

INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY



SEPTEMBER



2006

MISSION STATEMENT

Institute of Tropical Medicine, 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



Preface

The Institute of Tropical Medicine, Nagasaki University, established in 1942, is a unique government-assisted institution for the research on tropical medicine, both in the basic and applied fields. Its reorganization led to the first collaborative institute in medical science in Japan in 1989, and designation as one of the Centers of Excellence in 1995 by Ministry of Education, Science and Culture. Present organization of the institute is composed of 3 major research fields (11 departments, 1 domestic visiting department, 1 overseas visiting department), 2 centers, and 1 clinical unit.

According to the first external review in 1996, the institute worked out its Mission Statement as shown on a back cover. To fulfil our mission, we continue the research and other related activities. The highlights are as follows.

* Activities on the Mission“ Spear-head research in tropical medicine and international health ”

- 1 . Strategic researches have been conducted to develop the novel weapon against tropical diseases; analysis of genomic structure of Japanese encephalitis and dengue viruses, structure and function of the receptors for bacterial enterotoxins, mechanisms for expression and activation of superoxide degenerating NADPH oxidase system, and immuno-genetical analysis of tropical diseases.
- 2 . Epidemiological studies and control have been carried out on malaria, dengue fever / dengue hemorrhagic fever, SARS acute respiratory infections, Kaposi's sarcoma and schistosomiasis in Southeast Asia and Africa.
- 3 . Environmental factors, such as vector and socio-economic problem, which cause the spread of tropical diseases in the developing countries have been studied.

* Activities on the Mission“ Global contribution through diseases control and health promotion in the tropics by applying the fruits of the research ”

- 1 . When the world was suffering from a severe outbreak of SARS in 2003, the institute dispatched 3 researchers to P.R. China and other countries in respond to a request of WHO.
 - 2 . And in 2005, the institute dispatched the investigation team to make a survey of possible outbreak of infectious diseases in Indonesia and Sri Lanka, the countries that met disaster of tsunami.
- Thus the staffs have given their technical co-operation to disease control program in developing countries as WHO short-term consultants, JICA experts and other consultants.

* Activities on the Mission“ Cultivation of the researchers and specialists in the above fields ”

- 1 . Staffs of the institute conduct the doctorate and master degree course which belongs to Graduate School of Bio-medical Sciences in Nagasaki University.
- 2 . Since 1978, the institute offers a 3-month course of Tropical Medicine and Related Studies.
- 3 . Since 1983, the institute holds one year training course for foreign participants entitled“ Research in Tropical Medicine ”sponsored by JICA.

Based on the achievement mentioned above, in1993 ,Department of Virology has been designated as WHO Collaborating Centre for Reference and Research on Tropical Viral Diseases, and since 2000 the Institute has played a role of core university in JSPS cooperative research program with Vietnam.

In 2003 ,Institute of Tropical Medicine and Graduate School of Biomedical Sciences made a joint application to the 21st Century Center of Excellence Program supported by Ministry of Education, Culture, Sports, Science and Technology. Our research program“ Global Control Strategy of Tropical and Emerging Infectious Diseases ”successfully obtains a Governmet Grant of 5 years.

In 2005, the overseas research laboratories of the Institute of Tropical Medicine has been established in Kenya Medical Research Institute, Nairobi, Kenya and National Institute of Hygiene and Epidemidogy, Hanoi, Vietnam. The overseas research laboratories promise an extensive and longitudinal studies on tropical diseases.

In addition, the institute has a home page by which we educate the public why tropical medicine is important for the future well being of humankind and information on the tropical diseases in the world.

This pamphlet is one of our advocacy efforts to the public. It offers a brief but intelligible explanation on our research activities and other related social activities. Any suggestions and supports will be gratefully appreciated.

September, 2006
Yoshiki Aoki M. D., D. M. Sc.
Dean and Professor
Institute of Tropical Medicine
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 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 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.



Successive Deans of the Institute

(East Asian Research Institute of Endemics)

Susumu Tsunoo	May .4 ,1942-Aug 22 ,1945
Kohei Koyano	Dec 22 ,1945-Jan 23 ,1948
Kiyoshi Takase	Jan 24 ,1948-Aug 31 ,1948
Noboru Tokura	Sept .1 ,1948-May 30 ,1949

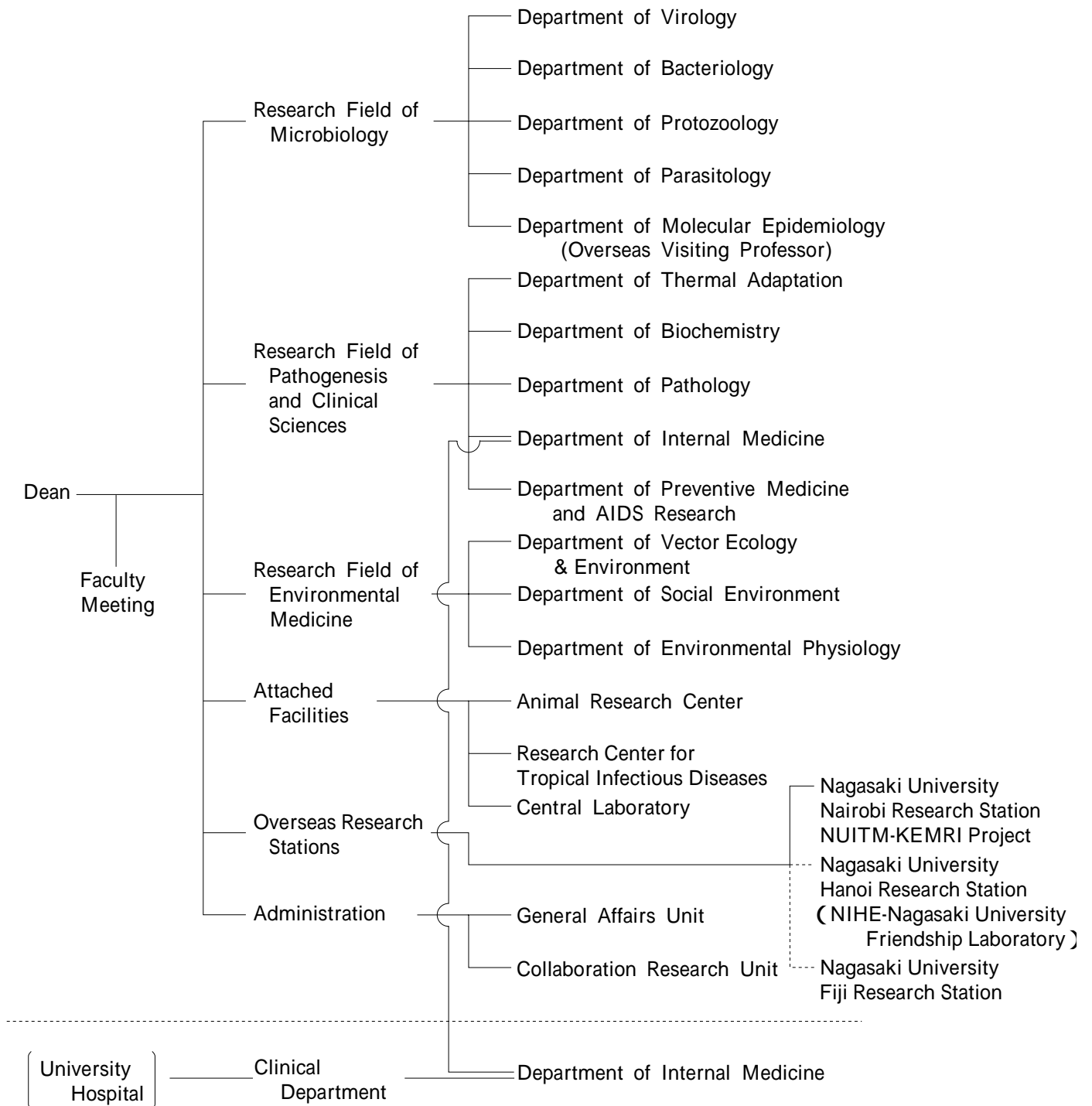
(Research Institute of Endemics)

Noboru Tokura	May 31 ,1949-Aug 31 ,1958
Nanzaburo Omori	Sept .1 ,1958-Nov 30 ,1963
Hideo Fukumi	Dec .1 ,1963-May 31 ,1967

(Institute of Tropical Medicine)

Hideo Fukumi	June .1 ,1967-Nov 30 ,1969
Daisuke Katamine	Dec .1 ,1969-Nov 30 ,1973
Kaoru Hayashi	Dec .1 ,1973-Nov 30 ,1977
Tatsuro Naito	Dec .1 ,1977-Nov 30 ,1979
Daisuke Katamine	Dec .1 ,1979-Apr .1 ,1981
Keizo Matsumoto	Apr .2 ,1981-Apr .1 ,1991
Hideyo Itakura	Apr .2 ,1991-Apr .1 ,1993
Mitsuo Kosaka	Apr .2 ,1993-Apr .1 ,1997
Akira Igarashi	Apr .2 ,1997-May 31 ,2001
Yoshiki Aoki	Apr .1 ,2001-Up to the present

Organizational Chart



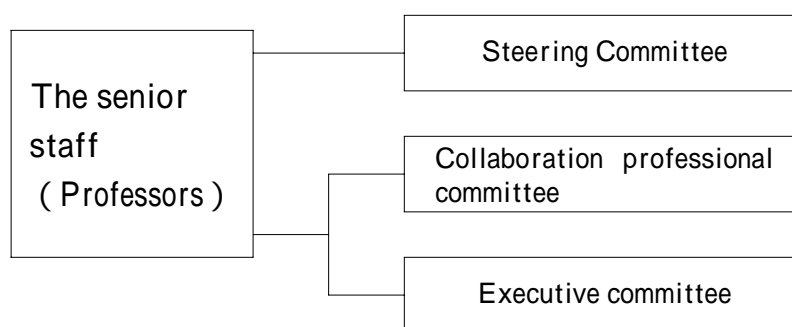
Collaboration research

The institute has conducted research in the field of tropical medicine for the past 62 years since its establishment in 1942 . The institute was reorganized to make extensive collaboration with other universities and institute in the field of interdisciplinary tropical medicine with molecular biology, entomology, anthropology, social medicine, etc.

These activities of the institute are expected to contribute to remarkable progress of tropical medicine.

The senior staff composed of professors of the institute and the executive committee make plans for research work. The steering committee and the collaboration professional committee composed of experienced scientists coordinate the various collaboration researchs.

