INSTITUTE OF TROPICAL MEDICINE
NAGASAKI UNIVERSITY

through Scientific Discovery and its Application Solving the World Health Problem

JULY 2014
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

General View of the Institute

Coverpage Photo : Kajiado County, Kenya  (by Mitsuru Toda, Kenya Station)
Preface

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, 2014
Kouichi Morita
Dean and Professor
Institute of Tropical Medicine (ITM)
Nagasaki University
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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 Clinics, 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 the present one 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 Depriva-tion Experiment Laboratory was promoted to be-come 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 desig-nated as Center of Excell-ence in the forefront of scientific research in 1995, and a new research Department, Molecular Epide-miology, 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 build-ing 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.

In April, 2014, Tropical Medicine Museum was relocated to Nagasaki University Museum of Medicine.
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
Organizational Chart

Department of Virology
Department of Emerging Infectious Diseases
Department of Bacteriology
Department of Protozoology
Department of Parasitology
Department of Molecular Epidemiology
(Overseas Visiting Professor)
Department of Immunogenetics
Department of Host-Defense Biochemistry
Department of Pathology
Department of Preventive Medicine and AIDS Research

Department of Eco-epidemiology
Department of International Health
Department of Global Health Development Policy Sciences
Department of Vector Ecology and Environment

Department of Clinical Medicine
Department of Pediatric Infectious Diseases
Department of Clinical Product Development
Center for Infectious Disease Research in Asia and Africa
Kenya Research Station
Vietnam Research Station
Tropical Medicine Museum
Central Research Laboratory
Office for Training and Education

Department of Infectious Diseases

Nagasaki University Hospital
Internal Medicine

Faculty Meeting

Dean

Microbiology and Parasitology

Host and Vector Biology

Public and Environmental Health

Clinical Medicine and Research

Associated Facilities

Kenya Research Station
Vietnam Research Station
Tropical Medicine Museum
Central Research Laboratory
Office for Training and Education

Overseas Visiting Professor
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 34 applications for collaborative researches, out of which 24 were adopted.

There were 3 applications for collaborative researches specified research area, out of which 3 were adopted.

There were 1 applications for research meeting, out of which 1 were adopted.
Concept Diagram

The Institute of Tropical Medicine

Dean

The Tropical Medicine Research Center Committee

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

Researchers’ Communities

Discuss important matters on its management

Expert advisors

Discuss specialized matters that are inquired

Support for its management and follow the intention of the committee

The Tropical Medicine Research Center Office

Research Grants

A collaborative Research Topic

A collaborative Research Topic

A collaborative Research Topic

Advice / Report

A collaborative Research Topic
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

Atomic Bomb Disease Institute
Professor Noboru Takamura

Committee Member inside the institute

Institute of Tropical Medicine
Professor Toshiya Hiyayama

Institute of Tropical Medicine
Professor Taro Yamamoto

Institute of Tropical Medicine
Professor Koya Ariyoshi

© : 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 six master and 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, 22 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
Three-month Course on Tropical Medicine

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, implementing 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 186 medical doctors, and 269 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 2014) 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.

Public communication

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 2013, we had 3 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.

Publications

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. Japanese Brochure (in Japanese yearly since 1977, PDF files are available at our web page.)
3. English Brochure: INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY (this copy. 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.)
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, Severe Fever and Thrombocytopenia Syndrome virus (SFTS) and H5N1 avian influenza virus are being conducted in Viet Nam, Japan and other countries in the South East Asia.

**Activities as a WHO Collaborating Center**
The Department of Virology is designated as a WHO Collaborating Center for Reference and Research on Tropical Viral Diseases' since 1993 and re-designated in 2003. 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.

