INSTITUTE OF TROPICAL MEDICINE NAGASAKI UNIVERSITY





2005

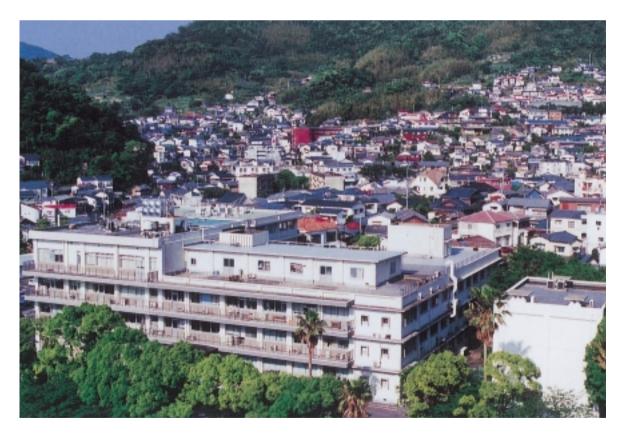
MISSION STATEMENT

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
- $\ensuremath{\mathsf{3}}$. Cultivation of the researchers and specialists in the above fields



General view of the Institute

Coverpage: Growth monitoring of young children in Savannakhet Province, Lao, P.D.R. (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 con-

tinue 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, 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 degree course which belongs to Graduate School of Biomedical 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 21 st 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.

August, 2005 Yoshiki Aoki M. D., D. M. Sc. Dean and Professor Institute of Tropical Medicine Nagasaki University

Contents

Preface	. 1
Contents	. 2
Historical Review	. 3
Successive Deans of the Institute	. 4
Organizational Chart	. 5
Collaboration research	. 6
Institute of Tropical Medicine Steering Committee	. 7
Institute of Tropical Medicine Collaboration Professional Committee	. 8
Scope of Activities	. 9
Postgraduate School	. 9
Three-month Course on Tropical Medicine and Related Studies	. 9
Training Course in Research of Tropical Medicine	.10
Public Lectures at the Institute	.10
Publications	.10
The 21st Century Center of Excellence Program	.11
Department of Virology	.12
Department of Bacteriology	.13
Department of Protozoology	.14
Department of Parasitology	.15
Department of Thermal Adaptation	
Department of Host-Defense Biochemistry	.17
Department of Pathology/Division of Clinical Investigation	.18
Department of Internal Medicine	.19
Department of Preventive Medicine and AIDS Research	.20
Department of Vector Ecology & Environment	.21
Department of Social Environment	.22
Department of Molecular Immunogenetics	.23
Department of Internal Medicine (University Hospital)	.24
Animal Research Center for Tropical Infections	.24
Research Center for Tropical Infectious Diseases	.25
Central Laboratory	.26
Administration	.26
Number of Staff	.27
Accounting	.27
Grant-in-Aid for Scientific Research from the Ministry of Education,	
Culture, Sports, Science and Technology	.27
External Funding	.28
Site and Buildings	.28
Agreement of Educational, Scientific and Scholaly Exchange	.28
Location map of the Institute of Tropical Medicine on Sakamoto Campus	
of Nagasaki University	.29
Telephone Number	.30

Historical Review

The Institute of Tropical Medicine, Nagasaki University was originally founded in March 1942, as the East Asian Research Institute of Endemics, 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 in mainland China, performed by several department such as Pathology, Bacteriology, Internal Medicine and Dermatology of Nagasaki College of Medicine. Unfortunately, all the facilities and research materials were completely destroyed instantaneously along with the Medical School by the atomic bomb which exploded on August 9 th, 1945. As a result, development of the institute and its research activities were severely inhibited.

In April 1946, the institute was named as the Research Institute of Endemics attached to Nagasaki College of Medicine, and moved to Isahaya City in May in order to resume its research activities. In accordance with the Act on the Foundation of National Schools in May 1949, the institute was renamed as the Research Institute of Endemics, Nagasaki University. Becauce of the severe flood in Isahaya City, the construction of the new building in Sakamotomachi, Nagasaki City was started in 1960, and the institute moved to new building in April, 1961. At that time, there were only two departments, Pathology and Clinics, however, since 1964, new departments were established every Year, such as Epidemiology, Parasitology, Virology and at the end of 1966, the first extension of the building was completed.

