# INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY





2007

## 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

Coverpage: Suba area DSS (Demographic Surveillance System) operation group, Nairobi Research Station, Kenya. (Health Development Study in Lao, P.D.R.)

### 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. In 2006, a one-year course of the Master of Tropical Medicine opened for medical doctors.
- 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 appeal the public how tropical medicine is important for the well being of humankind and offer the information on the tropical diseases.

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.

June, 2007 Kenji Hirayama M. D., Ph. D. 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 9 th, 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

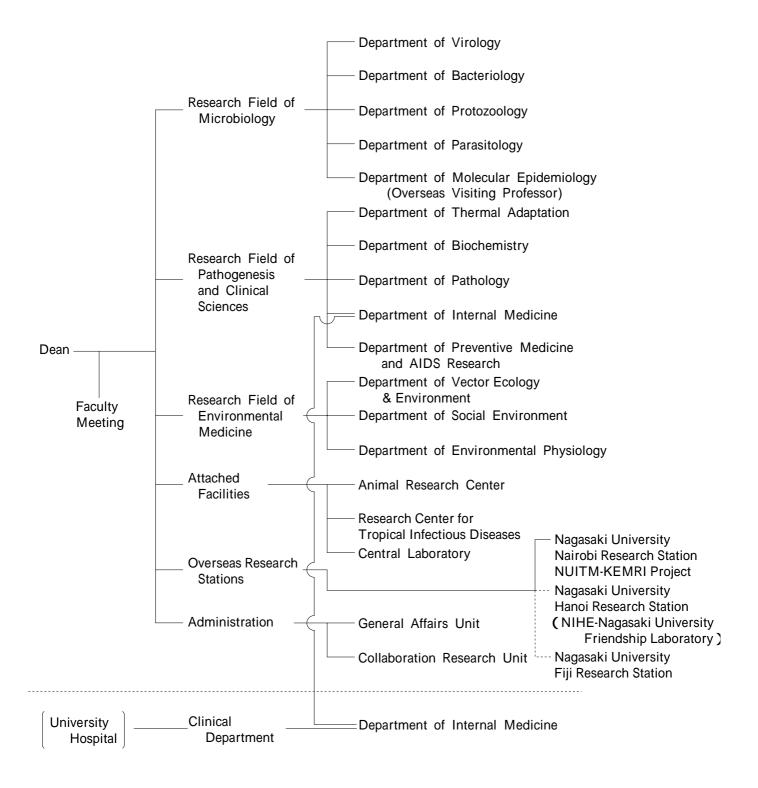
#### (Research Institute of Endemics)

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-May 31 2007
Kenji Hirayama	Apr .1 2007-Up to the present

### Organizational Chart



### Collaboration research

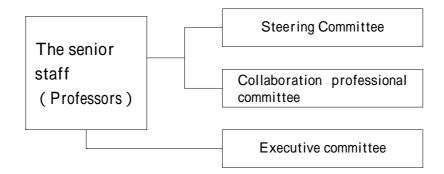
The institute has conducted research in the field of tropical medicine for the past 62 years since its establishment in 1942. The institute was reorganized to make extensive collaboration with other universities and institute in the field of interdisciplinary tropical medicine with molecular biology,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

In the FY2006 a total of 19 selected projects were carried out.



