on the unique molecules belonging to Schistosoma spp.

A research project on filariasis was also carried out in Mbita and Kwale, Kenya, in cooperation with KEMRI. In order to contribute to "Filaria Elimination Program" by WHO, we collaborate with Aichi Medical College. In the laboratory, Brugia malayi, B. pahangi and the vector mosquito, Aedes aegypti have been maintained for many years.

2. Amoebiasis, Leishmaniasis, Trypanosomiasis etc.

Genetic epidemiology and cohort studies on amoebiasis and leishmaniasis are carried out in cooperation with the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR, B.) and the University of Virginia. Field sites include Dhaka and rural areas of Bangladesh. In addition to genetic factors, we aim to elucidate various environmental factors that determine and/or influence the outcome and transmission of the infection. In the laboratory, we study host defense mechanisms against Leishmania major, L. donovani, Trypanosoma cruzi, and T. congolense, and in the process, have elucidated the function of the IL-12 cytokine family such as IL-27/WSX-1 during infection. After we developed animal models of intestinal amoebiasis together with Prof. Houpt at University of Virginia, we elucidated the pathogenicity of Entamoeba moshkovskii, and now are devoting ourselves to the study on molecular basis of pathogenicity of E. histolytica, E. moshkovskii and host defense mechanisms to Entamoeba spp.

3. Cohort study using HDSS on infectious diseases in Mbita and Kwale area in Kenya

We carried out cross-sectional study on infectious diseases in Mbita and Kwale area using HDSS (Health and Demographic Surveillance System) as the collaboration with Osaka City University and Department of Eco-epidemiology. In 2011, the feasible studies on schistosomiasis, other helminthic and protozoan infections, HIV/AIDS, tuberculosis and so on were launched.

One of our field site in Nepal, South Asia
Department of Immunogenetics

This department is focusing on the pathogenic genetic factors of the host and the parasite in the most important tropical infectious diseases by using immunology and genetics.

Research activities:
To clarify the molecular mechanisms in the protective and/or pathogenic host response to human pathogens such as Dengue Virus, Malaria, Trypanosoma cruzi and Schistosoma, the following research projects are going on in our laboratory.

1. Malaria
   1) Genetic susceptibility to severe forms of malaria (cerebral malaria, severe anemia) is analyzed by case-control study in South East Asia, South Pacific and West Africa.

2. Schistosomiasis
   1) Immunological regulation of the pathogenic anti-egg response in the resistant and susceptible persons, to post schistosomal liver fibrosis in China and Philippines.

3. Chagas disease
   1) Genetic susceptibility to different clinical types of chronic Chagas disease, namely, indeterminate, cardiac, and digestive forms, is analyzed by case control study in Bolivia where Chagas disease is still highly endemic.
   2) Host and Parasite factors influencing on the reactivity to the chemotherapy in the paediatric patients with chronic Chagas Disease.
   3) Genetic analysis of Trypanosomes in Latin Americas by using local isolates and molecular biology.

4. Dengue fever: Pasteur Institute HCMC (Vietnam)
   1) Pathogenesis of the DHF (Dengue Hemorrhagic Fever)
      Host factors will be detected by the Population genetic analysis of the patients with DHF and non DHF.

5. Vaccine development for Malaria, Dengue, Chagas disease.

Collaborations:
The research here is performed based on the well-arranged collaborative projects with the following facilities.

1. Malaria: Thammasat University (Thailand), Noguchi Memorial Medical Research Institute (Ghana), Karolinska Institute (Sweden), Kenya Medical Research Institute (KEMRI).

2. Schistosomiasis: Jiangxi Provincial Institute of Parasitic Diseases (China), Jiangsu Provincial Institute of Parasitic Disease (China), Univ. Philippines and RITM (Philippines).

3. Chagas Disease: Center of Tropical Medicine, Sirani Clinic, and Hospital Japones (Bolivia), IICS University of Asuncion (Paraguay).

Professor
Associate Professor
Senior Assistant Professor
Assistant Professor
Assistant Professor
Technologist
Assistant
Assistant
Assistant
Graduate Student
Graduate Student
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Graduate Student
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Kenji Hirayama
Nguyen Huy Tien
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Mihoko Kikuchi
Cherif Mahamoud Sama
Shuaibu Mohammed Nasir
Tetsuo Yanagi
Junko Hayashima
Shuji Miyazaki
Shino Chikatoshi
Kuniko Shimoda
Lam Quoc Bao
Mbancfo Evaristus Chibunna
Dang My Nhi
Nat Koonrungsesomboon
Vasquez Velasques, Clara Aleíandra
Yukimi Katagami
The Japanese Government has been making efforts under its second and third Science and Technology Basic Plans to create a world-class intellectual platform. In FY 2002 the Ministry of Education, Culture, Sports, Science and Technology (MEXT) implemented the National BioResource Project (NBRP) to construct the framework for systematic collection, preservation, and distribution of bioresources, with a focus on those that required strategic development by the National Government.