In June 1967, according to the partial alteration of the Act on the Foundation of National Schools, the name of the institute was changed to the present one, in order to perform basic as well as applied studies on tropical medicine. At the same time, the Department of Internal Medicine of the institute with 20 bed facilities was opened in the University Hospital. In 1974, Department of Bacteriology and Reference Center as an attached facility were opened. In 1978, the Department of Preventive Medicine suppoeted by visiting staff and the Training Course of Tropical Medicine were started. In 1979, Ward of Infectious animals became Animal Research Center. In March 1980, the 2 nd extension of the main building was concluded. In September 1983, the Training Course in Research for Tropical Medicine by JICA was opened. In 1984, Department of Protozoology was established. In July 1985, the 3 rd extension of the building was completed. In 1987, Department of Medical Entomology was established. In 1989, the institute was reorganized to a collaboration research institute. In 1991, Department of Biochemistry was added. In March 1994, the 4 th extension of the building was completed, and in April, 1994, the institute was reorganized to 3 research fields, Tropical Microbiology, Pathogenesis and Clinical Sciences, and Environmental Medicine, with addition of 2 new research departments, Thermal Adaptation and Social Environment, and the institute has 12 research departments at present. In 1995, the Institute was designated as one of the " Centers of Excellence " in the forefront of scientific research. In 1996, a new research department, Molecular Epidemiology, was established under the Research Field of Microbiology to invite an overseas visiting professor. In 1997, the Reference Center was abolished and in its place the Information and Reference Center of Tropical Medicine was established, then in 2001 ,it was abolished and in its place the Research Center for Tropical Infectious Diseases was established. In March 2003 ,the 5 th extension of the building was completed, symbolizing continuous consolidation and reorganization of the Institute.



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

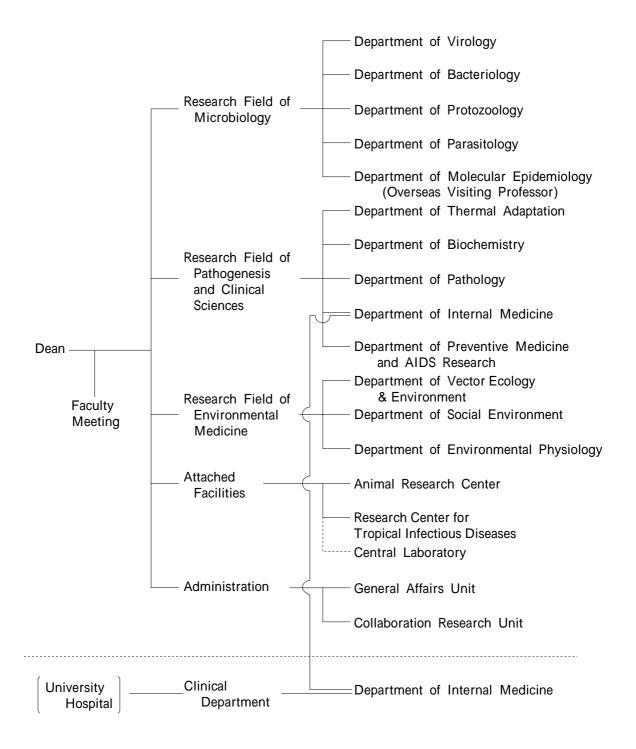
(Research Institute of Endemics)

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

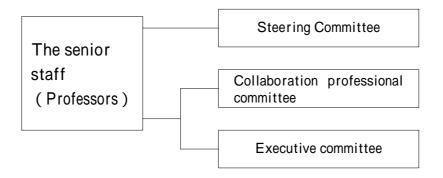


Collaboration research

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 Emetitus	Akira Igarashi
National Institute of Infectious Diseases	Duputy 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	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	Pegent	Shigeru Katamine
Graduate School of Biomedical Sciences	Dean	Koutaro Taniyama
Institute of Tropical Medicine	Dean	Yoshiki Aoki
11	Professor	Kouich Morita
11	Professor	Toshiya Hirayama
11	Professor	Hiroji Kanbara
11	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
"	Professor	Osamu Kunii
		e t 1

: 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 Internationa	I Studies	
	Professor	Akira Oki
Graduate School of Medicine The University of Tok	уо	
	Professor	Kiyoshi Kita
Graduate School of Veterinavy Medicine, Hokkaido	University	
	Professor	Ikuo Takashima
Chiba University Research Center for Pathogenic and	nd Microbial To	oxicoses
	Professor	Kazuko Nishimura
Tsuda College Undergraduate Courses	Professor	Chizuru Misago
Kobe University Graduate School of Medicine	Professor	Haku Hotta
The Japan Center for Area Studies, National Museu	m of Ethnology	
Assistan	t 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
		• Chair

: Chairman

Scope of 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.