#### Collaboration Research Sytem

# Institute of Tropical Medicine Steering Committee

Nagasaki University	Professor Emetitus	Akira Igarashi
Tayama Institute of Health	Director	Takeshi Kurata
International Medical Center	President	Takehiko Sasazuki
Keio University School of Medicine	Professor	Tsutomu Takeuchi
Research Institute for Humanity and Natur	re Director	Narifumi Tachimoto
Research Institute for Microbial Diseases	s Osaka University	
	Professor	Takeshi Honda
National Museum of Ethnology		
	Director - General	Makio Matsuzono
The Institute of Medical Science		
The University of Tokyo	Director	Motoharu Seiki
Graduate School of Biomedical Sciences	Professor	Shigeru Katamine
Graduate School of Biomedical Sciences	Dean	Masao Tomonaga
Institute of Tropical Medicine	Dean	Kenji Hirayama
11	Professor	Kouich Morita
11	Professor	Toshiya Hirayama
11	Professor	Osamu Kaneko
11	Professor	Yoshiki Aoki
11	Professor	Michio Nakamura
11	Professor	Koya Ariyoshi
11	Professor	Naoki Yamamoto
11	Professor	Masahiro Takagi
11	Professor	Tsutomu Mizota
11	Professor	Masaaki Shimada
11	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 In	ternational Studies	
	Professor	Akira Oki
Graduate School of Medicine The Univers	ity of Tokyo	
	Professor	Kiyoshi Kita
Graduate School of Veterinavy Medicine, H	Hokkaido University	
	Professor	Ikuo Takashima
Tsuda College Undergraduate Courses	Professor	Chizuru Misago
Kobe University Graduate School of Medio	cine Professor	Haku Hotta
Center for Integrated Area Studies (CIAS), Kyoto University		
	Associate Professor	Kenichi Abe
Nagasaki University	Pegent	Kazumi Matsuoka
Graduate School of Biomedical Science	ces Professor	Isao Kouno
Institute of Tropical Medicine	Professor	Kouichi Morita
"	Professor	Toshiya Hirayama
"	Professor	Osamu Kaneko
"	Professor	Yoshiki Aoki
"	Professor	Michio Nakamura
"	Professor	Koya Ariyoshi
"	Professor	Naoki Yamamoto
"	Professor	Masahiro Takagi
"	Professor	Tsutomu Mizota
"	Dean	Kenji Hirayama
"	Professor	Masaaki Shimada
11	Associate Professor	Kan Toriyama
		_

: 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, by the grants from Ministry of Education, Sports, Culture, Science and technology (MEXT), the extensive and longitudinal studies on tropical diseases are on the progress. 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 oversea 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 from 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 29<sup>th</sup> course held in 2006, 336 personnel (including 137 medical doctors, and 199 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**

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. To accumulate know -how of risk communication on tropical infectious diseases in our institute, we are planning to introduce " science cafe " sessions 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 )English Brochure: INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY (this copy. yearly since 1977, PDF files are available at our Web page.)

3 )Japanese Brochure (in Japanese yearly since 1977, PDF files are available at our Web page.)

4) Report of Nation-wide Cooperative Research Projects (Information of research activities and achievements as a nation-wile cooperative research center for tropical medicine is compiled.)

5 ) Tropical Medicine (An academic Journal issued since 1967 are now suspended since 2002 . PDF files are avairable at http://naosite. lb. nagasaki-u.ac.jp/ dspace/handle/10069/6. Electric files of Annals of Endemic Diseases (in Japanese, 1959-1966, the predecessor of Tropical Medicine) are also available at the same Web page.)

6 )Special memorial volumes of the 20 th , 30 th and 50 th anniversary (in Japanesse)

### The 21<sup>st</sup> 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 diseases, HIV/AIDS, drug-resistant infectious diseases, Helicobacter pyroli-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

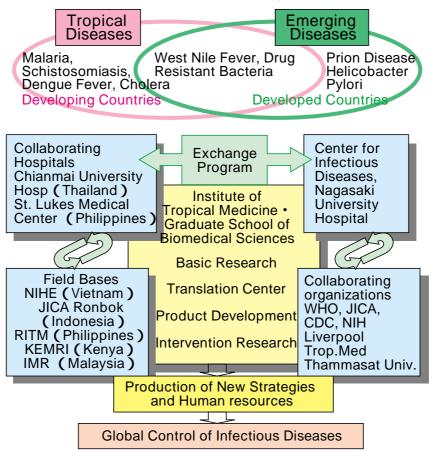
- 2 ) Hidden morbidity of schistosomiasis haemtobia
- 3 ) Mechanism of thrombocytopenia caused by dengue hemorrhagic fever
- 4 ) Drug-resistance mechanisms of respiratory infectious diseases
- 5 ) Some factors that induce endemic or epidemic malaria

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. py-lori* 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

- A total of 30 medical doctors took clinical training programs conducted at the Hospital of Chen-Mai 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 pathogenecity 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.

#### Research on emerging viral infectious diseases

Studies on the development of diagnostic methods and epidemiology on SARS virus, Nipah virus and H 5 N 1 avian influenza virus have been conducted in Viet Nam and other countries in the South East Asia.