Since 2002 Institute of Tropical Medicine (NEKKEN), Nagasaki University has been taking of Division of Protozoa in Pathogenic Microorganisms of a Core Facility Upgrading Program under Chiba University’s Medical Mycology Research Center. NEKKEN NBRP contributes the services to researchers; (1) information of owners and strains of pathogenic protozoans in Japan on database Website, (2) supply of protozoans for users from NEKKEN NBRP, (3) deposits of protozoans to NEKKEN NBRP and preservation in NEKKEN NBRP, (4) supply of protozoan specimens for laboratory practice of medical educational institutions, (5) acceptance of examination for protozoan infections from medical facilities.

To promote life sciences it is important researchers share the various bioresources necessary for pursuing research and development. The resources produced in years with painstaking labor will make foundation for future researches. The NBRP deals with the bioresources, which will not be able to be restored again if once they are lost. We would like to ask the access to our Project Website. Your cooperation and support for the project would be highly appreciated.

Project Representative: Kenji Hirayama
Collaborator: Shinjiro Hamano
Collaborator: Richard Culleton
Technician: Tetsuo Yanagi
Information Desk: Shiho Chikatoshi

http://www.nbrp.jp/
http://www.pathogenic.lab.nig.ac.jp/ns.jsp
April 2008, the Research Center for Tropical Infectious Diseases was reorganized and transformed into four groups i.e. two departments in the Research Field of Environmental Medicine, Tropical Medicine Museum and the Kenya station of Overseas Research Stations.

Therefore, Eco-epidemiology department inherited its philosophy of research from the Research Center for Tropical Infectious Diseases, as one of the departments in the Research Field of Environmental Medicine. The mission is to contribute to the global control of the tropical infectious diseases by analyzing the complex factors that regulate the endemics and/or epidemics of the diseases to find appropriate control measure of the infection.

The concept of eco-epidemiology is based on the view of recognizing tropical diseases as a system of infection. The aim of our research is to understand the process of interaction between microorganisms, vectors and human beings in the system. Therefore, the staffs mainly work in the field at the Kenya Research station of Overseas Research Stations.

Human beings and vectors, so-called hosts as a niche of pathogens, exist not statically but dynamically in time and space. In addition, there is an infinite diversity in the characteristics of hosts. We study how microorganism survive, maintain, proliferate, diminish, disappear and emerge through the niches.

The ultimate purpose of the department is to form a theory for a better understanding of the interrelationship between hosts and pathogen and its consequences, diseases.

Ongoing activities are 1) research using Health and Demographic Surveillance System (HDSS), 2) Establishment of African center for multiple assay method, surveillance system and integrated control programs for a wide range of pathogens of neglected tropical diseases (NTDs), 3) A child health cohort study from the viewpoint of sociology, anthropology and epidemiology in a marginal area of Africa, 4) Application of the vein pattern authentication system to epidemiological studies and social identification in developing countries, 5) Countermeasure of Problem Regarding Health in Sri Lanka. As a social action program, 6) a project for support communities in Lao People’s Democratic Republic with Research Institute for Humanity and Nature (Kyoto) and Hitachi, Ltd by Grant Assistance for Grass-roots Human Security Projects, the Ministry of Foreign Affairs in 2013.

Professor Satoshi Kaneko
Assistant Professor Yoshito Fujii
Assistant Professor Kensuke Goto
Research Fellow Masashi Miura
Research Fellow Chihiro Tanigawa
Visiting Researcher Nugegoda Gabadage Sujeewa Panditharatne (Sri Lanka)
JSPS Ronpaku Researcher Samson Nzou Muuo (Kenya)
Assistant Junichi Tanaka
Graduate Student Tomonori Hoshi

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Child health survey with finger vein authentication system
Nairobi laboratory for multiple assay for a wide range of pathogens of neglected tropical diseases
A scene at health and demographic surveillance system (HDSS) in Lao PDR
Department of International Health has started its activities since 2008, following the internal reform of Institute of Tropical Medicine. Department of International Health has its basis on Research Center for Tropical Infectious Diseases (RECTID) of Institute of Tropical Medicine established in 2001, Information and Reference Center in 1997, and Reference Center in 1994.

It says that RECTID, a precursor of our department, had following three activities; 1) developing the museum of tropical medicine, 2) collecting and disseminating information on tropical infectious diseases and 3) promoting joint research projects and doing epidemiological studies. Out of which, Department of International Health takes over research activities and adds to its mandate an international collaboration as a social responsibility anew.

Thus, Department of International Health, as a newly established department, has two pillars, e.g. research and social responsibility. Research was composed of three units; 1) research on infectious diseases in ecosystem, 2) research on the environment including climate change and Asian dust related to health, 3) research on biological evolution of microorganisms from the adaptation or fitness view point. The umbrella concept or key word linking above three research units is to reconstruct infectious diseases "temporally" and "spatially" alike. Infection is the biological 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.

Another pillar 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.

Our department raises following three activities as international contribution; advocacy on international health at national and international level, health promotion activities and empowerment at the community/ grassroots’ level and emergency relief. What our department thinks of important in those activities is to make solidarity in order to improve people’s health and contribute to people’s sustainable development. It is our department’s goal.