Collaboration Research Sytem



Institute of Tropical Medicine Steering Committee

Nagasaki University	Professor Emeritus	Akira Igarashi
National Institute of Infectious Diseases	Deputy Director	Takeshi Kurata
International Medical Center	President	Takehiko Sasazuki
Keio University School of Medicine	Professor	Tsutomu Takeuchi
Research Institute for Humanity and Nature	Director	Toshitaka Hidaka
Research Institute for Microbial Diseases Osaka University	Professor	Takeshi Honda
National Museum of Ethnology	Director - General	Makio Matsuzono
The Institute of Medical Science		
The University of Tokyo	Director	Tadashi Yamamoto
Nagasaki University	President	Shigeru Katamine
Graduate School of Biomedical Sciences	Dean	Masao Tomonaga
Institute of Tropical Medicine	Dean	Yoshiki Aoki
"	Professor	Kouich Morita
"	Professor	Toshiya Hirayama
"	Professor	Hiroji Kanbara
"	Professor	Michio Nakamura
"	Professor	Takuya Iwasaki
"	Professor	Koya Ariyoshi
"	Professor	Naoki Yamamoto
"	Professor	Masahiro Takagi
"	Professor	Tsutomu Mizota
"	Professor	Kenji Hirayama
"	Professor	Masaaki Shimada
"	Professor	Kazuhiko Moji
		: Chairman

Institute of Tropical Medicine Collaboration Professional Committee

The Institute of Medical Science The University of Tokyo	Professor	Aikichi Iwamoto
Meiji Gakuin University The Faculty of International Studies	Professor	Akira Oki
Graduate School of Medicine The University of Tokyo	Professor	Kiyoshi Kita
Graduate School of Veterinary Medicine, Hokkaido University	Professor	Ikuo Takashima
Chiba University Research Center for Pathogenic and Microbial Toxins	Professor	Kazuko Nishimura
Tsuda College Undergraduate Courses	Professor	Chizuru Misago
Kobe University Graduate School of Medicine	Professor	Haku Hotta
Center for Integrated Area Studies (CIAS), Kyoto University	Assistant Professor	Kenichi Abe
Nagasaki University		
Faculty of Fisheries	Professor	Kazumi Matsuoka
Graduate School of Biomedical Sciences	Professor	Isao Kouno
Institute of Tropical Medicine	Professor	Kouichi Morita
"	Professor	Toshiya Hirayama
"	Professor	Hiroji Kanbara
"	Professor	Yoshiki Aoki
"	Professor	Michio Nakamura
"	Professor	Takuya Iwasaki
"	Professor	Koya Ariyoshi
"	Professor	Naoki Yamamoto
"	Professor	Masahiro Takagi
"	Professor	Tsutomu Mizota
"	Professor	Kenji Hirayama
"	Professor	Masaaki Shimada
		: Chairman

Character of research organization and activities

Based on the following research organization and intimate linkages with other research institutes and universities, the institute aims at accomplishing a mission “Spear-head research in tropical medicine and international health”.

To study comprehensively the tropical diseases which are raging in the developing countries, research organization of the institute consists of 3 major research fields which deal with the classical triad of “human-agent-environment” determinants of infectious diseases and Research Center for Tropical Infectious Diseases.

The research of tropical medicine faces the inevitable fact that “the bench is in the bush”. Therefore the institute has a close linkage with the overseas institutes in Asia, Africa and South Americas and continues the joint studies. Memorandums of academic exchange programs were signed between Nagasaki University and 8 overseas institutes. Since the overseas research laboratories of the institute has been established in Kenya Medical Research Institute, Kenya and National Institute of Hygiene and Epidemiology Vietnam in 2005, the extensive and longitudinal studies on tropical diseases will be promoted. The exchange program under the core university system of JSPS established between our Institute and National Institute of Hygiene and Epidemiology in Vietnam in 2000 has been renewed in 2005 and lasts for 5 years more.

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.

Postgraduate School

In April, 2002, the system of Doctor Courses in Nagasaki University has been changed. In the new

system the Graduate School of Medical Science, Dental Science and Pharmacology were integrated into the Graduate School of Biomedical Science consisting of four courses. All the departments in the Institute belong to the Course of Infection Research. Students who want to study tropical medicine in the Institute are required to apply to the office of the Graduate School of Biomedical Science through the professor of each department.

In addition to the PhD course, in 2006 Master of Tropical Medicine (MTM) course opened in the Nagasaki University graduate school of Biomedical Science and 12 students from various countries were admitted to the school in April. The curriculum is constructed by three parts namely (1) 4 months lecture and practice on Clinical Trop Med and Tropical Public Health, (2) 1 month overseas training on tropical clinical medicine and public health in Thailand, Vietnam and or Philippines, and (3) 6 months dissertation preparation for each student's subject.

For the clinical training in the tropics, we set up 2 weeks training course at three affiliated hospitals, Chianmai University Hospital, Thailand, Choray Hospital, Ho Chi Minh City, Vietnam, and San Lazaro Hospital, Manila, Philippines. The application form is available through our homepage. Briefly, the applicant should have more than two years clinical training as a medical doctor, and should have enough communication skill in English.

Three-month Course on Tropical Medicine and Related Studies

This is the only one short-course of tropical medicine in Japan. This course aims to support medical and paramedical personnel who are working or will work in the tropics by providing opportunities to learn a broad range of skills and knowledge relevant to practicing medicine, conducting disease control programs and conducting medical research in tropical and developing countries.

The course began in 1978. Up to the 28th course held in 2005, 321 personnel (including 132 medical

doctors, and 189 paramedical such as nurses, community-health nurse, midwives, pharmacist) from all over Japan have completed the course. Fifteen participants are accepted to attend the course in each year. 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 member of the ITM and several guest lecturers provide the 14 weeks (June to August) of lectures, laboratory practicals and field work in the field of virology, bacteriology, protozoology, parasitology, medical entomology, environmental physiology, biochemistry, pathology, host-genetics, epidemiology, human ecology, social medicine, clinical medicine and also geography and culture in tropics. Participants who completed the course successfully are awarded the Diploma in Tropical Medicine.



Admission ceremony in 2006

Training Course in Research of Tropical Medicine

Arrangements for conducting the course in this Institute are administered by Japan International Cooperation Agency, commissioned by the Government of Japan to execute Technical Cooperation Programs from 1983 .

This course is conducted by the Government of Japan as a part of its Technical Cooperation Programs for developing countries with a view of contributing to upgrading their standards in tropical medicine and to promoting friendly relations to the countries.

The purpose of this course is to help the control

of endemic and epidemic diseases infesting the Torrid Zone. Through the guidance of the staff of the Institute, the participants will enrich their fundamental knowledge and practical techniques for various medical problems in the tropics.

Individual participants will study on a selected subject in the responsible department for a year. Capacity of each department is normally limited to one person.

Public communication

We hold lectures for the citizens with an irregular schedule. Pupils and students are invited every year to learn tropical medicine at our museum, by audiovisual aids and by lectures.

To accumulate know-how of risk communication on tropical infectious diseases in our institute, we are planning to introduce a science cafe where we have frank communication with the citizens on the present state of tropical medicine.

Publications

Our major publications are Bulletin of Nagasaki University Institute of Tropical Medicine (In Japanese, yearly since 1964, compiled from 1971-1979, PDF is available at HP), Brochure (Both in Japanese and English, since 1977, PDF is available at HP) and Report of collaborative study (since 1989). Special memorial volumes of the 20 th, 30 th and 60 th anniversary were also published.

The publication of our English Science Journal, Tropical Medicine (since 1967), was suspended since 2002. Annals of Endemic Diseases (from 1959-1966), the predecessor of Tropical Medicine, is being input to the electronic database of University Library. Literatures and documents being kept for decades in our depository will soon be open at our HP.

The 21st Center of Excellence Program Global Control Strategy of Tropical and Emerging Infectious Diseases (2003-2007)

Outline of the program

Tropical and Emerging Infectious Diseases have been posing public health problems and social and economic burdens on developing countries. The urgent need for countermeasures, therefore, has been longed for. This program aims at developing tools and strategies for the control of 10 major infectious diseases: malaria, dengue fever, West Nile fever, schistosomiasis, cholera, prion disease, HIV/AIDS, drug-resistant infectious diseases, *Helicobacter pylori*-infection, and SARS, and at cultivating researchers and specialists in the field.

The research project features three kinds of interactive studies such as laboratory vs. field, basic vs. clinic, and developing countries vs. advanced countries. The research members are grouped under six major pathogens: virus, bacteria, fungus, prion protein, HIV, and parasite. The organizing committee of the program makes sure that those six groups keep close contact with each other, and carry out other responsibilities including international symposia, publicity, and academic agreements between Nagasaki University and other overseas research institutes.

Highlights of research and education completed so far

Research works in the area where the diseases exist

- 1) Genetic factors that control the gravity of ma-

laria and dengue hemorrhagic fever

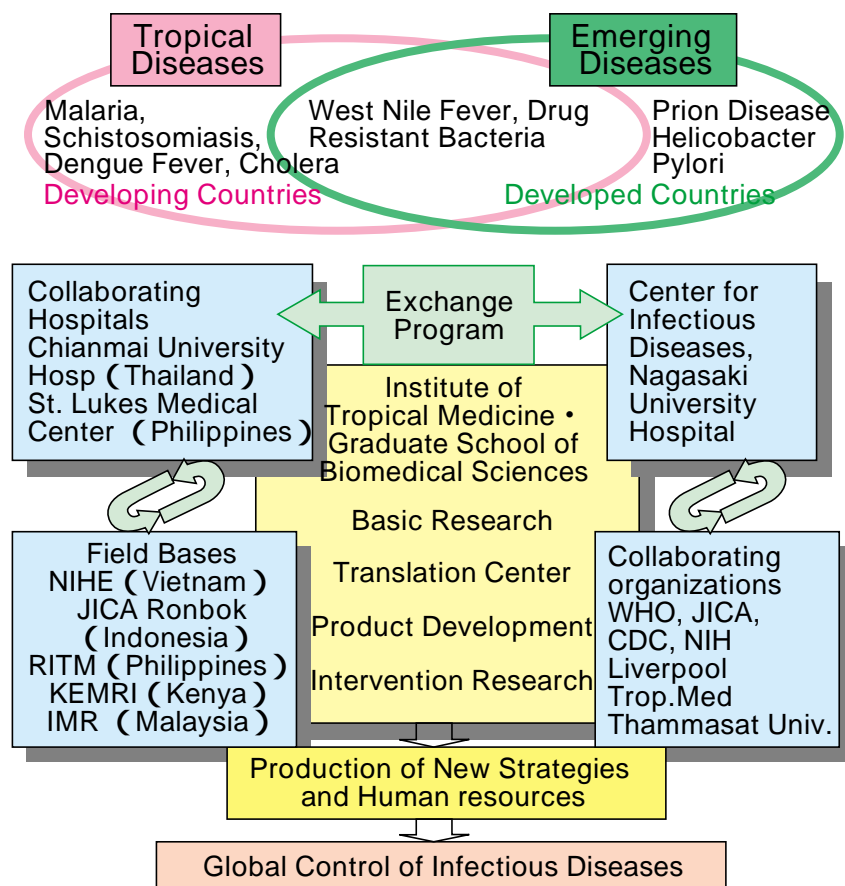
- 2) Hidden morbidity of schistosomiasis haemtobia
- 3) Mechanism of thrombocytopenia caused by dengue hemorrhagic fever
- 4) Drug-resistance mechanisms of respiratory infectious diseases
- 5) Some factors that induce endemic or epidemic malaria

Strategic research including the development of diagnostic tools, drugs, and vaccine

- 1) Miniature pigs as disease models for schistosomiasis japonicum
- 2) Protective immunological response against liver-stage malaria parasites
- 3) Pathogenesis of *Cryptococcus neoformans*
- 4) Mechanism of gastric mucosa injured by *H. pylori* vacuolating cytotoxin
- 5) Mechanism of retrovirus invasion of the cells
- 6) Development of anti-prion drugs by bioinformatics and screening of sea weeds
- 7) Development of diagnostic kits for West Nile fever and SARS
- 8) Development of vaccine for West Nile fever
- 9) Development of the method for evaluation of mosquito control using satellite landscape

Cultivation of human resource

- 1) A total of 30 medical doctors took clinical training programs conducted at the Hospital of Chienmai University in Thailand as well as San-Lazaro Hospital and St. Luke's Medical Center in Philippines.
- 2) In April, 2006, the Master Course of Tropical Medicine (one-year course) was established in Nagasaki University.