Professor (Project) | Kouichi Morita
Assistant Professor | Shingo Inoue
Assistant Professor | Fuxun Yu
Assistant Professor | Takeshi Nabeshima
Visiting Research Fellow | Daisuke Hayasaka
Visiting Associate Professor | Buerano Corazon Cerilla
Visiting Researcher | Masanobu Ago
Technologist | Toru Kubo
Research Fellow | Mitsu Torada
Research Fellow | Guillermo Posadas Herrera
Research Fellow | Mya Myat Ngwe Tun
Research Fellow | Muhareva Raekiansyah
Assistant | Yuki Takamatsu
Assistant | Kazumi Joda
Graduate Student | Takako Chiba
Graduate Student | Akira Yoshikawa
Graduate Student | Reo Uchida
Graduate Student | Ulanday Giinne Eduard Limbo
Graduate Student | Adungo Ferdinand
Graduate Student | Aung Kyaw Kyaw
Graduate Student | Satoshi Shimada
Graduate Student | Phu Ly Minh Huong

Epidemiological study of tick-borne viruses
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.

Professor Jiro Yasuda
Assistant Professor Yohei Kurosaki
Assistant Professor Shuzo Urata
Assistant Professor Saori Sakabe
Postdoctoral Fellow Yukiko Uno
Research Fellow Sayaka Okada
Research Assistant Mayuko Kobayashi
Assistant Tomomi Kamiyama
Graduate Student Chisato Narahara
Graduate Student Yukiko Hirota
Graduate Student Sayuri Nakamae

Molecular Mechanism of Marburg virus budding

Collaboration research work in the South Africa BSL-4 facility
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 adeno-carcinoma cell lines AZ-521 and G401 [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 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].

**References:**

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 red blood cell (RBC) invasion and the phenomenon of cytoadherence of parasite-infected RBCs using human malaria parasite *Plasmodium falciparum* and rodent malaria parasite *Plasmodium yoelii*. In addition, we are also conducting research aimed at elucidating the intracellular survival strategy of *Trypanosoma cruzi* that cause Chagas disease and *Babesia* parasites that cause Babesiosis in cattle.

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 RBCs
   3) Transcriptional control in malaria parasites
   4) Recrudescence of malaria parasites
   5) Calcium signaling in malaria parasites
   6) Establishment of a continuous *Plasmodium vivax* culture system
   7) Molecular epidemiology of malaria parasites in endemic countries
   8) Transmission dynamics of *Plasmodium 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. **Babesia**
   1) Molecular basis of host cell invasion and modification
   2) Establishment of gene manipulation techniques on Pirolasma parasites

*P. falciparum* expressing a calcium biosensor. Fluorescence resonance energy transfer (FRET) signal from the same parasite is shown in pseudocolor before (left) and after (right) adding an inhibitor of calcium-dependent ATPase.

Recombinant protein (green) expressed in *P. falciparum* co-localized with Maurer’s cleft protein (red) seen in the RBC cytosol outside of the malaria parasite. Nucleus is visualized with blue color.
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

In 2011, in cooperation with Kenya Medical Research Institute (KEMRI), we started a 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. congoense*, 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 Niigata University and Department of Eco-epidemiology. In 2011, the feasible studies on shistosomiasis, other helminthic and protozoan infections, HIV/AIDS, tuberculosis and so on were launched.

- Professor: Shinjiro Hamano
- Assistant Professor: Yoshinori Mitsui
- Assistant Professor: Kentaro Kato
- Assistant Professor: Risa Sonoda
- Technologist: Kyoko Masuda
- Assistant: Megumi Hamasaki
- Assistant: Tomoko Takaya
- Assistant: Fumie Hara
- Assistant: Hiromi Oda
- Graduate Student: Shumpei Kambe
- Graduate Student: Sachiyu Nagi
- Graduate Student: Yombo Dan Justin Kalenda
- Graduate Student: Kenichi Nobusue
- Graduate Student: Taeko Moriyasu
- Graduate Student: Sharmina Deloe
- Graduate Student: Eman Sayed Mohammed Hassan
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)
      TLR-9, IgGR, TNF-alpha
   2) Vaccine development
      Py Legumain (Transamidase18p)DNA vaccine with nanoparticle delivery system

2. **Schistosomiasis**
   1) Vaccine and Drug target molecules identification by genomics and proteomics
      SEA motif bearing gene family

3. **Chagas disease**
   1) Genetic susceptibility to different clinical types of chronia Chagas disease, namely, indeterminate, cardiac, and digestive forms
      HLA-B14 haplotype as resistant against chronic complications
   2) Host and Parasite factors influencing on the reactivity to the chemotherapy in the paediatric patients with chronic Chagas Disease. On going
   3) Compound library screening by using in vitro culture of T.cruzi
      Astellas open innovation network including U.Tokyo, Tokyo Institute of Technology, AIIST(National Institute of Advanced Industrial Science and Technology), and DNDi