Professor Taro Yamamoto
Associate Professor Junko Okumura
Assistant Professor Takayuki Wada
Visiting Researcher Liang Qin
Visiting Researcher Zhuo Zhang
Visiting Researcher Taijin Kaku
Visiting Researcher Tomoo Ichikawa
Visiting Researcher Katsuyuki Eguchi
Visiting Researcher Sengchanh Kounnavong
Visiting Researcher Md Ubydul Haque
Assistant Akiko Hayashi
Assistant Satoko Arai
Graduate Student Katsura Igai
Graduate Student Kenji Mizumoto
Graduate Student Vu Hai Ha
Graduate Student Shuko Takahashi
Graduate Student Yoshihiro Takayama
Our research interests include anything from ecology to molecular biology of medically important arthropods, particularly mosquitoes that transmit diseases such as malaria and dengue. We are also interested in their relationships with environmental variables and development of environmentally friendly vector control strategies.

1. Dengue vectors
As dengue vectors are extending their geographic distribution, the spread of the disease is being concerned. It has been suspected that the expansion of vector distribution is due to environmental factors such as climate change. We are currently mapping their distributions in Vietnam and Kenya, and examining the relationship with environmental factors, and examining the key environmental factors that contribute to epidemics in Hanoi and Nya Trang.

2. Malaria vectors
Main malaria vectors belong to a group of sibling species, and members within a group are morphologically indistinguishable. We are examining ecological and physiological differences among the members within the Anopheles gambiae complex group and the Anopheles funestus complex group in East Africa including Malawi. We are also investigating their geographic distributions in East Africa. This extensive field survey was designed to understand the effects of climate and the Great Rift Valley on their distributions and evolution.

3. Vector control measures
The coverage of insecticide treated bed nets has considerably increased in Africa. We are investigating whether local residents properly use and maintain bed nets, and how long bed nets last. We are also investigating the effects of bed nets on the species composition of vectors and their behavior, and monitoring their insecticide resistance in Kenya and Malawi. For control tools, we are testing two new types of mosquito nets (ceiling net and eave net).

4. Detection of virus in mosquitoes
We collaborate with National Institute of Infectious Diseases in Japan and National Institute of Hygiene and Epidemiology in Vietnam to detect new viruses from a variety of mosquito species.

Professor Noboru Minakawa
Associate Professor Hitoshi Kawada
Assistant Professor Toshihiko Sunahara
Assistant Professor Yukiko Higa
Assistant Professor Takashi Tsunoda
Assistant Professor Kyoko Futami
Assistant Professor Ataru Tsuzuki
Assistant Professor Chaves Sanabria Luis Fernando
Assistant Chiaki Tsurukawa
Assistant Emiko Kawashima
Assistant Naoko Mori
Assistant Kogomi Minagawa
Assistant Junko Sakamoto
Graduate Student Endang Pujiyati
Graduate Student Koji Yamada
Graduate Student Hanako Iwashita
Graduate Student Yusuke Sumita
Graduate Student Eugenio Fonzi
Graduate Student Huynh Thi Thuy Trang
Graduate Student Nozomi Imanishi
Graduate Student Owuor Gabriel Owino
Our research interests are tropical infectious diseases, respiratory infectious diseases including TB, and HIV/AIDS. We conduct a wide range of multi-disciplinary studies from basic research with animal models to clinical epidemiology research in and outside Japan. Specific research activities are described as follows:

1. Respiratory Infections Diseases and Tuberculosis

We have developed molecular assays to identify multiple pathogens causing respiratory infections and to quantify pneumococcus bacterial load. These novel assays are now being applied for several clinical studies including a large epidemiological study for adult pneumonia in Japan. Furthermore we are now developing a novel assay to evaluate cellular immune responses to various TB antigens. Our goal is to better-understand mechanisms causing severe and treatment-refractory pneumonias at molecular levels toward development of a novel treatment strategy. We are also working on basic research for pulmonary infection. We hypothesize that an impaired process in inducing the cessation of inflammation and repair of damaged tissues plays a central role in the pathogenesis of pneumonia. Our interest focuses on macrophage function, which is responsible for clearing apoptotic cells from the inflammation site.

2. Pediatric Infectious Diseases in Vietnam

We have conducted studies regarding to clinical and microbiological diagnosis, antimicrobial susceptibility and molecular epidemiology in collaboration with National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. Since 2005, we started a large-scale community-based survey targeting all residents in Nha Trang city and its adjacent Nin Hoa district in the Central Vietnam. During the survey, we collected information regarding environment and common diseases burden (pneumonia, diarrhea, dengue fever), health utilization pattern. Since 2006, we have dispatched a research clinician to the site and have been monitoring all pneumonia cases admitted to the pediatric ward at Kan Hoa General Hospital. In 2009, we commenced a birth cohort study, recruiting 2,000 pairs of mothers and new-born babies, with the objective of facilitating mother-to-child transmission studies of various infections and studies of host-gene polymorphisms associating the severity of pediatric infectious diseases.