Department of Virology

This Department has been conducting basic and applied research on mosquito-borne flaviviral diseases such as Japanese encephalitis (JE), dengue fever (DF) / dengue hemorrhagic fever (DHF), as well as SARS virus.

Analysis on the structure and function of JE and dengue viral genome

Nucleotide sequence analysis and molecular expression of JE and dengue viral genome have been carried out together with long PCR techniques in order to study molecular epidemiology, epitope analysis, biological activity of nonstructural proteins, and virulent viral gene responsible for viral pathogenesis.

Analysis on apoptosis induced by flavivirus infections.

Flavivirus infection induces apoptosis of the infected cells. Characterization of apoptosis and its relation to pathogenicity has been studied in cell line and animal model.

Development of rapid diagnosis of flaviviral diseases

Viral genome detection and identification by PCR and LAMP methods, preparation of diagnostic antigen from infected cell culture fluid, and simplification of IgM antibody detection have been carried out.

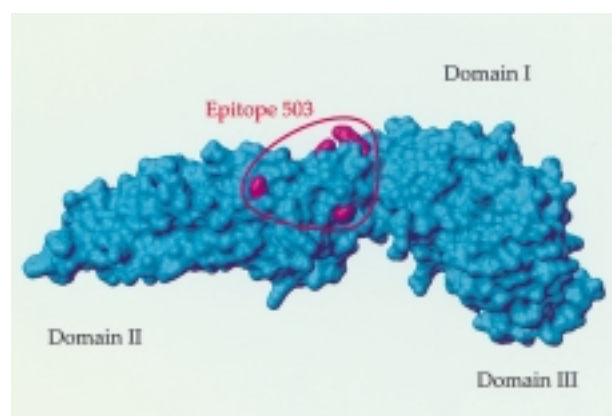
Activities as a WHO Collaborating Center

Dr. S. T. Han, former Regional Director of

WHO Western Pacific Region (WPR) designated, the Department of Virology, Institute of Tropical Medicine, Nagasaki University as a WHO Collaborating Center for Reference and Research on Tropical Viral Diseases on 23 Nov. 1993. On 9 August 1994, the Inauguration Ceremony was held at the Pompe Hall with Dr. Han and approximately 120 guests in attendance, this was followed by the WHO Workshop "Epidemiology and Control on DF /DHF and JE".

The Department has received WHO fellows from Vietnam, Fiji, and the Philippines, and dispatched WHO short-term consultants on the subjects relevant to its terms of reference. Dr. Kouichi Morita was appointed as the Regional Adviser on Communicable Diseases, WHO/WPR, from 16 May 1995 to 15 May 1998. Dr. Futoshi Hasebe was dispatched to the WHO Western Pacific Regional Office to collaborate in the global emerging infectious disease control program from March 2004 to March 2006.

Professor	Kouichi Morita
Associate Professor	Futoshi Hasebe
Visiting Associate Professor	Maria del Carmen Parquet
Research Associate	Shingo Inoue
Guest Research Fellow	Nabeshima Takeshi
Guest Research Fellow	Edward G. Mathenge
Guest Research Fellow	Yu Fuxum
Technician	Kazumi Jodai
Postgraduate student	Hitomi Kinoshita
Postgraduate student	Guillermo Posadas Herrera
Research Student	Mya Myat Ngwe Tun



Newly identified JE neutralizing epitope 503



P 2 Level laboratory

Department of Bacteriology

Our major research interest is to elucidate the etiologic agents isolated from pathogenic bacteria related to the worldwide emerging and re-emerging diseases.

Studies on the cellular and molecular mechanisms of diarrhea induced by bacterial enterotoxins and *Salmonella*:

Aeromonas sobria hemolysin is important in the pathogenesis of diarrhea caused by this enteropathogenic bacterium. Glycosylphosphatidylinositol-anchored glycoprotein was identified as a receptor for *A. sobria* hemolysin on Intestine 407 cells (Int. J. Med. Microbiol (2005) 294, 427).

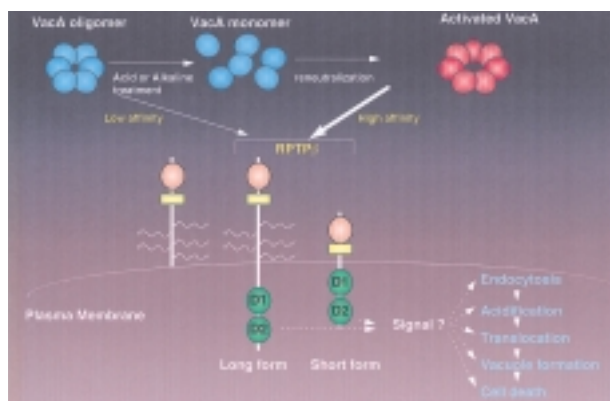
Focusing on the molecular mechanisms of the diarrhea induced by heat-stable enterotoxins (STa) of enteropathogenic bacteria, we are studying 1) interaction of *Escherichia coli* heat-stable enterotoxin with its receptor and 2) activation of guanylate cyclase (GC-C) by STa. Inflammation caused by *Salmonella* is also investigated (J. Biol. Chem. (2004) 279, 12213 J. Immunol. (2004) 172 : 3051)

Studies on the pathogenesis of *Helicobacter pylori*:

To investigate a potential mechanism of how *H. pylori* establishes infection, we investigate the host-parasite relationships of *H. pylori*, focusing on vacuolating cytotoxin A (VacA) and Cag pathogenicity island (CagPAI).

1) In cells transiently transfected with a carboxyl-terminal transmembrane domain (dominant-negative) syntaxin 7 mutant, VacA failed to induce vacuolation, suggesting that SNARE is involved in the intracellular vacuolation induced by VacA (J. Biol. Chem. (2003) 278:25585-25590).

2) VacA induced bone marrow-derived mast cells to produce proinflammatory cytokines, TNF- α , macrophage-inflammatory protein-1 α , IL-1 β , IL-6, IL-10, and IL-13 in a dose-dependent manner without causing degranulation (J. Immunol. (2002) 168: 2603-2607).



Cytotoxicity of VacA toxin through its binding to receptor-protein tyrosine phosphatase β

3) Mice deficient in protein tyrosine phosphatase β do not show mucosal damage by VacA, although VacA is incorporated into the gastric epithelial cells to the same extent as in wide-type mice (J. Biol. Chem. (2003) 278:19183) ibid (2004) 279: 7024, ibid (2004) 279: 51013 Nat. Genet. (2003) 33:375-381).

In addition, we found that VacA induces cell death through Bax and Bak activation leading to cytochrome C release (J. Biol. Chem. (2006) 281:11250)

4) Human β -defensin-2 (hBD-2) is an antimicrobial peptide which belongs to one of the most important host defence systems against bacterial infection in several epithelial tissues. We studied the effect of *H. pylori* on the expression of hBD-2 mRNA in MKN 45 gastric mucosal cells. *H. pylori*, but not culture filtrate, increased hBD-2 mRNA level in MKN 45 cells, whereas the inductive effect of *H. pylori* was not detected when Intestine 407 cells were incubated with *H. pylori*. Among the tested strains of *H. pylori*, which lacks Cag PAI, did not induce hBD-2 mRNA in MKN 45 cells. These results suggested that Cag PAI of *H. pylori* is important for inductive expression of hBD-2 mRNA through NF- κ B activation in MKN 45 cells.

Exposure of MKN 45 cells to *Salmonella typhimurium*, *S. enteritidis*, *S. typhi*, and *S. dublin*, but not *Escherichia coli* ML 35, resulted in remarkable induction of hBD-2 mRNA. (Cell. Microb. (2001) 3: 115 J. Immunol (2004) 173: 5398)

Studies on the development of cholera vaccine:

The overexpression of fimbriae of *Vibrio cholerae* O 1 is under study for use in cholera vaccine trial.

Professor	Toshiya Hirayama
Assistant Professor	Akihiro Wada
Research Associate	Masahiko Ehara
Technologist	Mamoru Iwami
Postgraduate Student	Jyunzou Hisatsune
Researcher	Eiki Yamasaki
Technician	Kayo Maeda
COE Technician	Kumi Tamura



Laboratory

Department of Protozoology

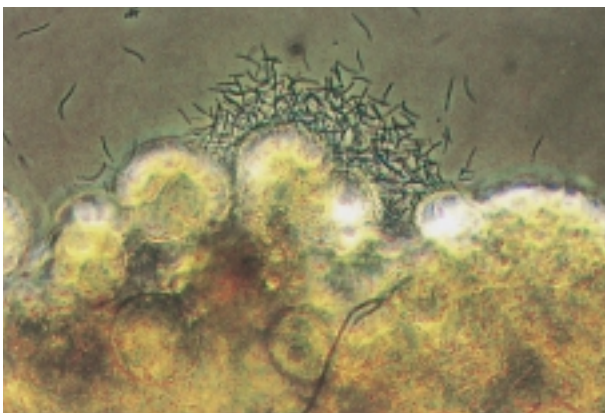
Our main purpose is to clarify infection mechanisms of intracellular protozoan parasites.

Study of malaria parasites

- 1) Specific immune reaction in malaria.
- 2) Surviving strategies of *Plasmodium falciparum* in mammalian hosts.
- 3) Epidemiology of human malaria.



Laboratory for culture



Plasmodia sporozoites from ruptured oocysts in Anopheline mosquito

Study of trypanosomes

- 1) Functions and expression mechanism of trans-sialidase.
- 2) Adaptation mechanisms of *Trypanosoma* species to environments.
- 3) Modification of infected host-cells by *Trypanosoma cruzi*.

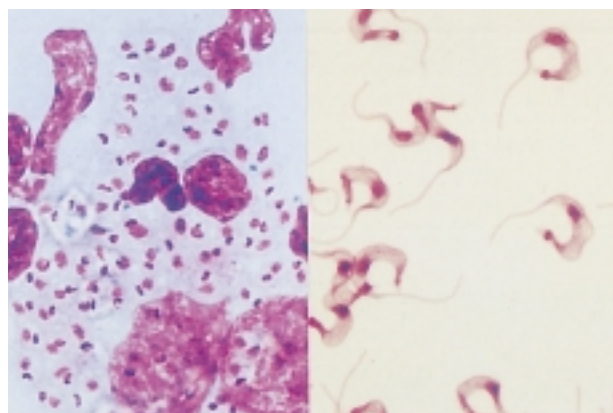
Study of Leishmania

- 1) Characterization of *Leishmania donovani* isolates from Nepal.
- 2) Establishment of animal models of visceral leishmaniasis.