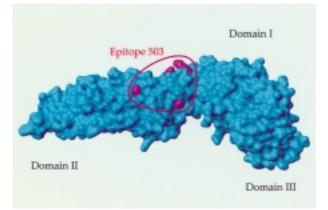
#### Activities as a WHO Collaborating Center

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 Professor Visiting Associate Professor Assistant Professor Assistant Professor Assistant Professor Guest Research Fellow Guest Research Fellow **COE** Researcher Technician Technician Postgraduate student Postgraduate student Postgraduate student Postgraduate student Research student Research Student

Kouichi Morita Futoshi Hasebe Maria del Carmen Parquet Shingo Inoue Toru Kubo Yu Fuxum Nabeshima Takeshi Edward G. Mathenge Dewi Beti Ernawati Kazumi Jodai Tomomi Yamaguchi Hitomi Kinoshita Guillermo Posadas Herrera Chikako Kataoka Dinh Tuan Duc Murao Lyre Anni Espada 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 reemerging diseases and to know the virulence mechanisms of bacterial pathogens.

1. 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 p 38/ATF-2mediated signal pathway [4] are independent of VacA effects on cellular vacuolation.

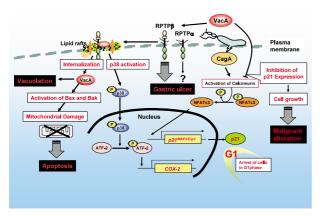
Analysis of VacA receptors provided new insights into the molecular basis of VacA function. We reported that two VacA proteins, termed m 1 VacA and m 2 VacA, which were defined by sequence differences in the middle of the molecules, interacted with target cells by binding to two types of receptorlike protein tyrosine phosphatases (RPTPs), i. e., RPTP $\alpha$  and RPTP $\beta$ , resulting in toxin internalization and vacuolation of the human gastric adenocarcinoma cell lines AZ-521 and G 401 [5, 6, 7]. By analysis of the pathological responses of wild type and RPTP $\beta$ -deficient mice to oral administration of VacA, we found that RPTP $\beta$  functions as a receptor for VacA and produces the disease associated with VacA toxicity including gastritis and gastric ulcer [3]. Receptor-dependent translocation of VacA to lipid rafts is critical for signaling pathways leading to p 38 MAP kinase/ATF-2 activation and vacuolation [8].

To know a potential mechanism of how *H. pylori* establishes infection, we also investigate the hostparasite relationships of *H. pylori*, focusing on VacA as well as CagA, which is an effecter protein injected by its type IV secretion system into host cells. Consistent with suppression of nuclear translocation of nuclear factor of activated T cells, NFAT, in Jurkat T cells, VacA counteracted CagA-induced activation of NFAT in AGS cells, suggesting that the two major *H. pylori* virulence factors inversely control NFAT activity [9]. Deregulation of NFAT, either positively or negatively, may contribute to cellular dysfunctions that underlie diverged clinical manifestations caused by *H. pylori* infection.

References: [1] Microb. Pathog. 31: 29-36, 2001, [2] J. Biol. Chem. 281, 11250-11259, 2006, [3] Nat. Genet. 33: 375-381, 2003, [4] J. Biol. Chem. 279, 7024-7028, 2004, [5] J. Biol. Chem. 278: 19183-19189, 2003, [6] J. Biol. Chem. 279: 51013-51021, 2004, [7] Cell Microbiol 7, 1285-293, 2005, [8] Infect Immun. 74, 6571-65 80, 2006, [9] Proc. Natl. Acad. Sci. USA. 102, 9661-9666, 2005.

2. The fimbriae of Vibrio cholerae is under study the possibility for use in cholera vaccine.

Professor	Toshiya Hirayama
Senior Assistant Professor	Akihiro Wada
Assistant professor	Masahiko Ehara
Technologist	Mamoru Iwami
Technician	Kayo Maeda
COE Technician	Kumi Tamura
Postdoctral Fellow	Masaaki Nakayama
Postgraduate Student	Jyunzo Hisatsune



Virulence mechanism of *Helicobacter pylori* vacuolating cytotoxin, VacA.



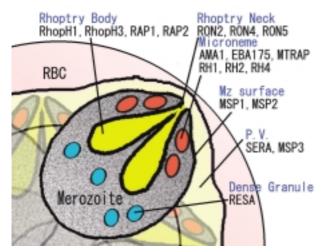
Laboratory

### Department of Protozoology

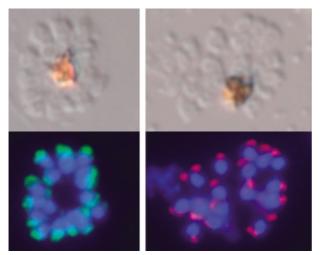
Our goal is to clarify the infection mechanisms of the intracellular protozoan pathogens, such as *Plasmodium* malaria parasites, *Trypanosoma* spp, and *Leishmania donovani*.