Three-month Course on Tropical Medicine and Related Studies

The course aims to provide participating persons with a better understanding of the health problems in tropics, to increase their ability to cope with them, and to give a fuller knowledge of the cultures and the life of the people in tropics.

Physicians and professionally qualified persons working in health and related fields may apply for admission to the course. Fifteen candidates are accepted to the course in a year. The course consists of 13 weeks (June-August) of instruction and examination. Teaching is undertaken by the full-time staff and guest lecturers.

The course provides lectures and laboratory and field practices in virology, bacteriology, protozoology, parasitology, medical entomology, environmental physiology, biochemistry, pathology, genetics, epidemiology, human ecology, social medicine, internal medicine, and geography and culture in tropics. Candidates who completed successfully the course are awarded the Diploma in Tropical Medicine.



Adomission ceremony in 2005

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 Lectures at the Institute

Annually, the Institute of Tropical Medicine holds public lectures for the citizens. The lectures address issues pertaining to travellers to regions endemic to tropical diseases. It is intended to prepare the public to maintain good health abroad. The other aim is to open our intellect and knowledge to the public.

Publications

Tropical Medicine

This is a quarterly journal with publications of original articles from the Institute. The journal was first published in March 1959 as "Endemic Diseases Bulletin of Nagasaki University ". In 1967, the name was changed to "Tropical Medicine". The publication has been suspended since 2002.

Institute of Tropical Medicine, Nagasaki University

The first English guide for foreign visitors was printed in 1971. A revised edition is published every year.



Adomission ceremony in 2004

The 21st Century Center of Excellence Program

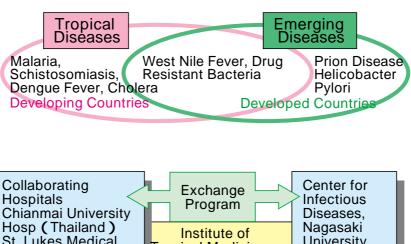
Program Title : Global Control Strategy of Tropical and Emerging Infectious Diseases

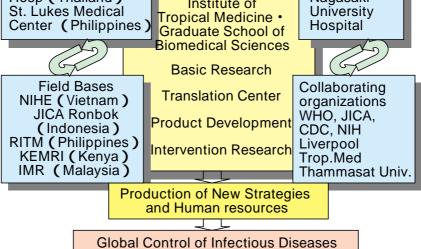
The core courses to form the program : Institute of Tropical Medicine, Graduate School of Biomedical Sciences Program Leader : Yoshiki Aoki

《Program Summary》

Global strategy for the control of tropical and emerging infectious diseases is urgently required by the world community. This program is designed to help our COE (Center of Excellence) to be one of the world top five centers for advanced research and education in this field within 5 years under the support of Ministry of Education, Sports, Culture and Science, Japan. Our COE is coordinated by three institutions of Nagasaki University and started in 2004. Institute of Tropical Medicine will focus on the field based research and education. Graduate School of Biomedical Sciences will mainly perform laboratory based research. The infectious disease center will be responsible for the field or clinical practice and trial. The three institutions will be coordinated to find and establish a new strategy for the control of the disease.

We have established several field sites in Southeastern Asia and Africa. For producing the experts in this field, we will set up the master degree course of tropical medicine in addition to already existed Ph.D. course. For the medical doctors' training, we opened a clinical training short course this year in the infectious disease center as well as in the affiliated hospitals located in the tropical countries such as Philippines and Thailand.





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

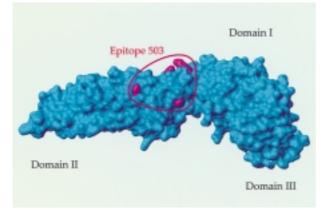
Viral genome detection and identification by PCR and LAMP methods, preparation of diagnostic antigen from infected cell culture fluid, and simplification of IgM antibody detection have been carried out.

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 was designated 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 of 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. in March 2004, Dr Futoshi Hasebe was dispatched to the WHO Western Pacific Regional Office to collaborate in the global emerging infectious disease control program.