Other studies

- 1) Epidemiology of intestinal protozoan infection.
- 2) Experimental *Entamoeba histolytica* infection in rats.

Professor	Hiroji Kanbara
Assistant Professor	Haruki Uemura
Research Associate	Shusuke Nakazawa
Technician	Miki Kinoshita
Technician	Megumi Morisaki
Postgraduate Student	Toshio Miyazaki
Postgraduate Student	Kishor Pandey



Amastigotes (left) and trypomastigotes (right) of *Trypanosoma cruzi*

Department of Parasitology

The research activities are concentrated on filariasis, schistosomiasis, and intestinal helminthiasis which constitute the major public health problems in the tropics.

Filariasis

Brugia malayi (Cheju strain, periodic form), *B. pahangi* and the vector mosquito, *Aedes aegypti* (Liverpool strain) have been maintained in the laboratory for many years. Highlights of recent studies are as follows.

1) Development of a simple and sensitive method for determination of serum concentration of ivermectin (IVM) and diethylcarbamazine (DEC):

IVM and DEC modified partially in their chemical structure successfully produced the antibody against drugs. Therefore the serum concentration (5 ng/ml) of IVM and DEC can be determined by EIA.

2) Screening of antifilarial drugs from medical plants:

Vernonia amygdalina from Africa, *Neurolaena lobata* from Guatemala and *Cardiospermum halicababum* from Thailand, were effective in vitro on *B. pahangi* adult worms and microfilariae.

3) Epidemiology and control of bancroftian filariasis:

A research project was carried in Kwale, Kenya, in cooperation with Kenya Medical Research Institute (KEMRI) during the period of 1990 and 1996. Transmission potential and morbidity were studied. Mass-chemotherapy with combination of DEC and NaHCO₃ was evaluated.

4) Chemotaxis of filarial infective larvae:

We first reported *B. pahangi* infective larvae show chemotaxis to serum. The peculiar chemotactic movement, the signal transduction involved in chemotactic response and serum characteristics that cause chemotactic response of larvae have been studied.

Schistosomiasis

Schistosoma mansoni (Puerto Rican strain and Kenyan strain), *S. haematobium* (Kenyan strain) and

some strain of vector snails have been maintained in the laboratory. Highlights of recent studies are as follows.

1) Swimming behavior of miracidia:

cAMP is involved in the control of ciliary beating and chemotaxis of miracidia, and the vigorous swimming of miracidia inside the egg-shell is a key factor for hatching of miracidia.

2) Mechanisms of penetration of cercariae into skin:

The studies suggest the involvement of protein kinase C in proteolytic enzyme release from cercariae.

3) Epidemiology and control of *S. haematobium* infection:

Since 1981, the research project on Schistosomiasis haematobia was carried out in Kwale, Kenya, in cooperation with KEMRI for 25 years. The highlights of our studies are human water contact study, cercarial concentration in natural water, ecology of *Bulinus globosus*, usefulness of urinary reagent strips, new immunodiagnostic test (urine ELISA, modified COPT), effect of piped water supply, KAP study (knowledge, attitude and practices), health education, morbidity studies using ultrasound, environmental modification for snail control, prevalence of bladder cancer and liver fibrosis, and qualitative and quantitative studies on difficulty of urination in the community.

Intestinal helminthiasis

Since 2000, epidemiological studies on intestinal helminthiasis has been taken up. The studies aim to show that mode of transmission is different in countries and main determinant is human behaviour.

Professor	Yoshiki Aoki
Research Associate	Kanji Watanabe
Research Associate	Yoshinori Mitsui
Technologist	Mitsumasa Miura
Technician	Satomi Tominaga
Postgraduate Student	Tomoharu Ohki
Postgraduate Student	Teruyo Kusaba
Postgraduate Student	Mayumi Abe
Postgraduate Student	Xinsong Zhang



Examination of difficulty of urination by using Uroflow-meter in an endemic area of Kenya



Examination of contamination of soil by eggs and larvae of intestinal helminth in Vietnam

Department of Thermal Adaptation

The department was established in 1994 to study on the influence and damage of tropical environment on human and animals. Then study result is applied in protection and care of tropical disease for improving infection and symptom.

Study on short and long term heat acclimatization of human

On the short term heat acclimatization, it experiment to expose Japanese to heat in environmental chamber for period from spring to summer. They sweat too much and high electrolyte concentration in the sweat for surplus reaction, so they have big damage as compensation of body temperature control.

Heat loss responses of Tropical inhabitants are studied in the short term heat acclimatization. Their nonevaporative heat loss by blood circulation are effective, and their sweat is a little with low electrolyte concentration as comparison with Japanese it.

Therefore, they sweat minimum volume, and have heat tolerance (Left figure).

Victims by heat stroke decrease, who are mainly children and old men. Society and economy develop by ability adaptation for heat acquired, which increases working ability without discomfort and fatigue.

A study of effective defense method from ultraviolet rays

Ultraviolet rays (UV) contained by Sun light cause various damage in the living body, and UV is a large quantity and strong power in the Tropical Zone and the mountains in particularly. Therefore, the



Experiment of thermal sweating in the environmental chamber

creatures on earth acquired various defense methods for ultraviolet rays harmful to body in a process of evolution.

We have been promoting the study of defense methods from ultraviolet rays in wild animals which inhabit in a low latitude area, the desert and mountains (Right figure: black layer of body hair absorbs UV) in particular.

For the purpose, we study effective defense mechanisms for ultraviolet rays in wild animals, then we design the best defense method against ultraviolet rays with nature and harmless.

The influence of change in biophylaxis functions induced by ultraviolet radiation to infection of tropical disease

Skin cancer occurs by strong ultraviolet radiation for a long term. The exposure to more little amount of ultraviolet rays may be influence biophylaxis function to infection. UV in the Tropical Zone are strong, and many persons suffer from infectious disease. There are approximately 250 million patients with schistosomiasis in Tropical Zone.

In our experiment on infection of *Schistosoma mansoni* cercariae to mouse, ultraviolet radiation group by ultraviolet lamp (UV-B) was statistical difference in the number of *Schistosoma mansoni* cercariae invaded into skin and recovery the adult worms compared with nonirradiation group. We experiment the influence of ultraviolet rays in Sun light on it now.

This study elucidates influence of ultraviolet rays for infectious disease and contributes to the infectious disease control, in particular, in the Tropical Zone with strong ultraviolet rays.

Associate professor (Additional post)

Nobu Ohwatari



Pika inhabiting the mountains of 3200 m

Department of Host-Defense Biochemistry

Reserches in our laboratory are focused on the molecular regulations of the phagocyte NADPH oxidase system that generates active oxygens essential for killing invading microbes.

Selective expression mechaisms for gp 91^{phox}, a core component of the oxidase

The phagocyte NADPH oxidase is composed of membrane-integrated flavocytochrome b 558 containing gp 91^{phox} and p 22^{phox}, and cytosolic components such as p 47^{phox} and p 67^{phox}. Upon phagocytotic stimulation, cytosolic factors move to membrane to make an active complex with the flavocytochrome. Based on genetic analysis of *CYBB*, the gene encoding gp 91^{phox}, in a patient with chronic granulomatous disease, we found that PU.1, a transcriptional activator, bound to gp 91^{phox} promoter position centered to bp -53 was important for the expression of gp 91^{phox} in neutrophils, monocytes, and B lymphocytes, but not in eosinophils. On the other hand, GATA-1 bound to a position centered to bp -98 had an important role in the expression of the gene in eosinophils. We are now interested in the mechanism that can modulate the expression of *CYBB* in selected types of cells for improving primary defense system in inflammation and allergy.

A novel GT-mismatch binidng protein

In the analysis of a *cis*-element of gp 91^{phox} promoter, we found a novel GT-mismatched DNA binding protein. An addition of unlabelled competitor homoduplex with G/C at bp -177, generated, but not erased, a strong 'supershifted' band in EMSA using the labelled probe with A/T at bp -177. Newly paired heteroduplex with the unlabelled upper stand with G at bp -177 and the labelled lower stand with T at the same position recruited nGTBP. This protein

strictly required TRTGNB (R=purine, N=any base, B=not adenine, G paired with T) and 14-mer or longer for binding. G can be replaced by deaminated A, namely, hypoxanthine, suggesting deaminated C-6 is essential for nGTBP binding. Deamination of nucleotide bases are increased by high temperature and the repair of deaminated portions of DNA would be more important in tropical area than other areas.

Transitions appreciably occurred more at TRTRNB sites than at other sites in tumor suppressor protein p 53 exons, suggesting this particular sites were fragile in tumor-prone cells. Relative frequency of esophageal cancer due to transitions at p 53 non-GpG sites in Brazilian mate-drinkers was relatively higher than that in world-wide patients. Cloning and purification of this nGTBP are now urgent issues in our laboraatory.

Professor	Michiko Nakamura
Assistant Professor	Futoshi Kuribayashi
Research Associate	Yoshito Fujii
Research Assosiate	Shoichi Suzuki
	(...in suspension)
Technical assistant	Kanae Tanaka



Department of Pathology / Division of Clinical Investigation

In 1970, the Late Professor Toyosuke WATANABE classified tropical diseases into 4 groups:

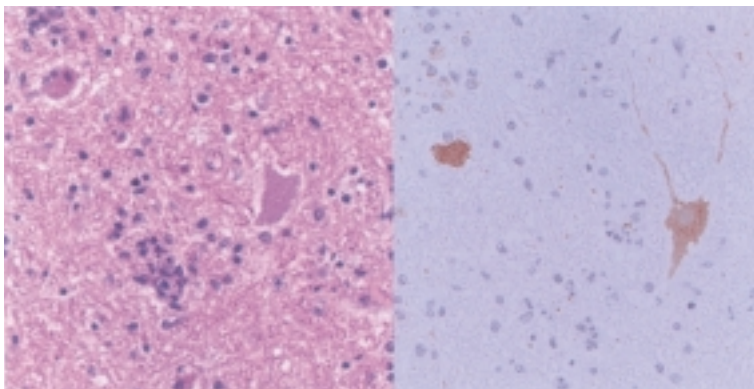
- 1 . Diseases caused by pathogens, uniquely present in the tropical areas.
- 2 . Diseases induced by environmental factors such as tropic climate.
- 3 . Diseases specific for some habitants in the tropical areas due to their high susceptibility.
- 4 . Diseases difficult to prevent in developing countries.

Now, we are investigating the pathogenesis of tropical diseases based on this concept and aim to establish the fundamental basis of their prevention and treatment.

Activities

Pathological diagnosis of infectious diseases.

We are developing various antibodies and molecular probes available for diagnosis of infectious diseases on the clinical specimens obtained at cytology, biopsy, necropsy and autopsy. We are also performing various animal experiments to obtain positive controls for this analysis and to analyze their pathogenesises.



Legend: The central nervous tissue of a cynomolgus monkey inoculated with enterovirus 71 (EV71) . Left: Hematoxylin - eosin stain. Right: Immunostaining for EV71 capsid antigens.