#### 1 .Malaria

1 )Molecular basis of the erythrocyte invasion of the malaria merozoites



Schematic of the malaria merozoite and its invasion-related molecules.



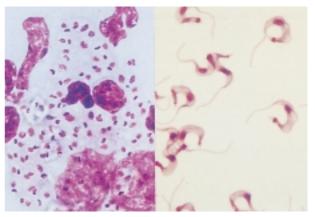
Newly identified malaria proteins were localized to the apical end of the merozoites. Blue is parasite nucleous, green and red are the location of the identified proteins. Upper panels are DIC images of the malaria parasite.

- 2 ) Molecular basis of the cytoadherence of the malaria-infected erythrocytes
- 3 ) Searching the parasite antigens that are the host immune target
- 4 ) Survival strategies of the malaria parasites in the host
- 5 ) Epidemiology of the drug-resistant *P. falciparum* malaria
- 2 .Trypanosoma
- 1 ) Functions and expression of transsialidase
- 2) Adaptation mechanisms of *Trypanosoma* spp to environments
- 3 ) Modification of infected host-cells by *Trypano*soma cruzi

#### 3 .Leishmania

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

Professor	Osamu Kaneko
Senior Assistant Professor	Haruki Uemura
Assistant Professor	Shusuke Nakazawa
Technician	Miki Kinoshita
Graduate Student	Kishor Pandey
Graduate Student	Akikocristina Salati



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

### Department of Parasitology

The research activities are concentrated on filariasis and schistosomiasis 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 Cardiospermun halicacabum 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 NaHCO<sub>3</sub> was evalualed.

4 ) Chemotaxis of filarial infective larvae:

We first reported *B pahangi* infective larvae show chemotaxis to serum. The peculiar chemotactic movement and the signal transudation involved in chemotactic response were also reported. Serum factors that cause chemotactic response of larvae are investigated.

#### Schistosimoasis

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.

 ${\bf 3}$  ) Epidemiology and control of  ${\it S.}$  haematobium infection:

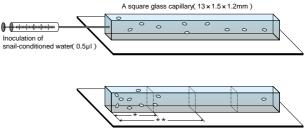
Since 1981, the research project on Schistosomiasis haematobia was carried out in Kwale, Kenya, in cooperation with KEMRI for 25 years. The highlights of our studies are human water contact study, cercarial concentration in natural water, ecology of *Bulinus globosus*, usefulness of urinary reagent strips, 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.

4) A novel tool for control of schistosomiasis, Decoy snails: Schistosome miracidia invade nonintermediate snails too. Presence of the huge number of decoy snails that attract powerfully miracidia, but do not allow miracidia to develop, is expected to block the life cycle of schistosome. The studies on decoy snails are carried on.

Yoshiki Aoki
Kanji Watanabe
Yoshinori Mitsui
Mitsumasa Miura
Satomi Tominaga
Masako Hayashida
Tomoharu Ohki
Teruyo Kusaba
Mayumi Abe



Examination of difficulty of urination by using Uroflowmeter in an endemic area of Kenya



Accumulation of miracidia at the first fourth( \* )and the first half( \*\* )of the tube.

Observation of the snail-conditioned water that has attraction for schistosome miracidia

### Department of Thermal Adaptation

The department was established in1994 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 mach 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 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 mount 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 warms 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



Experiment of thermal sweating in the environmental chamber



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<sup>phox</sup>, a core component of the oxidase

The phagocyte NADPH oxidase is composed of membrane-integrated flavocytochrome b 558 containing gp 91<sup>phox</sup> and p 22<sup>phox</sup>, and cytosolic components such as p 47<sup>phox</sup> and p 67<sup>phox</sup>. 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<sup>phox</sup>, in a patient with chronic granulomatous disease (CGD), we found that PU.1, a transcriptional activator, bound to gp 91<sup>phox</sup> promoter position centered to bp -53 was important for the expression of gp 91<sup>phox</sup> 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.

#### Analysis of NADPH oxidase

We are receiving blood samples to check whether the patients are CGD or not by testing genomic DNA and protein. And also we check mRNA to detect the length because there are skipping mechanisms to avoid pre-mature stop.