4. **Dengue fever**
   1) Pathogenesis of the DHF (Dengue Hemorrhagic Fever)
      HLA, Mast Cell derived factors, related to severity
   2) Early stage predictors for severe Dengue fever
      Free DNA, Chymase, VEGF

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

1. **Malaria:** Karolinska Institute (Sweden), Kenya Medical Research Institute (KEMRI), London School of Hygiene and Tropical Medicine, University of Liverpool
2. **Schistosomiasis:** Jiangxi Provincial Institute of Parasitic Diseases (China), Jiangsu Provincial Institute of Parasitic Disease (China), RITM (Philippines).
3. **Chagas Disease:** Center of Tropical Medicine, Sirani Clinic, and Hospital Japones (Bolivia), IICS University of Asuncion (Paraguay).
4. **Dengue Fever:** Ho Chi Minh Pasteur in Vietnam, Pasteur Paris, MacMaster University

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<tr>
<th>Position</th>
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<tr>
<td>Professor</td>
<td>Kenji Hirayama</td>
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<tr>
<td>Associate Professor</td>
<td>Nguyen Huy Tien</td>
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<td>Assistant Professor</td>
<td>Cherif Mahamoud Sama</td>
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<td>Assistant Professor</td>
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<td>Research Fellow</td>
<td>Mbanefo Evaristus Chibunna</td>
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<td>Postdoctoral Fellow</td>
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<td>Technologist</td>
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<td>Shihoko Chikatoshi</td>
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<td>Assistant</td>
<td>Kuniko Shimoda</td>
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<td>Graduate Student</td>
<td>Dang My Nhi</td>
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<td>Graduate Student</td>
<td>Vasquez Velasques, Clara Alejandra</td>
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<td>Graduate Student</td>
<td>Dao Huy Manh</td>
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<td>Graduate Student</td>
<td>Oumer Ali Ahmed</td>
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<td>Graduate Student</td>
<td>Eleonor F Avenido</td>
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**NEKKEN National BioResource Center**

The Government of Japan 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 bio-resources, 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 Medical Mycology Research Center, Chiba University. 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 from NEKKEN NBRP, (3) acceptance of protozoan deposit to NEKKEN NBRP and the preservation, (4) supply of protozoan specimens for laboratory practice of medical-educational schools, (5) examination for protozoan infections from any medical facilities.

To promote life sciences it is important that researchers share the various bio-resources 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 bio-resources, 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.

http://www.nbrp.jp/
http://pathogenic.lab.nig.ac.jp/ns.jsp
E-mail: protozoa@tm.nagasaki-u.ac.jp

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

**NEKKEN NBRP SERVICES**

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Department of Eco-epidemiology

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) Public health research on Dengue fever control in Sri Lanka and 6) Epidemiological investigation and surveillance development in the JICA non-communicable disease project in Sri Lanka.

Professor Satoshi Kaneko
Assistant Professor Yoshito Fujii
Research Fellow Masashi Miura
JSPS Ropaku Researcher Samson Nzou Muuo (Kenya)
Assistant Emi Nakayama
Graduate Student Tomonori Hoshi
Department of International Health

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 viewpoint and 4) research on the epidemiology from the historical viewpoint. The umbrella concept or key word linking above four 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. For examples, we would like to pursue the ways of analysis by various approaches such as molecular-evolutional technique, molecular epidemiology, detection of DNA footprint, next generation sequencer, bio-informatics, mathematical model. In addition to these researches of infectious diseases, we decided to add the historical approach based on documentary records in order to understand widely the relationship between creatures and societies.

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
Assistant Professor Takayuki Wada
Assistant Professor Tomoo Ichikawa
Research Fellow Mami Hayashita
Visiting Researcher Taijin Kaku
Visiting Researcher Md Ubydul Haque
Visiting Researcher Guoxi Cai
Assistant Rui Okabe
Assistant Yoshihiro Takayama
Graduate Student Yoshimi Misumi
Graduate Student Katsura Igai
Graduate Student Shuho Takahashi
Graduate Student Shihomi Yoshida
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 tools.