Virus infections of the central nervous system.

Flavivirus encephalitis, such as Japanese encephalitis and tick-borne encephalitis, and rabies are still big problems in the southeast and east Asia . Recently, enterovirus 71 infection among children is frequently associated with serious neurological manifestations in these areas. We are investigating the clinicopathological aspect of these infections and also performing animal experiments to establish their pathogenesis and prevention.

Carcinogenesis in papillomavirus infection.

Neoplasms, dysplasia and condylomas of the mucosa and skin are investigating for the presence of papillomaviruses using the molecular and pathological methods. In addition, we are developing an animal model of mucosal carcinogenesis using hamster.

Virus infections of the respiratory tract.

Human cases with airborne-infections such as influenza and measles are studied for pathological diagnosis and their pathogenesises.

Pathology of tropical diseases.

Epidemiological and histopathological studies are being done in the southeast Asia for tropical diseases and its sequelae.

Professor	IWASAKI, Takuya
Associate Professor	TORIYAMA, Kan
Research Associate	SENBA, Masachika
Research Associate	HAYASAKA, Daisuke
Research Associate	AGO, Masanobu
Technician	NAKAMURA, Masako

Department of Internal Medicine

Main objectives of research activities in the Department of Internal Medicine are to understand pathogenesis of tropical diseases and respiratory infectious diseases and to improve diagnosis, prevention and therapy for infectious diseases in developing countries. Various basic scientific research and international collaborative studies are on going as follows:

1. Respiratory Infections

Our goal is to better-understand mechanisms causing severe and treatment-refractory pneumonias at molecular levels toward development of a novel treatment strategy. We hypothesize that patients with severe and treatment-refractory pneumonia has an impaired process in inducing the cessation of inflammation and re-construction of damaged tissues. We, particularly, focus on the function of macrophage which is responsible for clearing apoptotic cells from the inflammation site using a mouse pneumonia model. We also conduct studies on biofilm formation and molecular epidemiology of pneumococcus, hemophilus influenza etc.

2. Pediatric Infectious Diseases in Vietnam

We have, so far, conducted studies on clinical and bacteriological diagnosis, antimicrobial susceptibility and molecular epidemiology in collaboration with National Institute of Hygiene and Epidemiology. Since 2005, we further collaborated with International Vaccine Institute and started a large-scale of census survey targeting all residents in Nha Trang city and its adjacent Nin Hoa district in the middle part of Vietnam. During the census, we also collect information regarding environment and diseases burden (particularly pneumonia, diarrhea, dengue fever), health care utilization pattern.

3. 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 in Lampang Hospital, northern Thailand. We are planning to facilitate host-gene polymorphisms, molecular immunology, molecular epidemiology and virology studies for a better understanding of HIV transmission and HIV pathogenesis.

4. Studies of Dengue Disease in the Philippines

In collaboration with St. Lukes Medical Center and San Lazaro Hospital in Metro-Manila, the Philippines, we have been studying pathogenesis and clinical and epidemiology aspects of dengue diseases. Our focus has been on mechanisms of thrombocytopenia, which is a characteristic feature of dengue virus infection.

5. Pneumococcal vaccine study for HIV-infected individuals in Uganda

As a collaborative study with the Joint Clinical Research Center in Kampala, Uganda, we have been evaluating the induction of specific antibody and opsonic activity in HIV-infected individuals after immunizing those with a 23-valent pneumococcal polysaccharide vaccine.

Professor	Koya Ariyoshi
Associate Professor	Konosuke Morimoto
Research Associate	Kei Miyagi
Research Associate	Kiwao Watanabe
COE Research Associate	Hiroshi Nakaoka
COE Researcher	Mariko Saito
COE Researcher	Sei Nishimura
Technician	Naoko Kirajima
Technician	Miki Magome
Secretary	Rika Nogawa
Postgraduate student	Jun Koyama
Postgraduate student	Takayuki Oike
Postgraduate student	Toshitaka Sukizaki
Postgraduate student	Yoshiyasu Yoza
Postgraduate student	Chen Meng
Postgraduate student	Vu Thi Thu Huong
Postgraduate student	Chiharu Kaji
Postgraduate student	Hiroaki Yoshii
Postgraduate student	Nanae Taguchi
Postgraduate student	Takeshi Yamamoto
Assistant Professor	Toru Matsubayashi (CICR)
Research Associate	LayMyint Yoshida (CICR)



San Lazaro Hospital (Manila)



Laboratory of molecular chemistry

Department of Preventive Medicine and AIDS Research

This department was newly added to the institute in 1978 as a research division open to visiting professors from other universities and institutes. It is run by concurrent research staff for the present. We have planned and started from August of 2002 a series of fundamental research to answer the question how and what mechanisms human immunodeficiency virus and murine leukemia virus enter into host cells. In addition, we are studying the application of these retrovirus to human gene therapy.

Study on the mechanism of viral entry into host cells by retroviruses

Human immunodeficiency virus (HIV) is known to be a causative agent for acquired immunodeficiency syndrome. After the HIV recognizes CD 4 and chemokine receptor, for example CXCR4 ,it enters into target cells mediated fusion between virus envelope and cell membrane. Murine leukemia virus (MLV) recognizes CAT 1 as the infection receptor, and enters into host cells by same manner. It is most likely that the environment around the receptors influences the infection efficiency. In this context, we are studying the effect of receptor glycosylation and lipid factors proximal to the receptor on the HIV and MLV infection.

On the other hand, there are some evidences

showing that actin-dependent clustering of the receptors is involved in the retrovirus infection. The receptors, however, do not directly associate with actin. We try to identify the cellular molecule that functions as a linker between the receptor and actin.

Application of HIV envelope gene to gene therapy

HIV enters into target cells by fusion between virus envelope and cell membrane. This reaction is catalyzed by envelope glycoprotein encoded by the viral genome. When the envelope gene is introduced to susceptible cells expressing CD 4 and CXCR4 , syncytium formation is induced by its membrane fusion activity, and die. Recently, CD 4 -independent HIV has been isolated. When the envelope gene of the CD 4 -independent HIV is introduced to cells expressing CXCR 4 but not CD4 ,syncytium and cell death was induced. It has been reported that CXCR 4 is up-regulated in mammary tumor. This suggests that the CD 4 -independent HIV envelope protein specifically induces cell death of mammary tumor cells. We are studying the application of the CD 4 -independent HIV envelope as a novel therapeutic gene for mammary tumor.

Visiting Professor	Naoki Yamamoto
Visiting Associate Professor	Hironori Sato
Assistant Professor	Yoshinao Kubo
Technician	Chika Tominaga



Laboratory for biochemical research



Laboratory for biochemical research

Department of Vector Ecology & Environment

Main interest of the department is analysis of environmental factors that affect the transmission of insect-borne diseases, and pursuing environmental friendly vector control strategy.

1 . Physiology and ecology of malaria vectors

A long-term monitoring on main vectors of malaria has been conducted at several fields in South-east Asian countries. Spatial and temporal changes in larval habitats, vegetation, and the impact of human activity on the environment are evaluated in relation to abundance of vectors, host preference, and other population parameters. The GIS/RS is introduced as a new tool to analyze the environment. Geographical strains of several *Anopheles* are comparatively studied by morphological, physiological, and genetic approach.

2 . Ecology and control of dengue vectors

Epidemiological studies have been conducted at several fields in Southeast Asian countries. Monitoring by oviposition traps and mark-release-recapture

experiment are performed to establish more realistic larval indices. In the laboratory *Aedes aegypti* and *Ae. albopictus* are studied on their ecological characters among geographical strains. Feeding behavior and population dynamics of these mosquitoes also are studied in the laboratory and fields.

3 . Vector control technique related studies

Basic study of copepods as a hopeful biological control agent against vector mosquito larvae. Biochemical approach to insecticide resistance in vector mosquitoes.

Professor	Masahiro Takagi
Assistant Professor	Hitoshi Kawada
Research Associate	Nobuko Tuno
COE Researcher	Kazunori Ohashi
Secretary	Toshiko Ueno
Technician	Chiaki Tsurukawa
Secretary	Junko Sakemoto
Postgraduate Student	Maiko Hasegawa
Postgraduate Student	Tran Vu Phong
Postgraduate Student	Yoshihide Maekawa
Postgraduate Student	Masaaki Sugiura
Postgraduate Student	Ataru Tsuzuki



Stereomicroscopic observation of mosquitoes



Ramp traps for collecting mosquitoes

Department of Social Environment

Specific Features of the Department

This Department covers under the 10th tenure interdisciplinary field of Environmental and Social Medicine related to health services and social welfare problems in developing countries.

Interdisciplinary approach includes studies in Social Sciences and Humanities. Further, methods and actual means of international cooperation toward developing countries has been sought to utilize in order to promote inter-departmental linkage for information accumulated with specific analysis and professional response to the public, particularly in the field of infectious diseases diagnosis and control.

Under this context, basic and applied research have been carried out in the following prospective themes from the view point of environmental and social aspects for the purpose of promoting assistance to minimize health problems in tropical areas:

Area of Research Activities:

- 1 . Study and analysis on social (incl. life style, political and economical) background which regulates frequency / areas / accumulation of diseases of the presence of epidemics.
- 2 . Study on the effect of individual and social environment toward endemic and epidemics.
- 3 . Standardization of human security measures in the field of health services from the view points of nutrition and 3 Es ie.economy, environment and education.
- 4 . Study on control of communicable diseases among the regional and international health care programs.
- 5 . Study on quantitative and qualitative values of medical and health services under the ODA ie. Official Development Assistance programs by Japanese government.
- 6 . Feasibility study on comprehensive information filing and network system for the sake of promoting health and social welfare services in developing countries, by epidemics, by regions, by administrative measures.



The Dept. often organizes Int'l Symposia.

7 . Reformation and coordination of health manpower training program / system to meet the need of tropical area in connection with Risk Management.

8 . Comparative studies on the control of emerging infectious diseases in tropical Asia such as West Nile and SARS or Avian Flu.

Specific themes of joint cooperative research designated to the Department in FY 2006 under the scheme of Research Institute for Nationally Joint-Use are listed below. The Technical and Management Committee recommended that interdisciplinary research collaboration should be realized from the viewpoint of middle and long-term range and managed not only by single department but also by the whole Institute as one of the important mandates.

Joint Research projects themes:

- a)Control and prevention measures for the Millennium Development Goals (MDGs) from the view point of tropical medicine and international health.
- b)Analysis of socio-environmental factors of the control and prevention of infectious diseases.

Noted results of research projects have often been integrated and fully utilized in the forms of seminar or symposium for covering valuable themes.

Research Forum theme:

Feasibility of technical cooperation for control of infections based on the understanding of socio-environmental changes.

Professor	Tsutomu Mizota
Research Associate	Susumu Tanimura
Research Associate	Kensuke Goto
Research Assistant	Tomomi Ikeda
Technician	Natsuko Imaoka
Visiting Researcher	Chizuko Suzuki
Postgraduate Student	Qin Liang
Postgraduate Student	Takeshi Yoda
Postgraduate Student	Kazuo Minematsu
JICA Trainee	Olga Maria Amiel
JICA Trainee	Lamine Bangoura



Joint Cooperative Research Members join in the meeting for preparing textbook.