#### A novel GT-mismatch binidng protein

In the analysis of a *cis*-element of gp 91<sup>phox</sup> 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 occured more at TRTRNB sites than at other sites in tumor supressor 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	Michio Nakamura
Visiting Professor	Tomoyuki Maekawa
Associate Professor	Futoshi Kuribayashi
Assistant Professor	Yoshito Fujii
Technical assistant	Kanae Tanaka



### Department of Pathology

Main purpose of our research is fundamentally pathological investigation of tropical diseases, mainly infectious diseases, focused on its geographical and ethnical peculiarities, namely interdisciplinary study on environmental pathology: environmental factors, human ecology and disease manifestation in the tropics, and establishes the basis of their treatment and prevention.

Pathological diagnosis of infectious diseases.

The pathology department is responsible for histological diagnostic pathology of surgical specimens, especially focused on bacterial, viral, protozoal and helminthous diseases in the tropics.

Carcinogenesis in oncogenic virus infections.

Cervical, cancer, malignant lymphoma, including Burkitt lymphoma, hepatocelluar carcinoma which are caused by oncogenic virus infection such as human papillomavirus (HPV), Epstein-Barr virus (EBV), hepatitis B and C virus (HBV, HCV), respectively are common and important malignant tumors in the tropics. We are carrying on an epidemiological research of these malignant tumors in tropical Africa and South-East Asia and also investigating carcinogenesis of these oncogenic viruses using the molecular and pathological methods.

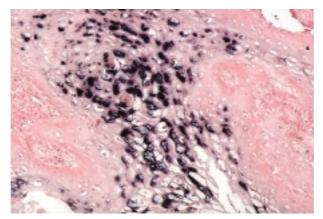
Hepatitis virus infection in South-east Asia

HBV and HCV infection is a world-wide public health problem. More than 2 billion people have been infected with HBV and around three quarters of the infection occur in Asia and Africa. We are carrying on a seroepidemiological research to know a risk assessment of HBV and HCV infection in northern Thailand and Lao PDR.

Clinicopathological study of the liver diseases.

In collaboration with First Department of Internal Medicine, Nagasaki University Hospital and Department of Pathology, Chiang Mai University, we are investigating liver biopsy specimens from both areas and comparing the clinicopathological manifestations.

Associate Professor Assistant Professor Technician Toriyama, Kan Senba, Masachika Nakamura, Masako



HPV in penile cancer (by ISH method)

### 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 are also developing a rapid and comprehensive assay to identify pathogens causing respiratory infections.

#### 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 pneumona, diarrhea, dengue fever), health utilization pattern. Since 2006, a research clinician has been dispatched from our department and monitoring all pneumonia cases admitted to the pediatric ward at Kan Hoa General Hospital in the above city.

#### 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 and maintained in Lampang Hospital, northern Thailand. So far, over 1200 people have participated. The main objectives of this cohort are to understand mechanisms of resistance to HIV infection among HIV-exposed but uninfected spouses living with HIV-infected patients and mechanisms of slow-progression among HIV-infected slowprogressors. These studies are being conducted in close collaboration with Thai counter parts and international experts in various fields such as hostgene polymorphisms, molecular immunology, molecular epidemiology and virology. Furthermore, based on this field setting, we are also conducting studies on frequencies of opportunistic infection, the effect of anti-retroviral drug therapy, and social need for children born to HIV-affected parents.

#### 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.

#### Department of Internal Medicine

Professor Associate Professor Assistant Professor Kei Miyagi Research Associate COE Assistant Professor Hiroshi Nakaoka COE Researcher COE Researcher Technician Technician Technician Secretary Postgraduate student Keita Oma Postgraduate student Postgraduate student Assistant Professor (Project) Lay Myint Yoshida Assistant Professor (Project) Motoi Suzuki

Koya Ariyoshi Konosuke Morimoto Kiwao Watanabe Mariko Saito Sei Nishimura Miki Magome Kanako Fujino Chen Meng Rika Nogawa Naho Tsuchiya Masahiko Mori Takayuki Oike Toshitaka Sukizaki Yoshiyasu Yoza Vu Thi Thu Huong Chiharu Kaji Hiroaki Yoshii Nanae Taguchi Takeshi Yamamoto



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 mechamism 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. 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 CD4 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 CD4-independent HIV is introduced to cells expressing CXCR4 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 CD4-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



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 trasmission of insect-borne diseases, and pursuing environmental friendly vector control strategy.

1 . Ecology and control strategy of dengue/DHF vectors

Ecological mapping of dengue/DHF vectors is conducted in Vietnam focusing to abandoned tires which are one of main breeding sources of the vectors. An epidemiological study also is conducted at several town blocks in NyaTrang city, southeast Vietnam, to clarify key breeding containers reflecting the life style of local people.