3. Clinical Research in Infectious Disease Hospitals in the tropics

In collaboration with the National Infectious Disease Hospital (San Lazaro Hospital), Manila, the Philippines, we have started research with objectives of improving diagnosis and management of leptospirosis, central nervous system infection and tuberculosis. In collaboration with the Department of Infectious Diseases, Bac Mai Hospital, Hanoi, Vietnam, we are conducting prospective studies aiming to disclose pathogens responsible for undiagnosed febrile illness.

4. HIV Cohort Studies in Northern Thailand

In collaboration with National Institute of Health, Thailand and National Institute of Infectious diseases, Japan, a large scale of cohort study targeting HIV-infected individuals and their spouses has been established and maintained in Lampang Hospital, northern Thailand; nearly 2000 people have participated. The main objectives of this cohort are to understand mechanisms of resistance to HIV infection among HIV-exposed but uninfected spouses living with HIV-infected patients and mechanisms of slow-progression among HIV-infected slowprogressors. These studies are being conducted in close collaboration with Thai counter parts and international experts in various fields such as hostgene polymorphisms, molecular immunology, molecular epidemiology and virology. Furthermore, we are conducting studies on frequencies of opportunistic infection, the effect of anti-retroviral drug therapy and the effect of other viral co-infection such as GBV, hepatitis B.

Professor Koya Ariyoshi
Professor Michio Yasunami
Associate Professor Konosuke Morimoto
Assistant Professor Motoh Suzuki
Assistant Professor Hikaru Saito
Research Associate Kiwao Watanabe
Visiting Professor Tomoyuki Maekawa
Visiting Professor Toshiyuki Miura
Visiting Researcher Akiko Takaki
Visiting Researcher Masahiko mori
Assistant Mitsuyo Kirie
Assistant Rina Shiramizu
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Graduate student Masahiro Takaki
Graduate student Sugihiro Hamaguchi
Graduate student Kensuke Takahashi
Graduate student Reiko Miyahara
Graduate student Le Nhat Minh
Graduate student Nobuo Saito
Graduate student Takaharu Shimazaki
Graduate student Ikumi Shimada
Graduate student Satoshi Kakuchi
Graduate student Tomoko Ishiuchi
Graduate student Dhubhadel Bhim Gopal
Graduate student Mai Izumida
Graduate student Hirotomo Yamanashi
Graduate student Ngo Chi Cuong
Graduate student Erni Kitashoji
Graduate student Kentaro Hayashi

Ward round in Khan Hoa Hospital
The Department of Pediatric Infectious Diseases is a recently expanded department under the Clinical Research Division at Institute of Tropical Medicine. We work on a wide range of infectious diseases with special attention on severe pediatric infectious diseases including pneumonia, diarrhea, dengue and malaria. Our research interests include integration of clinical, environmental and social issues at international, national and local levels.

Pediatric Respiratory Infections

Our department has a strong collaboration with the Department of Pediatrics of Nagasaki University. We regularly received clinical samples to identify viral and bacterial pathogens from pediatric cases admitted to the Nagasaki University hospital with severe respiratory infection. We are also conducting pneumococcal serotyping and antibiotic sensitivity testing of Streptococcal pneumoniae strains from cases with invasive pneumococcal diseases in Japan. Currently we are developing an advance molecular serotyping technique using nanofluidic technology to determine the S.pneumoniae serotype directly from clinical samples.

Cohort study on Pediatric Infectious Diseases in Vietnam

This study is conducted with funding from the Japan Initiative for Global Research Network on Infectious Diseases (JGRID). Our main counterpart in Vietnam is the National Institute of Hygiene and Epidemiology (NIHE), Vietnam. We have been conducting a large population based cohort study on Pediatric Infectious Diseases at Khanh Hoa Province, central Vietnam since 2006, to determine the etiology and risk factors for severe common pediatric infectious diseases (SPID) like acute respiratory infection (ARI), diarrhea and dengue which are the major causes of under 5 mortality. The study site covers a population of 353,525 residing in 75,826 households with 24,781 children less than 5 years. We conducted population census, demographic, social-behavioral data collection and disease burden study on SPID. We also obtained hospital databases from two hospitals covering the region. Utilizing these large databases, we were able to investigate on a variety of SPID in Vietnam. In addition, to determine incidence, viral etiology and risk factors for pediatric ARI/pneumonia, we are conducting a population based hospitalized Pediatric ARI surveillance at Khanh Hoa General Hospital, Nha-Trang since 2007.

Birth cohort study

Currently we are also conducting a birth cohort study on 2000 new born babies in Nha Trang, Vietnam. This study was conducted in collaboration with the Pediatric Department of Nagasaki University to study congenital infection and host genetic factors on physical-neurological development of the child and development of SPID.

Health impact of global environmental change

Our research interests cover most of environmental epidemiology. Current substantive research topics of interest, on which we work in collaboration with both international and Japanese colleagues, focus mainly on the impacts of weather and global climate change on health, but also include health risks of air pollution. Ongoing projects include: 1. Effects of flooding and weather on cholera, acute respiratory infections and other infectious diseases in Bangladesh. 2. Ocean-atmosphere interaction phenomenons including Indian Ocean Dipole and its association with malaria and cholera in the East Africa. 3. Health effects of Asian dust in the East Asia. 4. Intervention study to prevent heat-related illness in Japan. 5. Excess mortality due to influenza in Southeast Asia.