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 geographical distributions in South East Asia and Africa, and examining the relationships with environmental factors.

2. Malaria vectors

We are examining ecological and physiological differences among the members within the *Anopheles gambiae* complex group and the *Anopheles funestus* group in Kenya and Malawi. We are also investigating their geographic distributions, and monitoring their abundance in East Africa. This extensive field survey was designed to understand the effects of climate and develop a climate base malaria prediction model.

3. Vector control measures

The coverage of insecticide treated bed nets (ITNs) has considerably increased in Africa. We are investigating whether local residents properly use and maintain ITNs, and how long ITNs 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 East Africa.
Our main research interests are respiratory infectious diseases, tuberculosis (TB), HIV/AIDS and tropical infectious diseases. We are the only department of clinicians in NEKKEN and conduct a wide range of multi-disciplinary studies linking our strength of clinical epidemiology to laboratory-based microbiology and immunology studies both in- and outside Japan. Specific research activities are described as follows:

1. Respiratory Infections Diseases
   We have developed multiplex-PCR assays to identify 19 different viral and bacterial respiratory pathogens and also developed a novel nanofluidic real time PCR-based assay to determine 50 pneumococcus serotypes. These molecular assays are now being applied for several clinical studies including a multi-center epidemiological study for adult pneumonia in all over Japan and childhood acute respiratory infection study in central Vietnam. In 2009, we commenced a birth cohort studies, recruiting approximately 2,000 pairs of mothers and new-born babies, which facilitates studies of host-gene polymorphisms associating the severity of pediatric infectious diseases. For the development of a novel treatment strategy, we also investigate the pathogenesis of treatment-refractory pneumonia at molecular levels focusing on macrophage function, of clearing apoptotic cells from the inflammation site. We hypothesize that an impaired process in inducing the cessation of inflammation and repair of damaged tissues plays a central role.

2. Tuberculosis
   For better-diagnosis of latent MTB infection and tuberculosis, we are analyzing cellular immune responses to various TB antigens using a flowc Hammetero or a QFT combined with Luminex to evaluate a range of cytokines profile in various stages of TB infection and their contact cases both in Japan and the Philippines. Our goal is to clarify TB-specific cellular immune responses characteristic to a different clinical stage of TB infection. We are also investigating pathogens causing bacterial pneumonia and its impact on the survival prognosis of TB patients admitted to the National Infectious Diseases Hospital (San Lazaro Hospital) in the Philippines.

3. Clinical Research in Infectious Disease Hospitals in the tropics
   In collaboration with National Institute of Infectious Diseases, Tokyo, we are conducting undiagnosed febrile illness study in the Department of Infectious Diseases, Bac Mai Hospital, Hanoi, Vietnam by applying diagnostic tests for leptospirosis and various richetial diseases. In collaboration with the San Lazaro Hospital, the Philippines, we are conducting leptospirosis study to evaluate the new diagnostic test and to improve clinical management. We also run a bed-side clinical training course on tropical infectious disease with UK infectious disease consultants.

4. HIV Cohort Studies in Northern Thailand
   In collaboration with National Institute of Health, Thailand, we conducted a cohort study targeting HIV-infected individuals and their spouses in Lampang Hospital, northern Thailand between July 2000 and December 2010; nearly 2000 people 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. Data and sample analysis are still continuing as collaboration between Thai counter parts and international experts in hostgene polymorphisms, molecular immunology, molecular epidemiology and virology.

Bed-side clinical training course in San Lazaro Hospital
Activities
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.
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
Assistant Professor: Eduardo Jose Kawasaki
Visiting Professor: Kesara Na-Bangchang
Assistant: Ikumi Fritz
Graduate Student: Nut Koonrungsesesomboon
Kenya Research Station

Outline
Nagasaki University Kenya Research Station is an overseas research site that has been established through the Program to Establish Infectious Disease Research Network funded by the Ministry of Education (MEXT) in September 2005- March 2010. Since April 2010, the site received renewed funding from MEXT under the ‘Tropical Medicine, Emerging Infectious Disease and Clinical Epidemiological Research Program to Establish Education and Research System for the collaboration of Kenya and Japan’.