2 . Ecological, physiological and genetic studies on malaria vectors

Geographical distribution, ecological/physiological differences, and evolution of malaria vectors composed of the species complex are studied from molecular biological and genetic approaches focusing on *Anopheles gambiae* group in Africa and *An. minimus and An. dirus* groups in Asia. 3 . Basic studies on newly developed vector control measures

Efficacy of newly developed pyrethroid as a space repellent is evaluated in a laboratory and tropical fields. Improvement of mass rearing and planting techniques of *Mesocyclops*, which is a hopeful biological agent against dengue vector mosquito larvae, is challenged by laboratory and field trials in Vietnam. Status of insecticide resistance is continuously monitored.

#### 4 . Detection of virus in mosquitoes

Under collaboration with Department of Virology, ITM and Department of Medical Entomology, NIID detection of virus from a variety of mosquitoes is continued.

Professor	Masahiro Takagi
Senior Assistant Professor	Hitoshi Kawada
COE Researcher	Kazunori Ohashi
Resercher Fellow	Kohei Takenaka
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 11 th 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 admin-

istrative measures.

- 7 . Reformation and coordination of health manpower traning 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 2007 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 preventive measures for infectious diseases from the view point of the crisis management.
- b) Analysis on socio-environmental factors of the control and prevention of infections using the remote sensing and GIS.

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

We participated in various kinds of national or international meetings regardless of specific field barrier.

Professor Assistant Professor Assistant Professor Research Assistant Technician Visiting Researcher Visiting Researcher Postgraduate Student Tsutomu Mizota Kensuke Goto Takeshi Yoda Rie Ushitani Emi Nakayama Chizuko Suzuki Susumu Tanimura Kazuo Minematsu



The Dept. often organizes Int'l Symposia.



Lecture on' Development and Aid in the Master course of Tropical Medicine.

### 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 Waccine development for schitosomiasis 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 chronia 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 Latia

Americas 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: Tharmmasat University (Thailand), Noguchi Memorial Medical Research Institute (Ghana), Institute of Medical Research (Malaysia), Karolinska Institute (Sweden), Ehime University (Matsuyama), WHO/ TDR (Geneva Switzerland)
- 2 Schistosmiasis: 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 Hemorragic Fever)

Host factors will be detected by the Populational genetic analysis of the patients with DHF and non DHF.

#### Staffs

Professor Professor (Project) Associate Professor Senior Assistant Professor (Project) Mihoko Kikuchi Assistant Professor Research fellow **COE** Researcher Technician Technician Technician Ph. D. Student MSc Student

Kenji Hirayama Michio Yasunami Nobu Ohwatari Nguyen Huy Yien Huang Ming Guo Naoko Okuda Junko Hayashima Hitomi Horie Makiko Okamoto **Dujdow Songthamwat** Akiko Takaki Ekhlas hamed Abdel Hafeez Abdow Nguven Thi Phuong Lan Akiko Yamazaki Helegbe Gideon Kofi Edelwisa Segubre Mendoza Del Puerto rodas Ramona Florencia



Department of Molecular Immunogenetics



Clean Room for Cell Cuture

### 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 12<sup>th</sup> 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 neoplasmic 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, which includes a travel clinic. 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 bed-side 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.

#### Clinic at the University Hospital

Professor Associate Professor Assistant Professor Assistant Professor Assistant Professor Research Fellow Research Fellow Research Fellow Research Fellow Research Fellow Resident Physician Resident Physician Assistant Professor Assistant Officer Koya Ariyoshi Konosuke Morimoto Yoshiko Tsuchihashi Reiki Kuroki Akitsugu Furumoto Mayumi Terada Takeshi Tanaka Takahiro Nakama Yoshiro Yamashita Koji Yamada Tohru Ogasawara Nobuo Saito Kenichi Nobusue Shoko Honda Kozue Abiru

### 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 Regulation 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 Research Associate Technician Michio Nakamura Tetsuo Yanagi Junko Kawashima



Clinical conference



Mongolian gerbil (Meriones unguicalatus)

### 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. RECTID was established 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 ecoepidemiological 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 was renovated and opened on 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 researches. 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 Visiting Professor

Visiting Professor

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

Kazuhiko Moji Masaaki Shimada Masahiro Horio Nick Mascie-Taylor (Cambridge Univ) Pathom Sawanpanyalert (Thai NIH) Sumihisa Honda Hiroshi Nishiura Akiko Matsuyama Toshihiko Sunahara Masahiro Hashizume Nahumuki Nishikozi