Professor
Masahiro Hashizume

Associate Professor
Lay Myint Yoshdia

Research Fellow
Michiko Toizumi

Assistant
Nozomi Oka

Graduate student
Chisato Imai

Graduate student
Noriko Furuoya

Pediatric infectious diseases research in Vietnam
Environmental change and global health research in Bangladesh
This is a newly established department in response to the Global Strategy on public health, innovation and intellectual property (resolution WHA61.21). The resolution calls for the enhancement of health-needs driven research and development to address diseases that disproportionately affect developing countries. The establishment of this department was supported by the Department of Academic and Research Promotion, Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. MEXT continues to support the department until its full development.

The department focuses on:
1. building capacity of individuals for innovation in health product
2. strengthening capability of the local research institutions in providing an enabling environment, including infrastructure for product R&D
3. strengthening research institutes network for knowledge sharing and exchange, and for R&D technology transfer activities. The emphasis will be on developing products for public health needs to address the issues of inequity in health.
4. Development of health products

The operation of this department depends on the collaboration of existing offices and departments in NEKKEN and in Nagasaki University, e.g. Office for Training and Education, Immunogenetics, Toxicology, Clinical Pharmacy, Parasitology, Clinical Medicine, Clinical Paediatrics, Center for infectious disease research in Asia and Africa and the research institutions and universities in developing countries. The aim of its operation is to ensure that research priorities of research institutions are in line with their public-health needs, in particular the need for innovative research to address the health problems of their populations and to contribute to improved public health in other countries.

The activities:
1. Training
   1) Two-week course on Product Research and Development for public health needs;
   2) Three-day course on Bioethics
   3) PhD training as part of actual product development i.e. Shiunko for Cutaneous Leishmaniasis, Herbal Medicine for Cholangiocarcinoma and Malaria (see model below);
   4) PhD training as part of associated product development processes e.g. ethical issues in product development, clinical data management, good laboratory practice and etc.
2. Research
   1) Development of Shiunko for Cutaneous Leishmaniasis;
   2) Identification and further development of Herbal Medicine for Breast cancer, Cholangiocarcinoma and Malaria.
3. Network
   1) Coordination of Product Research and Development (PRD) Network
   2) Coordination of research ethics global network-Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)

Collaborations:
1. Drug Research Center, Thammasat University, Bangkok, Thailand
2. SIDCER, National Research Council of Thailand (NRCT), Bangkok, Thailand
3. Armauer Hansen Research Institute, Ministry of Health, Addis Ababa, Ethiopia
4. Institution of Human Research Protection, Ministry of Health, Thailand
5. Tokyo University, Tokyo, Japan
6. Government Pharmaceutical Organization, Bangkok, Thailand

Professor Juntra Laothavorn
Associate Professor Nguyen Huy Tien
Visiting Professor Kesara Na-Bangchang
Visiting Researcher Tullayakorn Plengsuriyakarn
Assistant Ikumi Fritz
Kenya Research Station

Outline

The Kenya Research Station was established by special funds for education and research of the Ministry of Education (MEXT), “Program to Establish Infectious Disease Research Network” in September 2005. After the program completed in March 2010, we have been on “Tropical Medicine, Emerging Infectious Disease and Clinical Epidemiological Research Program to Establish Education and Research System for the collaboration of Kenya and Japan” by MEXT since Apr 2010.

The goals of this project are to develop Kenya Research station, to provide trainings to young researchers and to conduct research on treatments and prevention of tropical and emerging infectious diseases with collaborative researchers.

Progress

1. Establishing of The Research Station
   We have worked on further development such as building and managing information network system, setting up labs (including the P3 lab in Nairobi), conference rooms and vehicles in Nairobi office and three research project sites in Mbita, Kwale and Busia.

2. Posting Researchers From Japan
   The members of the station include two professors (including a leader), three administrative staff. Also, an assistant professor and a researcher as JICA experts for STAREPS project, other four professors, another associate professor and four assistant professors have supported operating our project by short-term research visits.

3. Management for the Long-Term Research and Communities
   In Mbita district, Health and Demographic Surveillance System (HDSS) has been in operation collecting data of population, births, death toll and diseases. Also, Malaria Surveillance System (MSS) has been working on collection and analysis of data of malaria mosquitos in the area. Consequently, we began a new project of JICA Partnership Program focusing on school health in Mbita area as the last project completed its terms of three years, started in 2009.

   Meanwhile, HDSS and parasitology research have been running in Kwale since 2010. Science and Technology Researchers Program by JSPS which started in 2010 has completed in Apr 2013.

4. The Study of Tropical Medicine
   The research on malaria and mosquito transmission in Western Kenya, bacterial and viral diarrheal disease and mosquito-borne hemorrhagic fever has been operated at the P3 lab in Nairobi Office and KEMRI (Kenya Medical Research Institute) production department. In Kwale, epidemiological research of schistosomiasis haematobium has been conducted. As the project of JST-JICA (SATREPS) launched in March 2012, we completed setting up two of KEMRI’s labs in KEMRI Production Department and Busia. Meanwhile, we have begun equipping a lab for seroepidemiology project supported by MEXT which started in April 2013.