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, TB, Malaria, Trypanosoma cruzi, Schistosoma, and Filaria, 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)Malaria vaccine development using the immunological characteristics of resistant persons living in the endemic area in Asia 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.
- 2)Miniature pig schistosomiasis as a human model.
- 3)Vaccine development for schistosomiasis japonica and masoria using schistosomula antigens.
- 4)Production of the new diagnostic Kit for active infection.

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)Genetic analysis of Trypanosomes in Latin America by using local isolates and molecular biology.

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), Institute of Medical Research (Malaysia), Karolinska Institute (Sweden), Ehime University (Matsuyama), WHO/ TDR (Geneva Switzerland)
- 2 .Schistosomiasis: Jiangxi Provincial Institute of Parasitic Diseases (China), Jiangsu Provincial Institute of Parasitic Disease (China), Univ. Philippines and RITM (Manila, Philippines), Tokyo Medical Dental Univ. (Tokyo)
- 3 .Chagas Disease: Center of Tropical Medicine and Hospital Japones (Bolivia), IICS University of Asuncion (Paraguay)
- 4 . Dengu virus
 - 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.

Staffs

Professor	Kenji Hirayama
Professor (Project)	Michio Yasunami
Associate Professor	Nobu Ohwatari
Lecturer (Project)	Mihoko Kikuchi
COE Researcher	Kazunari Ishii
COE Researcher	Naoko Okuda
Technician	Junko Hayashima
Ph. D. Student	Dujdow Songthamwat
Ph. D. Student	Akiko Takaki
Ph. D. Student	Ekhlas hamed Abdel Hafeez Abdow
Ph. D. Student	Nguyen Thi Phuong Lan
Ph. D. Student	Akiko Yamazaki
MSc Student	Del Puerto rodas Ramona Florencia
MTM Student	Fernando Gerald Vera Gamez



Department of Molecular Immunogenetics



Clean Room for Cell Culture

Clinic at the University Hospital

The Department of Internal Medicine is the only one clinical department at the Institute of Tropical Medicine. It has a clinic and a medical ward with about 20 beds on the 12th floor of the Nagasaki University Hospital. We specialized in the Infectious Diseases and Chest Medicine; diseases that we handle are systemic infectious diseases, including "tropical" diseases and HIV infection, and pneumonia including tuberculosis, and various neoplastic and inflammatory respiratory diseases. We actively receive consultations regarding diagnosis and management of infectious diseases from other departments. The outpatient clinic is open two days a week where we started a travel clinic since April 2004. We are also involved in various clinical trials such as cancer treatment, antibiotics, GM-CSF therapy for pulmonary alveolar proteinosis. We have also responsibilities for training medical students (lectures and bedside teaching) and for postgraduate training programs for general internal physicians and infectious disease and chest medicine specialists. Since April 2006, we have been organizing a clinical case conference (in English) for tropical diseases as a part of Master of Tropical Medicine course.

Professor	Koya Ariyoshi
Associate Professor	Konosuke Morimoto
Assistant Professor	Hiroshi Watanabe
Research Associate	Yoshiko Tsuchihashi
Research Associate	Reiki Kuroki
Research Fellow	Mayumi Terada
Research Fellow	Takeshi Tanaka
Research Fellow	Reiko Mizutani
Research Fellow	Naho Tsuchiya
Intern	Yoko Tsumori
Research Associate	Shoko Honda



Clinical conference

Animal Research Center for Tropical Infections

The center makes it the principal aim to ensure the safety of animal experiments which deal with the pathogenic microorganisms and to build up the successful generation of experimental animals, microorganisms and parasites. The building consists of 7 breeding rooms for experimental animals, 2 laboratories, one breeding room for snails and insects, and two P 3-level biohazard laboratories. The air pressure is kept to be always negative to avoid outflow from inside even at entrance to building. Since the building has the most thorough ventilation through HEPA filter, any microbe cannot leak out to outside of the building. The used water is given chlorination and drained off. The breeding animals and experiments are done according to the Guideline for Animal Experiment edited by Nagasaki University. The laboratory animals bred in the center are mice, rats, hamsters, gerbils, rabbits, snails and mosquitoes.

Professor and Director	Michio Nakamura
Research Associate	Tetsuo Yanagi
Technician	Junko Kawashima



Mongolian gerbil (*Meriones unguiculatus*)

Research Center for Tropical Infectious Diseases(RECTID)

Research Center for Tropical Infectious Diseases, RECTID, was established in April 2001, as one of the outcomes of the Japanese government's commitment for promoting global parasitic disease control, on the basis of the Reference Center (since 1974) and Information and Reference Center (since 1997) of the Institute of Tropical Medicine. The founding head, Professor Masaaki Shimada is now the head of Nairobi Research Station for NUITM-KEMRI project in Kenya. RECTID has the following four fields of activities; 1) developing the museum of tropical medicine, 2) collecting and disseminating information on tropical infectious disease researches, 3) promoting joint research projects, and 4) conducting eco-epidemiological field studies as well as theoretical epidemiological studies.

First, RECTID is responsible for running an exhibition/audio-visual room. Our current exhibitions consist of panels of major tropical diseases such as malaria, diarrhea diseases, ARI, AIDS, TB, filaria, schistosomiasis, and specimen of parasites, vector arthropods and poisonous marine animals, etc. Pathological tissue specimens are also collected. References currently available are historical books, periodicals and documents, films, video/DCD/DVDs, photo slides, and photographs. The exhibition room has moved to the first floor in 2006, and many researchers and students are now visiting the exhibition room. In the near future we would like to expand the exhibition room to the museum of tropical medicine. The museum will enhance the unique function of risk communication for outbreak of tropical infectious diseases.

Second, RECTID gathers and analyzes biological, medical, socio-economic, and cultural information related to tropical diseases and disseminates information on researches on tropical medicine mainly through internet to all the staff researchers, graduate students and trainees, as well as members of the public at large. Materials in the exhibition room are now being digitized and are available through cyberspace. Professor Masahiro Horio is the curator of the exhibition room and also developing the RECTID website with other staff.

The third and forth missions of RECTID is to contribute to the global control of the tropical infectious diseases by promoting and conducting re-

searches. We analyze the factors that regulate the epidemics of the diseases to find appropriate control measure of the infection. RECTID organizes and carries out the integrated eco-epidemiological field studies on tropical diseases in Africa and Asia. We are trying to see the natural history and epidemiology of tropical infectious diseases in endemic areas by means of the combination of long-term field observation by using demographic surveillance system and theoretical epidemiology of infectious diseases. One of our main interests is the role of human behavior in the transmission of tropical infectious diseases. We would like to see the human ecological impacts of tropical infectious diseases both in the local and global perspectives.

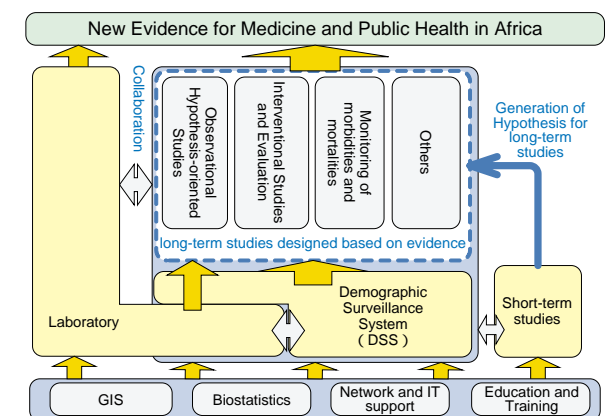
Professor and head
Professor
Professor/ Curator
Research Professor
Research Professor
Research Professor
Research Professor
Visiting Professor

Kazuhiko Moji
Masaaki Shimada
Masahiro Horio
Noboru Minakawa
Satoshi Kaneko
Yoshio Ichinose
Hideki Yanai
Yasuhiko Kamiya
Nick Mascie-Taylor
(Cambridge Univ)
Pathom Sawanpanyalert
(Thai NIH)

Visiting Professor

Assistant Professor
Assistant Professor
Assistant Professor
Research Associate
Research Associate
Researcher Fellow
Researcher Fellow
Researcher Fellow
Research Student
COE Researcher
Research Assistant
Research Assistant
Technician
Technician
Technician
Technician
Postgraduate Student
Postgraduate Student
Postgraduate Student
Postgraduate Student
Postgraduate Student
Postgraduate Student
Postgraduate Student
Postgraduate Student

Sumihisa Honda
Hiroshi Nishiura
Akiko Matsuyama
Eiko Kaneda
Toshihiko Sunahara
Kyoko Futami
Kouhei Takenaka
Masahiro Hashizume
Nobuyuki Nishikiori
Shouhei Takeuchi
Kyoko Sakitani
Kazuo Araki
Kiyomi Suda
Youji Shimizu
Akiko Komazawa
Shin Ryou
Yuko Nakao
Guoxi Cai
Tomoko Abe
Rieko Nakao
Magafu Mgaywa Damas
Osuke Komazawa
Ayumi Nomura
Etuko Hatagishi



GRAND DESIGN OF THE NUITM-KEMRI PROJECT



Exhibition Room of Tropical Medicine

Central Laboratory

There are equipments shared in the institute. Those equipments are maintained and operated by the staffs listed below. There are three major laboratories to be set up, namely electron microscope lab, P 3 and cell culture lab and molecular biology lab. Electron microscopies (TEM and SEM of jeol), a Ultramicrotome (Reichert), con-focal laser microscope system (LEICA DMIREZ), a flow cytometer (Becton), Bioimage analyzers (Hamamatsu Photonics, Bio rad GS-250 and Pharmacia Image master), DNA sequencers (Perkin-Elmer), a DNA/RNA extraction system (Qiagen), two P 3 rooms, and 2 dimensional protein purification system (Beckman). Following are the major equipments.

Professor	Kenji Hirayama
Assistant Professor	Akitoyo Ichinose
Technician	Hitomi Horie



Lab for Genetic Analysis

Infectious Diseases Research Program Nairobi Research Station, Kenya (A Special Grant from the Ministry of Education, Sports, Culture, Science and Technology, 2005 ~ 2009)

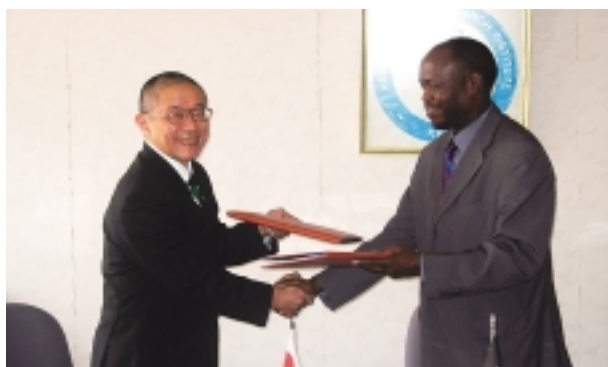
Outline of the program

The Institute of Tropical Medicine (ITM) has received a government grant for the promotion of research on tropical diseases and emerging and reemerging infectious diseases. With this special, ample grant of money, ITM established a research station in Nairobi, Kenya. The unique feature of the Nairobi Station's research program is long-term, extensive, and multidisciplinary studies based on the Japan-Kenya collaboration. The program provides training for young researchers both Japanese and Kenyan, and in collaboration with JICA, contributes to the disease control and health promotion in the tropics with the fruits of its research.