Professor Assistant Professor Research Associate **Research Associate** Research Fellow **COE** Researcher Guest Research Fellow Guest Research Fellow Senior Research Assistant Technician Postgraduate student Postgraduate student Postgraduate student Postgraduate student Assistant Staff Ronpaku Fellow **JICA Student**

Kouichi Morita Futoshi Hasebe Shingo Inoue Md Alimul Islam Takeshi Nabeshima Afjal Hossain Khan Maria del Carmen Parquet Edward G. Mathenge Tomomi Yamaguchi Kazumi Jodai Hitomi Kinoshita Thai Hong Thicam Yu Fuxum Leonora Salda Mariko Oniduka Paresh Sumatilal Shah Nemani Telemaitoga Yuming Jin



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 enteropathobacterium. Glycosylphosphatidylinositoldenic 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 investigates the hostparasite 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 (dominantnegative) syntaxin 7 mutant, VacA failed to induce vacuolation, suggesting that SNARE is involved in theintracellular vacuolation induced by VacA (J.Biol. Chem. (2003) 278:25585-25590).

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

3 Mice deficient in protein tyrosine phosphataseb 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) .

4 Human β-defensin-2 (hBD-2) is an antimicrobial peptide which belongs to one of the most important host defence system against bacterial infection in several epithelial tissues. We studied the effect of H. pyloli on the expression of hBD-2 mRNA in MKE 45 gastric mucosal cells. H. pylori, but not culture filtrate, increased hBD-2 mRNA level in MKN 45 cells, whereas thus 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-KB activation in MKN 45 cells.

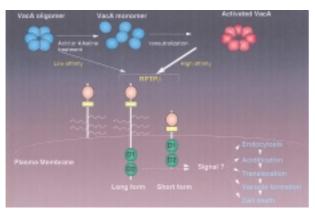
Exposure of MKN 45 cells to Salmonella typhimurium, S. enteritidis, S. typhi, and S. dublin, but not Escherichia coli ML 35, resulted in remarkable induction of hBD-2 mRNA. (Cell. Microb. (2001) 3: 115 J. Immuml (2004) 173: 5398)

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 Assistant Professor Research Associate Technologist Postgraduate Student Masaaki Nakayama Postgraduate Student Jyunzou Hisatsune PRESTO Researcher Eiki Yamasaki PRESTO Technician Kayo Maeda COE Technisian

Toshiya Hirayama Akihiro Wada Masahiko Ehara Mamoru Iwami Kumi Tamura



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



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 *Plamodium falciparum* in mammalian hosts.
- 3) Epidemiology of human malaria.

Study of trypanosomes

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

Stady of Leishmania

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

Other studies

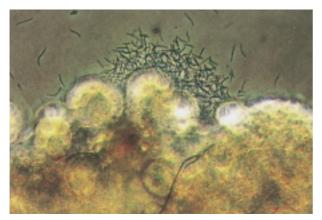
- 1) Epidemiology of intestinal protozoan infection.
- 2) Biological chracterization of microsporidia.



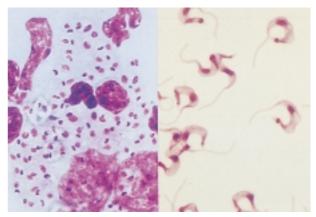
Hiroji Kanbara Haruki Uemura Shusuke Nakazawa Mohammed Nasir Shuaibu Miki Kinoshita Megumi Morisaki Toshio Miyazaki Kishor Pandey Ali Takadir Mtoro



Laboratory for culture



Plasmodia sporozoites from ruptured oocysts in Anopheline mosquito



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 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 NaHCO₃ was evalualed.

4) Chemotaxis of filarial infective larvae:

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

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.

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 20 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, epidemiologial 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
Technologist	Mitsumasa Miura
Technician	Satomi Tominaga
Postgraduate Student	Tomoharu Ohki
Postgraduate Student	Teruyo Kusaba
Postgraduate Student	Mayumi Abe
Postgraduate Student	Mayumi Abe
Postgraduate Student	Xinsong Zhang



Examination of difficulty of urination by using Uroflowmeter 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 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^{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 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
Assistant Professor
Research Associate
Research Assosiate

Technologist Secretary Michiko Nakamura Futoshi Kuribayashi Yoshito Fujii Shoichi Suzuki (...in suspension) Toshiyuki Moriuchi Mizue Nakamura



Department of Pathology / Division of Clinical Investigation

In1970 ,the Late Professor Toyosuke WATAN-ABE classified tropical diseases into 4 groups:

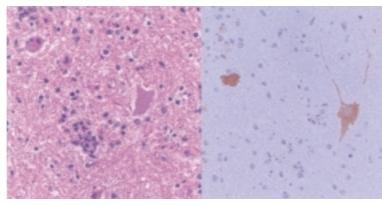
- 1 . Diseases caused by pathogens, uniquely present in the tropical areas.
- 2 . Diseases induced by environmental factors such as tropic climate.
- 3 . Diseases specific for some habitants in the tropical areas due to their high susceptibility.
- 4 . Diseases difficult to prevent in developing countries.