5. Educational Programs
   Three of researchers and doctors from Kenya graduated Master of Tropical Medicine at the Institute of Tropical Medicine in Nagasaki. Every year, we also give opportunities to study in field for three graduate students from school of International Health Development, Nagasaki University and medical school students from Osaka University Osaka City University, and Shiga University of Medical Science.

Project Members

Leader and Professor
Yoshio Ichinose (Kenya)
Professor
Noboru Minakawa
Professor
Shinjiro Hamano
Professor
Masaaki Shimada (Kenya)
Professor
Masahiro Horo
Professor
Satoshi Kaneko
Associate Professor
Hitoshi Kawada
Assistant Professor
Shingo Inoue (JICA Expert/ Kenya)
Assistant Professor
Yoshito Fujii
Assistant Professor
Kyoko Futami
Assistant Professor
Kensuke Goto
Assistant Professor
Shah Mohammad
Research Fellow
Mitsuru Toda (JICA Expert/ Kenya)
Research Fellow
Masashi Miura
Research Fellow
Chihiro Tanigawa
Staff
Yukie Saito (Kenya)
Staff
Haruki Kazama (Kenya)
Staff
Tadahisa Sakata (Kenya)
Staff
Tomoka Tawara
Staff
Chiharu Kamimura
Graduate Student
Shunpei Kanbe
Graduate Student
Shah Mohammad
Graduate Student
Gabriel Dida
Graduate Student
Ernest Apondi
Vietnam Research Station

Outline

NEKKEN and National Institute of Hygiene and Epidemiology, Vietnam (NIHE) jointly conducted a project from 2005 on clinical and epidemiological research on Emerging and Re-emerging Infectious Diseases (ERID) granted by the Ministry of Education, Science, Culture and Technology (MEXT) of Japan. Consequently, Vietnam Research Station was established and a number of research activities conducted by investigators from both NEKKEN and NIHE. In the framework of the collaborative project, researches on the environmental and social factors influencing outbreaks of zoonosis, vector-borne infectious diseases, diarrhoea, and childhood pneumonia have been carried out. Having achieved goals of aforementioned researches in the first phase project (2005-2009), the next research objectives was underlined, which is, clarifying the factors and their mechanisms in causation of infectious diseases including ERID. In the second phase, therefore, we aim to attain aforementioned objectives and consequently seek for medically and socially significant achievements by carrying out research activities. To conduct a worldwide study of infectious diseases, we have a scope to network research centers which were established in eight countries in tropical zone, under the framework of the Japan Initiative for Global Research Network on Infectious Diseases (J-GRID).

Research activities

The objectives of the entire project are to clarify the ecology of pathogens in nature and in human society, to clarify the pathogenic mechanism of human diseases, and to develop an intervention-based method to inhibit the spread of infectious diseases. Four research groups will conduct their researches pursuing their research objectives. Research agenda are as follows:

1. Diarrhoea research group:
   1) A molecular epidemiological study on kinetics of enteropathogens after rotavirus vaccine intervention
   2) A molecular epidemiological study of Vibrio cholerae in ecosystem in Vietnam
   3) Hospital based analysis of a broad range of etiological agents of diarrhoea in Vietnam

2. Vector-Borne Infectious Diseases Research Group:
   1) Study on biological properties, virulence and ecological significance of dengue viral quasispecies in mosquito vectors and humans
   2) A survey of Japanese encephalitis virus migration
   3) A study of the influence of arbovirus on seasonal encephalitis of unknown origin
   4) A survey of climate change, mosquito vectors, and virus infection
   5) A study of mosquito vectors, pathogenic mechanism of dengue fever, and anti-infection measures
   6) Inter-regional study on dengue virus and vector mosquitos
   7) A study of simian malaria in Vietnam

3. Clinical Research Group:
   1) Pediatric acute respiratory infection cohort research study
   2) A birth cohort study
   3) An immunogenetical analysis of severe dengue fever at Choray Hospital
   4) Establishment of a clinical and epidemiological research data collection system for analysis of the fever of unknown origin

4. Zoonosis Research Group:
   1) A viral epidemiological study of bat-borne infectious diseases
   2) A molecular epidemiological study of rabies
   3) An epidemiological study of hantavirus
   4) Development of human monoclonal antibody with neutralizing activity against avian influenza (H5N1) strain
   5) An epidemiological study of avian influenza

NIHE-Nagasaki University Friendship Laboratory (NNFL) staff

Leader and Professor: Tetsu Yamashiro
Professor: Futoshi Hasebe
Assistant Professor: Takashi Tsunoda
Assistant Professor: Kozue Hotta
Assistant Professor: Taichiro Takemura
Assistant Professor: Asako Tokizawa
Research Fellow: Michiko Toizumi
Staff: Takahiro Nakao
Research Assistant: Dang Thi Dinh
Research Assistant: Le Thi Thuyen
Research Assistant: Phan Hoai Linh
Research Assistant: Uong Thi Hong
Research Assistant: Bui Thi Tra
Secretary: Yumiko Fukuiwa
Assistant: Kanae Tanaka

Staff of Vietnam research Center
Japanese staff is providing a basic technique to perform PCR to a Vietnamese staff
A surveillance for mosquito which potentially transmit dengue viruses
Tropical Medicine Museum

Museum of Tropical Medicine was preceded by the Tropical Medicine Reference Centre, which was established in 1974 and was reorganized in 1997 as Tropical Medicine Reference and Information Center. In 2001, it was renamed as Research Center Tropical Infectious Diseases (RECTID) and in 2008 it was established as an auxiliary institution. The institution performs the following 2 functions.