The goals of this project are to strengthen the Kenya Research station, to train young researchers on research of emerging and re-emerging infectious diseases, and to collaborate with local researchers on long-term research projects.

Progress
1. Establishing of The Research Sites
We have made progress on setting up the Kenya Research Station in Nairobi (including setting up the Biosafety Level 3 laboratory and other laboratories) and field research sites in Mbita, Kwale, Kisumu and Busia. Building renovation, setting up conference rooms and information systems, and vehicle procurement are currently ongoing.

2. Posting Researchers From Japan
The members of the station include two professors (including a representative), two assistant professors, and three administrative staff members. An assistant professor and a researcher are working as JICA experts for STAREPS project. Five professors, another associate professor and three assistant professors have supported our project through short-term visits.

3. Management for the Long-Term Research and Communities
In Mbita area, Health and Demographic Surveillance System (HDSS) has collected data on population, births and death rates, and incidences of diseases. Mosquito surveillance System (MSS) has collected and analyzed data on malaria mosquitos in the area. We began a new project through JICA Partnership Program focusing on school health in Mbita area that has been ongoing since 2009.

HDSS and parasitology research have continued in Kwale since 2010.

4. The Study of Tropical Medicine
Research on malaria and mosquito transmission in Western Kenya, bacterial and viral diarrheal disease and mosquito-borne hemorrhagic fever has continued at the P3 lab in Nairobi Office and at the KEMRI (Kenya Medical Research Institute) Production Department. In Kwale, epidemiological research of schistosomiasis haematobium has been conducted. As the ‘The Project for Development of Rapid Diagnostics and the Establishment of an Alert System for Outbreaks of Yellow Fever and Rift Valley Fever in Kenya’ of JST-JICA (SATREPS) launched in March 2012, we completed setting up two KEMRI labs at the KEMRI Production Department and in Busia. Meanwhile, a lab for seroepidemiology project focusing on NTD (neglected tropical diseases) was set up with a fund by Japan Science and Technology Agency, and the project started in April 2013.

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

Project Members
Leader and Professor: Yoshio Ichinose (Kenya)
Professor: Noboru Minakawa
Professor: Shinjiro Hamano
Professor: Masahiro Hashizume
Professor: Masaaki Shimada (Kenya)
Professor: Masahiro Horio
Professor: Satoshi Kaneko
Associate Professor: Hitoshi Kawada
Assistant Professor: Shingo Inoue (JICA Expert/ Kenya)
Assistant Professor: Kyoko Futarni
Assistant Professor: Yoshito Fuji
Assistant Professor: Mohammad Shah
Assistant Professor: Rei Takeuchi (Kenya)
Assistant Professor: Peter Larson (Kenya)
Research Fellow: Mitsuru Toda (JICA Expert/ Kenya)
Research Fellow: Masashi Miura
Administrative/HR Manager: Yukie Saito (Kenya)
Chief Accountant: Masayuki Kotani(Kenya)
Adminstrator (Coordinator): Haruki Kazama(Kenya)
Administrator: Tomoka Tawara
Contracted Administrator: Mitsuo Takatoh (Kenya)
Graduate Student: Shunpei Karbe
Graduate Student: Gabriel Dida
Graduate Student: Ernest Apondi
Vietnam Research Station

Outline

NEKKKEN 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 NEKKKEN and NIHE. In the framework of the collaborative project conducted by two institutes, 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 and a community based studies 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 mosquitoes
   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

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<tr>
<td>Leader and Professor</td>
<td>Tetsu Yamashiro</td>
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<td>Professor</td>
<td>Futoshi Hasebe</td>
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<td>Assistant Professor</td>
<td>Takashi Tsunoda</td>
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<td>Assistant Professor</td>
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<tr>
<td>Staff</td>
<td>Takahiro Nakao</td>
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<tr>
<td>Research Assistant</td>
<td>Phan Hoai Linh Ly</td>
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<td>Yumiko Fukuiwa</td>
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<td>Assistant</td>
<td>Mayumi Ogawa</td>
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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. In addition, the present museum was relocated to Nagasaki University Museum of Medicine. The institution performs the following 2 functions.