Progress of the program

1 . Research station in Kenya

The Research station was set up in the Kenya Medical Research Institute (KEMRI), Nairobi. KEMRI is one of the overseas research organizations with which ITM has long been doing a cooperative research. Based on the academic agreement between Nagasaki University and KEMRI, the signing ceremony for the new research program's Memorandum of Understanding was held on September 13, 2005. The Research Station is now partially equipped to facilitate bio-medical and epidemiological studies in tropical diseases. In the very near future, the P3 laboratory and Demographic Surveillance System will be completed.



Signing ceremony on September 13, 2005

2 . Dispatch of Japanese researchers

Four professors, one is a program leader, and one administrative staff member work in the Nairobi Station. They are to be provided with special logistic support by one professor and one associate professor of ITM.

3 . Study areas for the long-term and extensive research work

The Demographic Surveillance System (DSS) will be put into operation in two regions, the Suba area in Western Kenya and the Kwale area on the Coast. The research proposal of DSS has been approved by the scientific and ethical committee of KEMRI and ITM.

4 . Studies in infectious tropical diseases

Research projects on schistosomiasis and malaria were launched. The projects include studies in epidemiology of schistosomiasis, hidden morbidity of schistosomiasis haemoglobinuria, and malaria vector control in Kenya.

5 . Training program

Under the patronage of JICA, four Kenyan researchers and doctors were given a chance to visit ITM and were trained in research on tropical medicine. Professors of ITM served as advisers in the JICA-sponsored International Parasite Control which took place in Kenya.

Program Staff

Program Leader and Professor Masaaki Shimada (Nairobi Station)

Professor Yasuo Ichinose (Nairobi Station)

Professor Noboru Minakawa (Nairobi Station)

Professor Satoshi Kaneko (Nairobi Station)

Professor Masahiro Horio (Institute of Tropical Medicine)

Associate Professor Hiroshi Nishiura (Institute of Tropical Medicine)

Administrative Staff Shiho Honda (Nairobi Station)

Post-doctorate Fellow Kyoko Futami (Nairobi Station)



Nairobi Research Station, Nairobi, Kenya

Research Center: Clinical Epidemiology of Emerging and Reemerging Infectious Diseases Laboratory in Hanoi, Viet Nam (A special research program of the Japanese Government for the establishment of a research center for emerging and reemerging infectious diseases, 2005 ~ 2009)

Outline of the program

In 2005, the Government of Japan (Ministry of Education, Culture, Sports, Science and Technology) provided special funds to certain grant-winning Japanese universities for the purpose of establishing research centers for emerging and reemerging infectious diseases in order to make joint studies with overseas research institutions. Nagasaki University, one of the recipients, set up Research Centers in Nagasaki and Hanoi, Viet Nam to study clinical epidemiology of emerging and reemerging infectious diseases, including disease ecology, intervention, and protection and prevention, thereby contributing to the control and/or elimination of infectious diseases, which is today's global concern.

The Research Centers have been managed in collaboration with four institutions, the Institute of Tropical Medicine (ITM) of Nagasaki University, the International Medical Center of Japan, Tokyo, the National Institute of Hygiene and Epidemiology (NIHE), Hanoi, and Bach Mai Hospital, Hanoi, with ITM and NIHE playing a major role in the operation. NIHE has the NIHE-Nagasaki University Friendship Laboratory in which Japanese researchers are now carrying out infectious diseases research. In Nagasaki, the research projects focus on basic strategic research and product development, and

also provide guidance for ethical consideration and determining of perfect strategies to counter any potential infectious disease outbreak.

Meanwhile, the research work in Viet Nam will concentrate on the following areas:

- 1) zoonotic infectious diseases including avian influenza, hanta, nipah virus infection, and rabies;
- 2) vectorborne infectious diseases, including malaria and dengue virus infection;
- 3) fecal-oral infection including rotavirus, norovirus infection, and cholera;
- 4) human to human infection, including acute respiratory infections.

Update status

The project document has been approved by the Vietnamese Government, and the Friendship Laboratory has been equipped with apparatus for bio-medical and epidemiological studies on infectious diseases.

The Center had its opening ceremony on March 17, 2006 in Hanoi, and started epidemiological study on avian influenza and dengue fever infection while developing the Demographic Surveillance System for long-based and extensive infectious diseases studies.

NIHE-Nagasaki University Friendship Laboratory Staff

Project Leader and Professor	Koichi Morita
Professor	Tetsu Yamashiro
Professor	Futoshi Hasebe
Professor	Hideki Yanai
Research Fellow	Yukiko Higa
Research Fellow	Motoi Suzuki
Administrative Staff	Yoshio Furuya
Post Doctoral Fellow	Gen-ichiro Uechi



National Institute of Hygiene and Epidemiology (NIHE)



Opening ceremony of the Research Center in NIHE

Japanese support to the Pacific Immunization Program Strengthening (J-PIPS) Suva, Fiji

The Japanese support to the Pacific Immunization Program Strengthening (J-PIPS) is a 5-year project of JICA in 13 South Pacific island countries. The project aims to strengthen capacity development in the Pacific in the area of immunization services through resource development of EPI management staff and to upgrade the quality of EPI services provided. The Center for International Collaborative Research (CICORN), Nagasaki University, is responsible for the administrative management of J-PIPS. J-PIPS started operation in February 2005 under the leadership of Dr. Kouichi Morita as Chief Advisor, and who is Professor, Department of Virology, Institute of Tropical Medicine (ITM). In March 2005, four other professionals from CICORN and ITM were assigned to the project office in Suva, Fiji.

The project's two main objectives are: to strengthen the Pacific island countries' EPI program planning and monitoring system of vaccine-preventable diseases, such as poliomyelitis, measles, Hepatitis B and influenzae bacillus; and to establish a functioning regional training system for vaccine logistics, cold chain maintenance, injection safety and EPI waste disposal management.

As part of its capacity enhancement program, J-PIPS in cooperation with the Nagasaki University, coordinates a technology transfer program to assist the target countries. In March 2006 a Measles outbreak occurred in Fiji where J-PIPS actively participated in its containment by providing technical support and conducting supplementary immunization activity (SIA) campaigns in cooperation with the Government and international agencies. A staff from the Fiji Centre for Communicable Disease Control, the regional laboratory for communicable disease and center for diagnosis of virus diseases in the South Pacific, and an earlier recipient of the study program from ITM, was remarkably involved in laboratory diagnosis work during the outbreak containment activities having received capacity enhancement from the scheme. Thus, the benefit of technology transfer was

achieved not solely in Fiji but by the regional laboratory of the South Pacific countries, as well.

J-PIPS holds regular “regional trainings” in Suva for immunization project leaders, as well as supplementary health workers “country trainings” in each target country with the active participation and in collaboration with the Fiji Ministry of Health, WHO and UNICEF.

Annual surveys are conducted by J-PIPS in the 13 South Pacific island countries, in order to assess, determine and discuss with counterparts updates on occurrence of target communicable diseases and other project issues. Survey results are gathered and published as annual reports.

J-PIPS maintains close communication and collaboration with its international agency partners such as WHO, UNICEF, AusAID, NZAID, SPC and other international agencies to ensure a sustained maximum degree of effectivity in technical cooperation.

Significantly, the J-PIPS project serves as an avenue for communicable disease control activities, particularly vaccine-preventable diseases, in the Pacific island countries and, thus, is in conformity with the ITM mission to “spearhead research in international health” and make a “global contribution through health promotion by applying the results of research”; and is one of the “capacity strengthening” projects of CICORN and ITM.

Project Staff

Dr. Kouichi Morita, Professor, ITM
Dr. Yasuhiko Kamiya, Professor, CICORN/ITM
Mr. Tatsuhiko Tsukakoshi, CICORN
Mr. Kenzo Sasagawa, CICORN
Mr. Hiroshi Osawa, CICORN



First PIPS Regional Training (12-15 December, 2005)

Administration

Katsuhisa Jinno, Head Official

General Affairs Unit

Tsukasa Harada, Chief

Naomiki Yamamura, Sub-Chief

Ami Noda, Staff

You Kanai, Staff

Shiho Honda, Staff

Junko Suenaga, Assistant Staff

Asuka Mtsuo, Assistant Staff

Tomoko Takenouchi, Assistant Staff

Mariko Hirano, Assistant Staff

Etsuyo Uchida, Assistant Staff

Mamiko Akagi, Assistant Staff

Kumiko Shimizu, Assistant Staff

Collaboration Research Unit

Hidemitsu Noguchi, Chief

Fumiko Hashiguchi, Sub-Chief

Yumiko Matsumoto, Assistant Staff

Number of Staff

(as of May, 2006)

Divisions	Professor	Assistant Professor	Lecturer	Assistant	Sub total	Others	Total
Enrollment	12 (4)	6 (1)	3	17 (1)	38 (6)	8 (2)	46 (8)

() number of fixed-term staff

Accounting

Revenue (in 2005)

Divisions	Amount (in thousands)
Tuition and Matriculation Fee	1,974
Others	2,077
Industry-Academic Cooperation	76,855
Donation	16,502
Total	97,408

Expenditure (in 2005)

Divisions	Amount (in thousands)
Personnel expenses	514,068
the cost of equipment	485,113
Total	999,181

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

(in 2006)

Classification	Scientific Research on Priority Areas	Scientific Research (A)	Scientific Research (A)	Scientific Research (B)	Scientific Research (C)	Exploratory Research	Young Scientists (B)	Total
Number of Grants	0	1	1	4	1	5	1	13
Amount (in thousands)	0	18,330	26,390	18,400	1,800	7,600	800	73,320

External Funding

(in 2005)

Divisions	Cooperative Research	Commissioned Research	Grants and Endowments
Number of Sources	1 件	8 件	20件
Amount (in thousands)	3 ,500	50 ,684	16 ,502