Nobuyuki Nishikiori Shouhei Takeuchi Guoxi Cai Kyoko Sakitani Kazuo Araki Kivomi Suda Youji Shimizu Akiko Komazawa Yoshiki Hamada Akio Ohno Yuko Nakao Tomoko Abe Rieko Nakao Magafu Mgaywa Damas Osuke Komazawa Ayumi Nomura Etuko Hatagishi Mugen Ujiie



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 UItramicrotome (Reichert), con-focal laser microscope system (LEICA DMIREZ), a flow cytometer (Becton), Bioimage analizers (Hamamatsu Photonics, Bio rad GS-250 and Pharmacia Image master), DNA sequancers (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	Kouichi Morita
Research Associate	Akitoyo Ichinose
Technician	Takako Chiba



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)

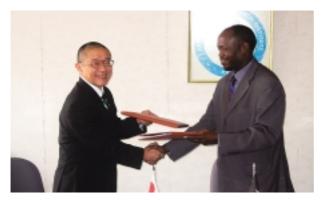
#### Outline of the program

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 haemtobia, 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



National Institute of Hygiene and Epidemiology (NIHE)

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 longbased 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



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 Takenobu Hayashida, Chief Naomiki Yamamura, Sub-Chief Kaori Nagatomo, Sub-Chief Fumiko Hashiguchi, Sub-Chief 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 Kumiko Shimizu, Assistant Staff

Collaboration Research Unit Hidemitsu Noguchi, Chief Yumiko Matsumoto, Assistant Staff Miyuki Yamashita, Assistant Staff

### Number of Staff

(as of May, 2007)

Divisions	Professor	Associate Professor	Lecturer	Assistant Professor	Assistant	Sub total	Others	Total
Enrollment	11 (4)	5 (1)	3	13 (1)	3	35 (6)	8 (2)	43 (8)

( ) number of fixed-term staff

### Accounting

Revenue (in 20 Divisions	Amount (in thousands)
Tuition and Matriculation Fee	2,265
Others	212
Total	2,477

Expedditure	(in	2006)	١
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Divisions	Amount (in thousands)
Personnel expenses	511,113
the cost of equipment	480,386
Total	991,499

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

(in 2007)

Classification	Scientific Re- search on Pri- ority Areas	Scientific Research (A)	Scientific Research (A)	Scientific Research (B)	Scientific Research (B)		Explora- tory Re- search	Young Scientists (Start Up)	Total
Number of Grants	1	2	1	6	1	3	4	1	19
Amount (in thousands)	7,700	32,760	24,180	38,220	5,460	6,630	7,000	1,350	123,300

# Grant-in-Aid for Scientific Research from the Ministry of Health, Labour and Welfare (in 2007)

Classification	International Medical Cooperation	Emerging and Reemerging Infectious Diseases	AIDS Control	Research Fund Project on Health Sciences focusing on Drug Innovation	Clinical Cancer	Total
Number of Grants	1	2	1	1	1	6
Amount (in thousands)	14,827	14,500	8,500	2,500	500	40,827

### Grant-in-Aid for Forming Research Locations etc (21 st Century COE Program)

Fiscal Year	2003	2004	2005	2006	2007
Amount (In thousands)	193,000	157,300	172,100	214,236	214,500