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 pathogeneses.



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 manifestaions 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 pathogeneses.

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
Postgraduate Student	HATAGISHI, Etsuko
Research Assistant	FUKUMA, Aiko
Technician	NAKAMURA, Masako

Department of Internal Medicine

Main objectives of research activities in the Department of Internal Medicine are to understand pathogenesis of tropical 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

We are investigating factors causing refractory respiratory infectious diseases, such as biofilm formation of causative pathogens and clearance mechanisms of apoptotic neutrophil by pulmonary macrophages. We also conduct studies on molecular epidemiology of pneumococcus, hemophilus influenza etc, acquired immunity against these pathogens in the lung, mucosal vaccine development.

2. 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.

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 further hostgene polymorphisms, molecular immunology, molecular epidemiology and virology studies for a better understanding of HIV transmission and HIV pathogenesis.

4. 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.

5. Acuter respiratory infections among pediatric patients in Vietnam

In collaboration with National Institute of Hygiene and Epidemiology, we are conducting studies on clinical and bacteriological diagnosis, antimicrobial susceptibility and molecular epidemiology.

Professor Associate Professor **Research Associate Research Associate** Technician Technician Secretary COE Researcher Postgraduate student Postgraduate student

Koya Ariyoshi Kazunori Oishi Takeshi Yamaryo Kiwao Watanabe Naoko Kitajima Miki Magome Rika Nogawa Mariko Saito Jun Koyama Takayuki Oike Toshitaka Sukizaki Yoshiyasu Yoza Chen Meng Chiharu Kaji Hiroaki Yoshii Keita Oma Natsuki Matsumoto



Research on bacteriology in BSL 2 laboratory



Laboratory of biochemical research

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 ProfessorNaoki YamamotoVisiting Associate ProfessorHironori SatoAssistant ProfessorYoshinao KuboCOE ResearcherMasaru YokoyamaTechnicianChika Tominaga



On the other hand, there are some evidences

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 . Physiology and ecology of malaria vectors

A long-term monitoring on main vectors of malaria has been conducted at several fields in Southeast 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 registance in vector mosquitoes.

ProfessorMAssistant ProfessorHResearch AssociateMCOE ResearcherTSecretaryTResearch AssistantHTechnicianCTechnicianCSecretaryJPostgraduate StudentTPostgraduate StudentTPostgraduate StudentTJICA StudentI

Masahiro Takagi Hitoshi Kawada Nobuko Tuno Toshihiko Sunahara Toshiko Ueno Kozue shimabukuro Chiaki Tsurukawa Emiko Kawashima Junko Sakemoto Maiko Hasegawa Tran Vu Phong Yoshihide Maekawa Isaac Mwangi Kimani



Stereomicroscopic observation of mosquitoes



Ramp traps for collecting mosquitoes

Department of Social Environment

Specific Features of the Department

This Department covers under the 9th 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.
- 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.

Specific themes of joint cooperative research designated to the Department in FY 2004 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)Social and Environmental Diagnosis of Tropical Diseases for its Control and Prevention.
- b)Study on Social bases of health care systems in developing countries.

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

Professor Research Associate Research Assistant Technician Postgraduate Student Postgraduate Student Postgraduate Student JICA Trainee Tsutomu Mizota Susumu Tanimura Tomomi Ikeda Natsuko Imaoka Chizuko Suzuki Qin Liang Takeshi Yoda HId Thein



" Dept. of Social and Environmental Medicine often serves as a secretariat for Int'l Symposia."



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

Department of Molecular Immunogenetics

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

1. Schistosoma japonicum

1) Pathogenesis of hepatosolenic disease

Immnopathology controlled by HLA-ClassII genes is analysed by T cell epitope, Tcell cloning, tetramer analysis, Cytokine network analysis, ELISPOT analysis, 4 color FACS, animal model of HLA Tg mini-pig system

Identification of pathogenic genes by Multiple families (MF) genetic analysis

Association analysis between disease and immune related polymorphic genes

2) Molecular analysis of protective immunity in humans

Protective antigens effective for humans are searched by checking reactivity of superresistant individuals in China.

Experimental animal model (pig)

Analysis of protective immunity in pig, and Vaccine development targetedto somula stage antigens.