The institute primarily functions as a museum and resource center for tropical disease. Currently, on the 1st floor of the Institute of Tropical Medicine Nagasaki University, there is a general section providing information on tropical diseases, parasites/bacteria/viruses/poisonous insects and specimen of dangerous animals, valuable books, and displays images of the data. Moreover, it has an audio-visual room accommodating a few numbers of people. Furthermore, a system is being developed for using this collection of resources to strengthen public science and risk communication with thousand points relating to the history and philosophy of tropical medicines and infection symptoms. In the near future we would like to expand the exhibition room to the museum of tropical medicine and can be used as an educational resource for society and educators and provide tropical disease related research and successful results for the public. In addition, we displayed Africa’s Nature, Development, and People, in March 2009, as part of the Ueno Yama Decade of Information series of National Museum of Nature and Science, Tokyo.

It also functions as an information center for the dispatch, collection, organization, and analysis of information on tropical medicine. This has become an essential component of the daily research activities related to tropical medicine. Due to infrastructure rearrangement in 2012, network tools were updated with technological innovation and long lasting safety; thus responding to every need of the users. We also serviced various databases, using a research evaluation system and a database of the tropical medicine museum. Moreover, we are trying to provide a similar environment to research universities overseas with VPN by including video conferencing system to promote international conferences and e-learning plans.

Head and Professor Noboru Minakawa
Professor Masahiro Horio
Technologist Kazuo Araki
Staff Akiko Akita
Assistant Kiyomi Suda

The database server

Tropical Medicine Museum

BSL-4 lab model
Investigation of the interactions between microbial pathogens, vectors and hosts at molecular or gene levels is important for the better understanding of pathogenesis of various infectious diseases. Molecular Biology Laboratory has been equipped with 16- and 48-cappilary sequencers for high-throughput and high-resolution genetic analysis of pathogens, vectors and hosts. In addition to general laboratory facilities such as pure water supply, ultracentrifuge, lyophilizer, Speed-Vac, French press, Bioruptor, sample storage in liquid nitrogen, bio-safety cabinet, autoclave, dark room and cold room, the laboratory is also equipped with several special analyzers such as laser confocal microscope, flowcytometer, digital cell sorter, Luminex bead-array system, fluorescence- and luminescence-multilabel counter, fluorescence- and luminescence-imager, mass spectrometry-based genotyping system, genome sequencer “GS junior” to meet a variety of demands of researches of the institute as well as those of visiting investigators. Further, capillary electrophoresis system “QIAxcel” has been introduced in year 2013.

Main purpose of our research is fundamentally pathological investigation of tropical diseases, mainly infectious diseases, focused on oncogenic microbes, and establishes the basis of their treatment and prevention. Although many investigators have proposed oncogenesis due to inflammation associated cancer development, the mechanisms underlying the relationship between chronic inflammation and cancer still remain unresolved. Therefore, our research focuses on the potential role of oncogenic microbes in the development of cancers, highlighting the recent advances in the understanding of the molecular mechanisms. The proportion of total cancer deaths attributable to infectious agents is estimated to be 20% to 25% in developing countries and 7% to 10% in industrialized countries. A causal relationship between chronic inflammation and cancer is widely accepted. Specifically, there is a strong association between tumor viruses and the development of human cancers. The mechanisms of oncogenesis associated with infection and inflammation have not been elucidated. However, many oncogenic mechanisms have been proposed for infection and inflammation. Activation of NF-κB is also involved cancer development and progression. Therefore, our research focuses on the molecular players during the development from chronic inflammation to cancer.

The electron microscope room is a NEKKEN-wide user facility for ultrastructural characterization of most microbial pathogens including viral, protozoal, and bacterial species. We offer high quality imaging services from conventional and immuno-electron microscopy to 3D tomography, and also provide training on sample preparation and use of equipment. This laboratory is equipped with transmission and scanning electron microscopes (from JEOL), high-pressure freezer (from LEICA), ultra-microtomes (from LEICA and REICHERT),
vacuum coater, critical point dryer system, and osmium plasma coater in addition to general laboratory facilities for a wide range application of electron microscopy. Here is also open to users from other universities and institutes.

**The Malaria Unit**

We are a small and highly driven malariology group focusing on many different aspects of malaria. Established in 2011, we believe in a multi-disciplinary approach to studying malaria, as this enables a broad understanding of the subject, and therefore facilitates the development of novel solutions for fighting the disease. Such a holistic approach to disease research can only succeed, however, on the foundation of a solid and detailed understanding of its multi-disciplinary constituents. Our core belief is that all our research should produce results that are of potential practical use for fighting the disease. We also strive to engage young researchers in studies on malaria, and hope to encourage them to develop enthusiasm for useful scientific research. We believe that scientific research should be fun, and try to foster a freethinking and engaging research environment for students working with us.