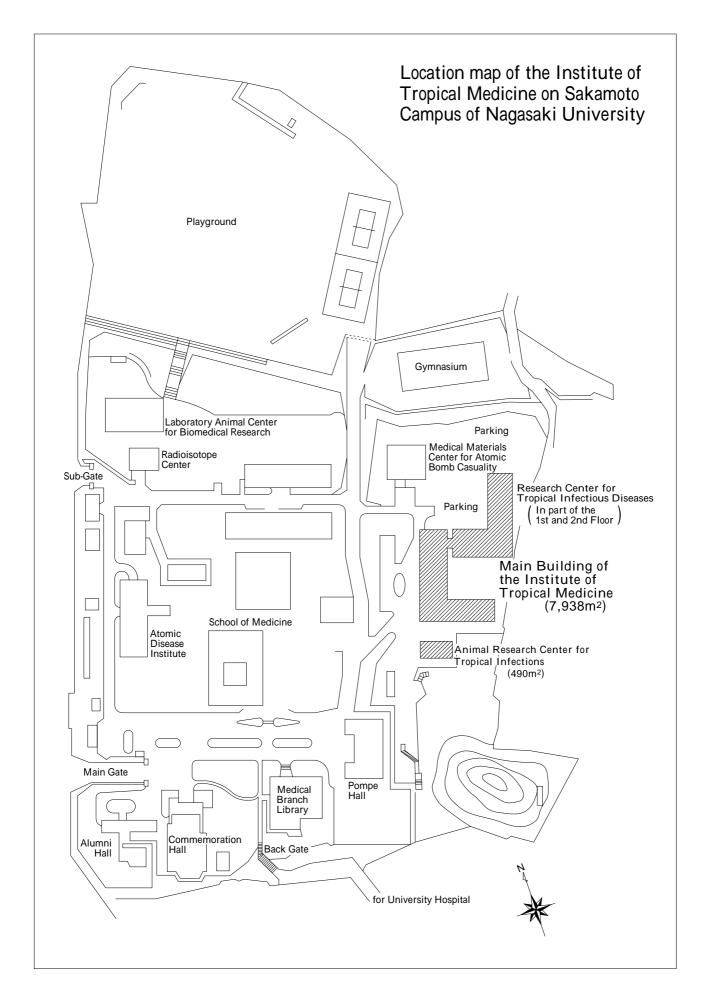
# External Funding

(in 2006)

Divisions	Cooperative Research	Commissioned Research	Endowments
Number of Sources	1	6	19
Amount (in thousands)	2 ,000	37 253	16 ,200

### 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



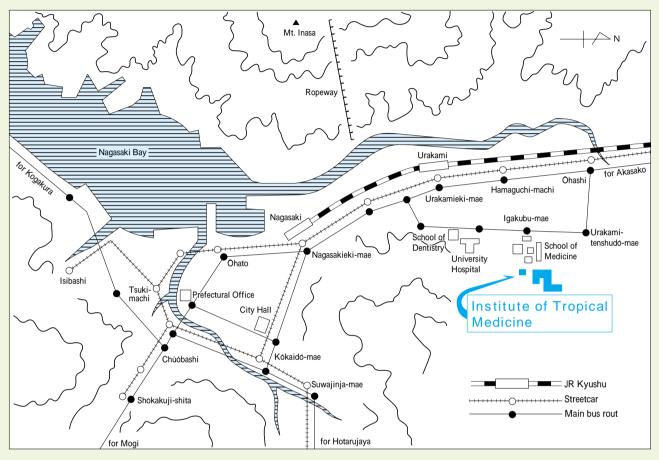
# Telephone Number

Institute of Tropical Medicine, Nagasaki University	
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Extens	ons
Dean	849 7801
Head of Administrative Office4701	849 7802
Chief of General Affairs Unit	
General Affairs Unit	849 7803
General Affairs Unit	
General Affairs Unit	849 7806
General Affairs Unit	
Chief of Collaboration Research Unit4709	
Collaboration Research Unit	849 7807
Facsimile	849 7805
Meeting Room	
Department of Virology	
Professor	849 7827
Associate Professor	849 7828
Information	849 7829
Facsimile	849 7830
Department of Bacteriology	
Professor	849 7831
Lab 2	849 7832
Lab 3	849 7833
Department of Protozoology	
Professor	849 7835
Lab 2	849 7836
Lab .1	849 7837
Information	849 7838
Department of Parasitology	
Professor	849 7822
Staff room	849 7823
Lab	849 7824
Information	849 7825
Department of Molecular Epidemiology	
Professor	849 7860
Department of Thermal Adaptation	
Professor (Concurrent)4726	849 7820
Department of Biochemistry	
Professor	849 7848
Lab .1	849 7849
Culture room	849 7850
Information	849 7851

Department of Pathology	Extensions	
Professor	4719	849-7813
Associate Professor	4720	849-7814
Staff room	4721	849-7815
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)

- ①Get on a bus (Nagasaki Bus, Line 8 ) at Nagasakieki-mae and get off at Igakubu-mae. Five minutes walk from the bus stop.
- ②Get 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.
- ③Ten minutes by taxi from the station.
- 2 . From Urakami Station (JR Kyushu)
  - 1 Twenty minutes walk.
  - <sup>(2)</sup>Five minutes taxi.
- 3 . From Nagasaki Airport
  - ①Get on limousine at the airport ( for Nagasaki ), and get off at Nagasaki-ekimae, and then continue to 1.
  - <sup>(2)</sup>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.
  - ③About 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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