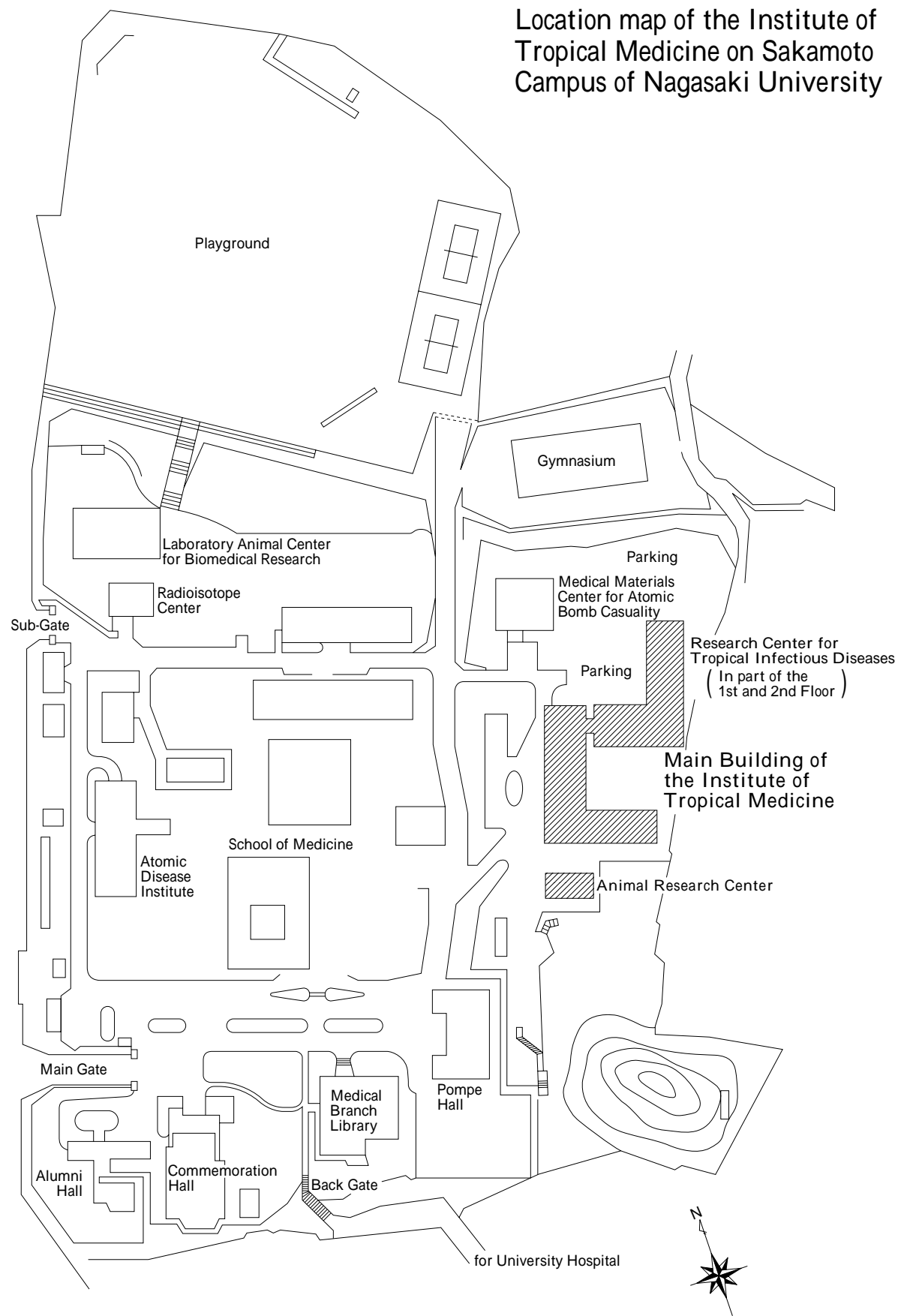
Site and Buildings

Location	12 - 4 Sakamoto 1 chome Nagasaki - city		
Buildings(m ²)	Institute of tropical medicine (7 ,663m ²)	Animal Research Center (490m ²)	

Agreement of Educational, Scientific and Scholaly Exchange

Name of organization of partner countries	Concluded date
Chiang Mai University (Thailand)	February ,1988
Mahidol University (Thailand)	November ,1999
Philippines University Diliman (Philippines)	April ,2001
Institute of Hygiene and Epidemiology (Vietnam)	June ,2001
Airlangga University (Indonesia)	January ,2004
St. Luke's Medical Center (Philippines)	February ,2004
SAH LAZARO HOSPITAL MEDICAL CEHTER (Philippines)	August ,2004
KENYA MEDICAL RESEARCH INSTITUTE (KENYA)	November ,2004
THAMMASAT University (Thailand)	March ,2006

Location map of the Institute of Tropical Medicine on Sakamoto Campus of Nagasaki University



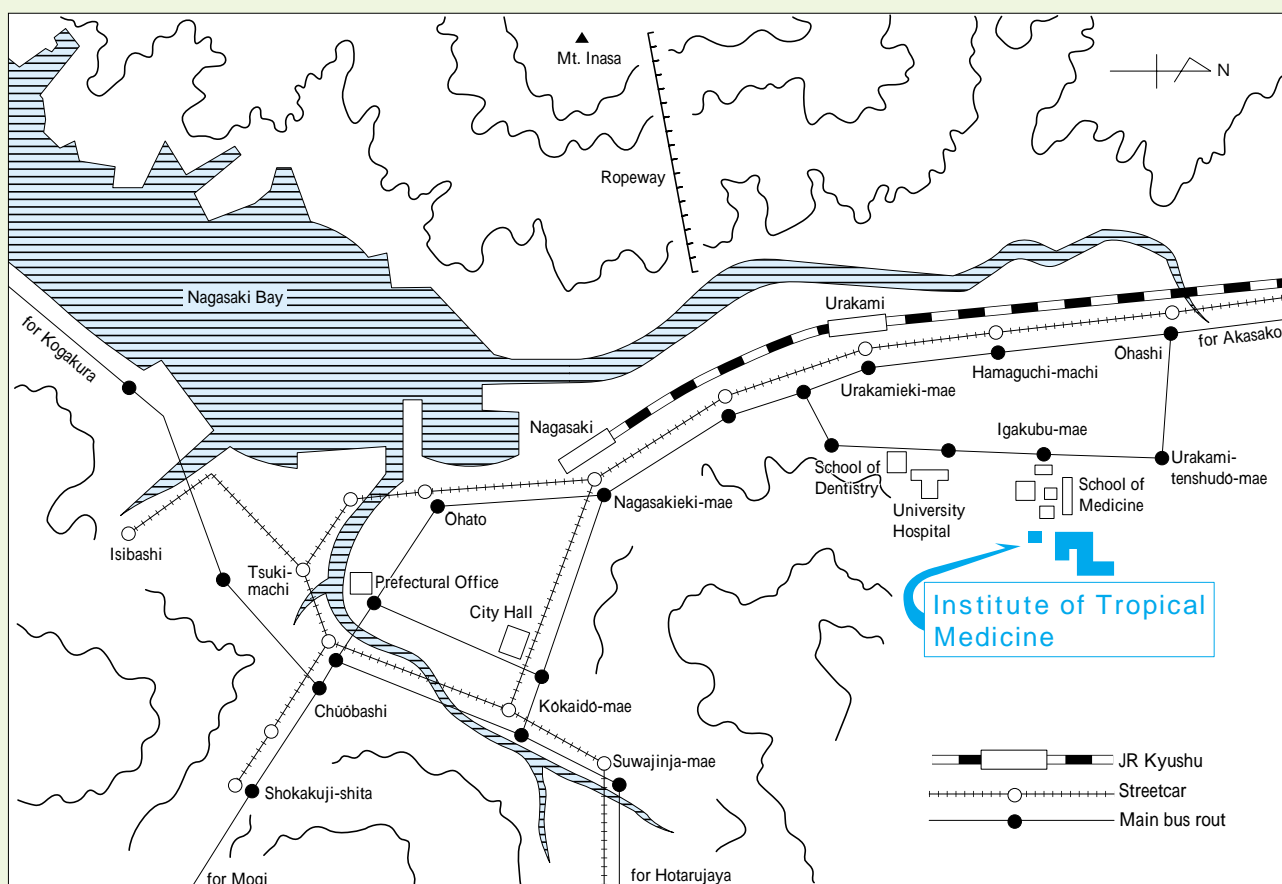
Telephone Number

Institute of Tropical Medicine, Nagasaki University095 (849) 7800

	Extensions	
Dean	4700	849 7801
Head of Administrative Office	4701	849 7802
Chief of General Affairs Unit	4702	
General Affairs Unit	4703	849 7803
General Affairs Unit	4706	
General Affairs Unit	4707	849 7806
General Affairs Unit	4708	
Chief of Collaboration Research Unit	4709	
Collaboration Research Unit	4710	849 7807
Facsimile	4705	849 7805
Meeting Room	4711	
Department of Virology		
Professor	4733	849 7827
Associate Professor	4734	849 7828
Information	4735	849 7829
Facsimile	4736	849 7830
Department of Bacteriology		
Professor	4737	849 7831
Lab 2	4738	849 7832
Lab .1	4739	849 7833
Department of Protozoology		
Professor	4741	849 7835
Lab 2	4742	849 7836
Lab .1	4743	849 7837
Information	4744	849 7838
Department of Parasitology		
Professor	4728	849 7822
Staff room	4729	849 7823
Lab	4730	849 7824
Information	4731	849 7825
Department of Molecular Epidemiology		
Professor	4770	849 7860
Department of Thermal Adaptation		
Professor (Concurrent)	4726	849 7820
Department of Biochemistry		
Professor	4754	849 7848
Lab .1	4755	849 7849
Culture room	4756	849 7850
Information	4757	849 7851

Department of Pathology	Extensions	
Professor	4719	849-7813
Associate Professor	4720	849-7814
Information	4721	849-7815
Staff room	4722	849-7816
Information	4780	849-7870
Department of Internal Medicine		
Professor	4746	849-7840
Associate Professor	4782	849-7873
Information	4747	849-7841
Information	4748	849-7842
Facsimile	4749	849-7843
Department of Preventive Medicine and AIDS Research		
Lab	4750	849-7844
Information1	4751	849-7845
Information2	4752	849-7846
Department of Vector Ecology & Environment		
professor	4716	849-7810
Staff room	4717	849-7811
Information	4715	849-7809
Facsimile	4718	849-7812
Department of Social Environment		
Professor	4774	849-7864
Research Associate	4775	849-7865
Information	4776	849-7866
Facsimile	4777	849-7867
Department of Environmental Pyhsiology		
Professor	4724	849-7818
Associate Professor	4725	849-7819
Information	4726	849-7820
Facsimile	4727	849-7821
Animal Research Center		
Information	4762	849-7856
Laboratory	4763	849-7857
Research Center for Tropical Infectious Diseases		
Lab .1	4778	849-7868
Lab .1	4779	849-7869
Lab 2	4714	849-7808
Museum	4759	849-7853
Central Laboratory		
Electron Microscope Room	4765	849-7859

Location map of the Institute of Tropical Medicine, Nagasaki University in Nagasaki City



How to get the Institute

- 1 . From Nagasaki Station (JR Kyushu)
 - ① Get on a bus (Nagasaki Bus, Line 8) at Nagasakieki-mae and get off at Igakubu-mae.
Five minutes walk from the bus stop.
 - ② Get on a streetcar at Nagasakieki-mae (for Akasako, Line 1 or 3) and get off at Hamaguchi-machi. Ten minutes walk from the streetcar stop.
 - ③ Ten minutes by taxi from the station.
- 2 . From Urakami Station (JR Kyushu)
 - ① Twenty minutes walk.
 - ② Five minutes taxi.
- 3 . From Nagasaki Airport
 - ① Get on limousine at the airport (for Nagasaki), and get off at Nagasaki-ekimae, and then continue to 1 .
 - ② Get on limousine at the airport (for Nagasaki), and get off at Ohashi, and then twenty minutes walk from the bus stop or 5 minutes by taxi.
 - ③ About one hour by taxi from the airport.

Location

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

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