First, it functions as a museum and resource center for tropical disease. 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
Assistant  Kiyomi Suda

The database server
Central Laboratory

The aim for Central Laboratory is operation and efficient managements for large equipment and general laboratory facilities. The laboratory had equipped that 16- and 48-cappillary sequencers, GS junior genome sequencer and mass spectrometry-based genotyping system for genome analysis, flowcytometer and digital cell sorter for cell function analysis, laser confocal microscope, fluorescence microscope, and fluorescence-luminescenceimager for visualizing analysis, and Luminex bead-array system and fluorescence-luminescence multilabel counter for multipurpose analysis. 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. Those facilities were used to support to researches of the institute and visiting investigators.

Eco-health Unit

In order to promote people’s health in the world, it is essential to understand the health in the context of social and ecological interactions (Eco-system). By such multi-disciplinary approach this unit explicates factors associated to ill-health, especially infectious diseases which are preventable by appropriate counter measures. Main focuses are: 1) Emerging antimicrobial resistant bacterium in aquatic environment, 2) Problems related to tuberculosis medication under conditions of conflict and large-scale disaster, 3) Rapid changes in Eco-system and morbidity pattern among ethnic minorities.

In October 2013, we initiated cohort studies (children under 5 years of age) to investigate risk factors influence on child health in Savannakhet province in Lao PDR. Since then we are following up the cohort every 2 weeks. This study will be continued until March 2018.

Pathology Unit

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.
Electron Microscope Unit

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.

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.

Head and Professor  Toshiya Hirayama
Associate Professor  Richard Culleton
Associate Professor  Junko Okumura
Senior Assistant Professor  Mihoko Kikuchi
Assistant Professor  Masachika Senba
Assistant Professor  Miako Sakaguchi
Assistant  Sarina Hokama
Assistant  Risa Tatsuhara
Clinic at the University Hospital

The department of clinical medicine, the Institute of Tropical Medicine has a clinic and is in charge of managing infectious disease ward in the Nagasaki University Hospital. Our ward has 16 beds with 8 negative pressure rooms, of which two can accommodate patients with BSL4 pathogens. We specialize in infectious diseases and respiratory diseases; we treat patients with systemic infectious diseases, including tropical infectious diseases, HIV/AIDS, tuberculosis, pneumonia, and various neoplastic and inflammatory respiratory diseases. We see well over 300 consultation cases a year in other wards, for giving advice on diagnosis and treatment of infectious diseases. Outpatient clinic is open twice a week where we also run a travel clinic for international travelers.

For training and education, we provide a number of lectures on infectious diseases and respiratory diseases to undergraduate students and bedside training programs for resident physicians. We organize 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
Koya Ariyoshi
Konosuke Morimoto
Akitsugu Furumoto
Maiko Kojiro
Takeshi Tanaka
Masahiro Takaki
Hiroshi Fuji
Takaharu Shimazaki
Kensuke Takahashi
Shungo Kato
Masaharu Nobuyoshi
Tomoko Hiraoka
Kazuma Iwata
Yumi Yamamoto
Ayako Matsuo

Infectious diseases conference

Staff Members
**Number of Staff**
(as of May 1, 2014)

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<th>Divisions</th>
<th>Professor</th>
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※（　）number of fixed-term staff

**Accounting**
(Fiscal Year 2013)

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Facilities & Administrative costs included

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(FY 2013)

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<th>Type of Research</th>
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<th>Scientific Research(C)</th>
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<th>Young Scientists(A)</th>
<th>Young Scientists(A)</th>
<th>Scientific Research on Innovative Areas</th>
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(FY 2013)

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(FY 2013)

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Facilities & Administrative costs included

**External Fund**

(FY 2013)

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Facilities & Administrative costs included

**Agreement of Educational, Scientific and Scholarly Exchange**

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<td>Defence Research and Development Establishment (India)</td>
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## Telephone Number

Institute of Tropical Medicine, Nagasaki University 095 (819) 7800

<table>
<thead>
<tr>
<th>Position/Department</th>
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<tbody>
<tr>
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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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