Estimation of mRNA expression in somula by SAGE method

3) Surveillance system

Development of novel methodology for the long term surveillance

Environmental research by GIS/RS is introduced to Hilly type schistosomiasis project

2. Malaria

1) Pathogenesis of Severe malaria

Functional analysis of the susceptible TNFP (TNF-alpha promoter) alleles to cerebral malaria

- 2) Protective Immunity in falciparum malaria HLA-Class I restricted CD 8 Tcell analysis in the immunity
- 3. Trypanosoma cruzi

Pathogenesis of the complications
 Human genetic factors to develop Chagas heart,
 or the Mega disease by using HLA-class I,
 MICA, B, TNFP, and other relevant genes.

 Pathogenicity of the parasite
 By Comparisons between three different patho genic parasite lines derived from human patients
 with different clinical types, cardiac, digestive,
 and no complication.

lar basis of the difference between intracellualr proliferative (Peru 1,2) and non-proliferative, (H 1, H 23) are analysed by 2 D

2) Protective immunity Identification of a resistant gene Analysis of the human T cell immunity Protection from transplacental fetal infection.

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 Associate Professor Assistant Professor COE Researcher COE Researcher Technician Postgraduate Student Postgraduate Student Postgraduate Student Postgraduate Student Postgraduate Student JICA Student Kenji Hirayama Nobu Ohwatari Mihoko Kikuchi Kazunari Ishii Naoko Okuda Junko Hayashima Dujdow Songthamwat Akiko Takaki Ekhlas hamed Abdel Hafeez Abdow Nguyen Thi Phuong Lan Akiko Yamazaki Saw Wut Hmone



Department of Molecular Immunogenetics



Clean Room for Cell Cuture

Department of Internal Medicine (University Hospital)

The Department of Internal Medicine is located on the 12th floor of University Hospital. It specializes in the Respiratory and Infectious Diseases. We treat patients with lung cancer, bronchial asthma, pulmonary fibrosis, sleep disorder, tuberculosis (TB) and other systemic infectious diseases, including "tropical" diseases. It has twenty beds and several others in the TB isolated ward. We have a ward round, clinical conference, and journal club every Broncho-scopic examination is being conweek. ducted regularly. We are actively involved in various clinical trials. The outpatient clinic is open two days a week where we started a travel clinic in April 2004. In addition to our educational duties for undergraduate medical students (lectures and bed-side teaching), we have a postgraduate training program for general internal physicians and infectious disease specialists.

Professor Associate Professor Assistant Professor Research Associate Research Associate Research Fellow Research Fellow Research Fellow Research Fellow Koya Ariyoshi Kazunori Oishi Hiroshi Watanabe Hiroyuki Yoshimine Yoshiko Tsuchihashi Shoko Honda Reiki Kuroki Tsuyoshi Kuramoto Reiko Mizutani

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 water used 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 Research Associate Technician Hiroji Kanbara Tetsuo Yanagi Junko Kawashima



Clinical conference



Mongolian gerbil (Meriones unguicalatus)

Research Center for Tropical Infectious Diseases

The Research Center for Tropical Infectious Diseases, Which Inherited its history from the information and Reference Center of Tropical Medicine, was established in April 2001. According to the history the center has three missions.

The center functions as a museum of tropical diseases, which is unique in Japan. Next, the center also provides necessary information and references related to tropical diseases to all the staff, graduate students, researchers and trainees, as well as members of the public who visit the Institute. The third mission of the center is to contribute to the global control of the tropical infectious diseases. We analyze the factors that regulate the epidemics of the diseases to find appropriate control measure of the infection.

References currently available at the center are books, maps, periodicals, pamphlets, films, videocassette tapes, photo slides, photographs, charts, exhibition panels, animal specimens as well as pathological tissue specimens. These materials are now being digitized and are provided to the public through cyberspace. The center also gathers scientific, social economic, and cultural information related to tropical diseases. Our current exhibitions consist of panels of major tropical diseases, diarrhea diseases, acute infectious diseases, AIDS related diseases, and specimen of parasites, vector arthropods and poisonous marine animals.

The center carries out eco-epidemiological studies on tropical diseases by means of fieldwork at the actual site of the problem. We also use computer science technology, such as the geographical information system, remote sensing and information exchanging system, which project the future of tropical infectious diseases from both local and global perspective. One of our main interest is the role of human behavior in the transmission of tropical infectious diseases.