We are interested in all aspects of malariology, and are currently actively engaged in research projects involving immunology, genetics, genomics, evolutionary theory, ecology, epidemiology, and molecular cell biology.

Collaborative projects with malaria researchers based in Japan and internationally are of enormous importance to us, and make up the bulk of the work we are currently engaged in. At present we are actively working with researchers from the USA, the Republic of Congo, Vietnam, Sri Lanka, Brazil, the UK and Saudi Arabia.

<table>
<thead>
<tr>
<th>Head and Professor</th>
<th>Toshiya Hirayama</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associate Professor</td>
<td>Richard Culleton</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td>Masachika Senba</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td>Miako Sakaguchi</td>
</tr>
<tr>
<td>Assistant</td>
<td>Junko Kawashima</td>
</tr>
<tr>
<td>Assistant</td>
<td>Sarina Hokama</td>
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</tbody>
</table>
Clinic at the University Hospital

This department is the only one department at the Institute of Tropical Medicine, which runs a clinic and a medical ward in the International Medical Center of Nagasaki University Hospital. Besides general ward, we have 8 negative pressure rooms and two of them accommodate patients with BSL4 pathogens. We specialized in Infectious Diseases and Respiratory Diseases; diseases that we handle are systemic infectious diseases, including tropical infectious diseases and HIV/AIDS, tuberculosis and pneumonia, and various neoplastic and inflammatory respiratory diseases. Each year, we receive approximately 300 consultations from other departments, regarding diagnosis and management of infectious diseases. The outpatient clinic is open once a week where we also run a travel clinic for international travelers.

For training and education, besides training programs for resident physicians, we provide a number of lectures on infectious diseases and respiratory diseases to undergraduate students. We are responsible for organizing a clinical case conference of tropical infectious diseases as a part of Master of Tropical Medicine course, Graduate School of Biomedical Sciences. Staff doctors and resident doctors are regularly dispatched for a long-term to abroad, San Lazao Hospital, the Philippines and the infectious disease ward in Bac Mai Hospital, Vietnam to accumulate our knowledge and experience with clinical tropical medicine.

Professor
Associate Professor
Senior Lecturer
Assistant Professor
Assistant Professor
Fellow Doctor
Fellow Doctor
Fellow Doctor
Fellow Doctor
Fellow Doctor
Senior Resident
Senior Resident
Assistant Ayako
Koya Ariyoshi
Konosuke Morimoto
Akitsu Furumoto
Maiko Kojiro
Nobuo Saito
Masahiro Takaki
Tomoko Ishifuji
Hirotomo Yamanashi
Satoshi Kakiuchi
Rena Osawa
Kota Mochizuki
Akira Nishiyama
Ayako Kitamura

Infectious diseases conference

Staff Members
Number of Staff  
(as of May 1, 2013)

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※ ( ) number of fixed-term staff

Accounting  
(Fiscal Year 2012)

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Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology  
(FY 2012)

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<th>Scientific Research(B)</th>
<th>Scientific Research(C)</th>
<th>Challenges Exploratory Research</th>
<th>Young Scientists(A)</th>
<th>Young Scientists(B)</th>
<th>Scientific Research on Innovative Area</th>
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Facilities & Administrative costs included

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<th>Strategic Young Researcher Overseas Visits Program for Accelerating Brain Circulation</th>
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## Agreement of Educational, Scientific and Scholarly Exchange

### Overseas

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<td>Mahidol University (Thailand)</td>
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<td>University of the Philippines Diliman (Philippines)</td>
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<td>National Institute of Hygiene and Epidemiology (Vietnam)</td>
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### Domestic

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Institute of Tropical Medicine, Nagasaki University 095 (819) 7800
Department of Eco-epidemiology

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Department of International Health

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Department of Vector Ecology and Environment

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Department of Clinical Medicine

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Department of Pediatric Infectious Diseases

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Department of Clinical Product Development

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Center for Infectious Disease Research in Asia and Africa

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Tropical Medicine Museum

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<td>The Malaria Unit</td>
<td>7 9 0 3</td>
<td>819 – 7903</td>
</tr>
</tbody>
</table>
Location map of the Institute of Tropical Medicine on Sakamoto Campus of Nagasaki University
Location map of Institute of Tropical Medicine, Nagasaki University in Nagasaki City

How to get the Institute

From JR Nagasaki Station
- Electric Tramway  Nagasaki Station → (bound for Akasako) → Hamaguchi-machi → 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) → Hamaguchi-machi → about 10-minute walk

From Nagasaki Airport
- Kenei Bus  Nagasaki Airport No.4 Bus Stop → (bound for Nagasaki City via Showa-machi and Urakami) → Urakami Station → refer to from JR Urakami Station above

Location
1-12-4 Sakamoto Nagasaki 852-8523
URL http://www.tm.nagasaki-u.ac.jp

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