Professor Professor Professor Assistant Professor Research Associate **Research Associate** Research Assistant Research Assistant Technician Technician Postgraduate Student Postgraduate Student

Masaaki Shimada Kazuhiko Moii Osamu Kunii Akiko Matsuyama Eiko Kaneda Nobuyuki Nishikiori Kyoko Sakitani Kazuo Araki Kiyomi Suda Satsuki Kunikane Tomoko Kisu Yoshiki Hamada Yuko Nakao Akio Ohno Sadako Nakamura Guoxi Cai Tomoko Abe Rieko Nakao Magafu Mgaywa Damas Osuke Komazawa



Exhibition room



Schistosomiasis transmission site (Collection of vector snails)

Central Laboratory

There are several equipments at this laboratory. It is open for collaboration research with all part of Japan followings are the equipments now available. Electron microscopies (TEM and SEM of jeol), a UItramicrotome (Reichert), con-focal laser microscope system (LEICA DMIREZ), a flow cytometer (FACScan), a cell sorter (FACSsatar plus), Laser scanning microscopies (Bio rad MRC 600 and Zeiss LSM), micromanipulation system (Nikon-Narishige and Zeiss-shimazu), Bioimage analizers (Hamamatsu Photonics, Bio rad GS-250 and Pharmacia Image master), a peptide synthesizer (Millipore 600 E), a peptide sequencer (Shimazu PPSQ-10), DNA sequancers (Perkin-Elmer 373-70 and Pharmacia AFL), a DNA/RNA extraction system (Perkin-Elmer 341-30), a real-time surface plasmon detecter (Fisons IAsys), two P3 rooms, Super sentrifugal machine (optima L-90 K). with other equipments, experiments on cell biology and histochemistry can be carried out.

Professor and Chief Research Associate Research Assistant Kenji Hirayama Akitoyo Ichinose Hitomi Horie



The TEM of electron microscope Laboratory

Administration

Kinichiro Makiyama, Head Official

General Affairs Unit Tsukasa Harada, Chief Naomiki Yamamura, Sub-Chief Ami Noda, Staff You Kanai, 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 Yasuo Sakanaka, Chief Fumiko Hashiguchi, Sub-Chief Yumiko Matsumoto, Assistant Staff

Number of Staff

(as of May, 2005)

Divisions	Professor	Assistant Professor	Lecturer	Assistant	Sub total	Others	Total
Enrollment	13	4	4	18	39	8	47

Accounting

Revenue (in 2004)

Divisions	Amount (in thousands)
Tuition and Matriculation Fee	1,853
Others	24
Industry-Academic Cooperation	66,541
Donation	14,342
Total	82,760

Divisions	Amount (in thousands)
Personnel expenses	566,026
the cost of equipment	352,688
Total	918,714

Expedditure (in 2004)

Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology (in 2

(in 2005)

Classification	Scientific Re- search on Pri- ority Areas	Scientific Research (A)	Scientific Research (A)	Scientific Research (B)	Scientific Research (C)	Explora- tory Re- search	Young Scientists (B)	Total
Number of Grants	3	1	1	6	3	2	2	18
Amount (in thousands)	17,400	1,600	18,200	23,700	3,600	2,300	2,900	69,700

External Funding

(in 2004)

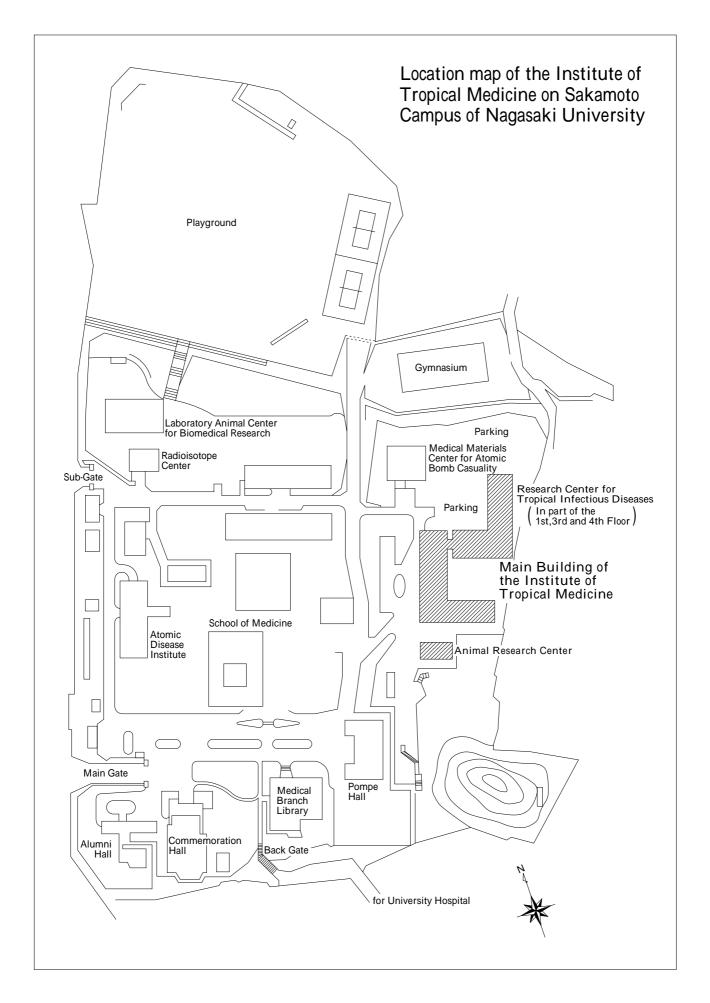
Divisions	Cooperative Research	Commissioned Research	Grants and Endowments
Number of Sources	4件	7件	18件
Amount (in thousands)	2 ,970	43 844	14 ,342

Site and Buildings

Location	12 - 4 Sakamoto 1 chome Nagasa	ki - city
Buildings(m^2)	Institute of tropical medicine (7 /463m ²)	Animal Research Center ($490\mathrm{m}^2$)

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



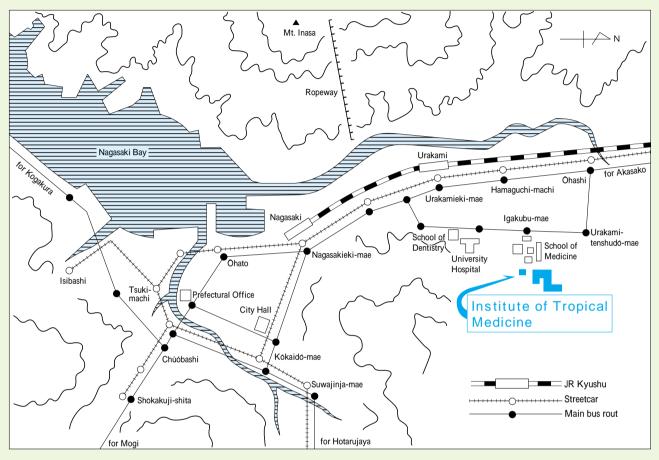
Telephone Number

Institute of Tropical Medicine, Nagasaki University	
-----------------------------------------------------	--

Extensi	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 Unit	
Collaboration Research Unit	849 7807
Facsimile	849 7805
Meeting Room 4711	
Department of Virology	
Professor	849 7827
Associate Professor	849 7828
Information	849 7829
Facsimile	849 7830
Department of Bacteriology	
Professor	849 7831
Lab 9	849 7832
Information	849 7833
Department of Protozoology	
Professor	849 7835
Associate Professor	849 7836
Lab 3	849 7837
Information	849 7838
Department of Parasitology	
Professor	849 7822
Associate Professor	849 7823
Research Associate	849 7824
Information	849 7825
Department of Molecular Epidemiology	
Professor	849 7860
Department of Thermal Adaptation	
Professor (Concurrent)	849 7820
Department of Biochemistry	
Professor	849 7848
Lab .1	849 7849
Lab 2	849 7850
Information	849 7851

Department of Pathology	Extensions	
Professor	4719	849-7813
Associate Professor	4720	849-7814
Lab 2	4721	849-7815
Information	4722	849-7816
Department of Internal Medicine		
Professor	4746	849-7840
Associate Professor	4747	849-7841
Information	4748	849-7842
Facsimile	4749	849-7843
Department of Preventive Medicine and AIDS Research		
Professor	4751	849-7845
Research Associate	4751	849-7845
Information	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
Information	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		
Professor	4778	849-7868
Professor	4779	849-7869
Professor	4759	849-7853
Lab .1	4714	849-7808
Computer Room(2)	4778	849-7868
Information		849-7854
Central Laboratory		
Electron Microscope Room	4765	849-7859
FACS Room	4767	
Section for Experimental Animals	4769	

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)
 - ①Twenty minutes walk.
 - ⁽²⁾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.
 - ②Get 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

Published on July 30, 2005 Edited by Institute of Tropical Medicine, Nagasaki University Printed by Showado Printing Co., 1007 2 Nagano machi, Isahaya 854 0036, Japan