

Research Activities of Japan Initiative for Global Research Network on Infectious Diseases (J-GRID)

Division of Infectious Disease Research
Department of Research Promotion

As of July 2018

[Thailand] Current Activities in Osaka University Laboratories

【Principal Investigator・Directors】



Principal Investigator

Affiliation: Research Institute for Microbial Diseases, Osaka University
Title: Director/ Professor
Name: Yoshiharu Matsuura

Main-Laboratory Director

Thailand-Japan Research Collaboration Center on Emerging and Re-emerging Infections (Thai NIH)

Sub-Laboratory Director

Mahidol-Osaka Center for Infectious Diseases (Mahidol University)



SA Professor
Masashi Tatsumi
(Resident)



Professor
Tatsuo Shioda
(Periodic Resident)

【Laboratories in Thailand】

Thailand Research Institute

- Main Laboratory: National Institute of Health, Thailand
7 Japanese researchers including 4 residents and 18 Thai researchers
- Sub Laboratory: Mahidol University
18 Japanese researchers including 1 resident and 4 Thai researchers



Researchers



Building 10 of Thai NIH



BSL-3 facility



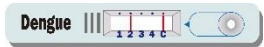
Confocal microscope



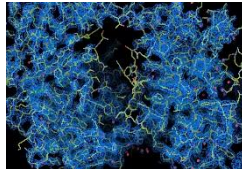
Next-generation sequencer

【Current Research Activities】

<Development of diagnostic and therapeutic measure against dengue and chikungunya fevers>

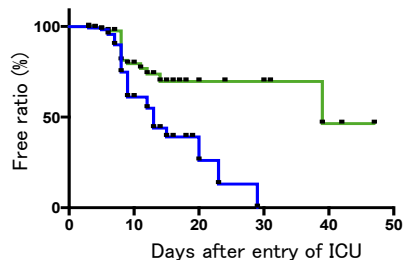


Development of rapid diagnostic kits for serotype distinction of dengue and detection of chikungunya.



Development of antivirals against dengue and chikungunya viruses

<Molecular epidemiology of Carbapenem-resistant bacteria>



Effect of early intervention by using a rapid detection method of Carbapenem-resistant bacteria on its spread in Thailand hospital

<Epidemiology, molecular epidemiology, and research on pathogenic mechanisms of diarrheagenic pathogens>



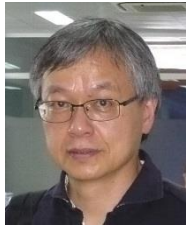
Detection of norovirus, rotavirus, Shigella, and Campylobacter from hospitalized patients as well as from healthy individuals and river water



Rapid detection of *Vibrio Cholerae* in the field

[Vietnam] Research Activity of Nagasaki University Project

【Project Leader ▪ Supervisor】



Project Leader
Prof. Kenji Hirayama, Dean,
Institute of Tropical Medicine,
Nagasaki University.



Supervisor
Prof. Futoshi Hasebe, Center
for Infectious Disease
Research in Asia and Africa,
Vietnam Research Station.
(Resident)

【Current situation of Vietnam Research Station】

- Location: Room 201(Lab), 210, 214, 219, High Tech Building, National Institute of Hygiene and Epidemiology (NIHE)
- Japanese Scientists : 29 (Resident : 4)
- Local Scientists : 54
- Sub-Research Station : Bach Mai Hospital
- Japanese Scientists : 23 (Resident 0)
- Local Scientists : 46



NIHE High Tech Build.



Bach Mai Hospital



NIHE-NU Lab.



MiSeq. (NGS)

【Research Subjects】

<Dengue Research>



- Molecular epidemiological study on dengue viruses.
- Elucidation of pathogenicity of severe dengue.
- Mosquito vector control.

<Research on diarrhea diseases>



- Hospital and community based studies of a broad range of etiological agents of diarrhea.
- Molecular epidemiological study of *Vibrio cholera* in Vietnam.

<Cohort study on pediatric infectious diseases in Nha Trang>



Determination of the etiology and risk factors for severe common pediatric infectious diseases (SPID).

<Research on avian influenza>



Molecular epidemiological study on avian influenza virus among poultry and wild bird.

<Research on drug-resistance bacteria>



- Molecular epidemiology of drug-resistance bacteria causing hospital infections.
- Development of early diagnostic method and novel therapeutic method.

<AIDS Research>



- Clinical research on side-effects of antiretroviral.
- Clinical research on HBV-HIV co-infection
- Analysis of determinants of QOL and depression among HIV patients.

<Research on tuberculosis in Vietnam>



- Study on transmission, response to therapy and recurrence of TB.
- Analysis of host factor, pathogenicity and epidemiological background relating to drug-resistance.

[China] The University of Tokyo Project Laboratories

【Project Director】



Project Director
Professor Yasushi Kawaguchi
The Institute of Medical Science,
The University of Tokyo
 (visits Labs in Beijing bimonthly)



Professor Jun-ichiro Inoue
 Chief of China-Japan
 Joint Laboratories in
 Beijing
 (visits Labs in Beijing
 bimonthly)



Professor Yoshihiro Kawaoka
 Chief of China-Japan
 Joint
 Research Group
 on Avian Influenza
 Virus
 (located in HVRI,
 CAAS)

Laboratory of Structural
 Virology and Immunology (LSVI),
 Laboratory of Molecular Immunology
 and Molecular Microbiology (LMIMM)
 (located in IBPCAS/IMCAS)

【Project Laboratories】

<Host Institutions>

The Institute of Biophysics (IBP) and the Institute of Microbiology (IM), Chinese Academy of Sciences (CAS)
 The Harbin Veterinary Research Institute (HVRI), Chinese Academy of Agricultural Sciences (CAAS)

<IBPCAS>

- Number of Japanese researchers : 10
 (including 1 dispatched researcher)
- Number of Chinese researchers : 8



IBPCAS

<IMCAS>

- Number of Japanese researchers : 9
 (including 3 dispatched researchers)
- Number of Chinese researchers : 8

<HVRI, CAAS>

- Number of Japanese researchers : 9
 (No dispatched researchers)
- Number of Chinese researchers : 2



IMCAS



September 23, 2015
 Signing Ceremony of the 3rd
 MOU between IMSUT and
 IBPCAS (in Beijing)

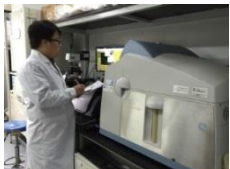
【Research Activities】

(1) Basic studies for controlling infection with enveloped viruses including Dengue virus

In IBPCAS, studies are conducted aiming to develop membrane fusion inhibitors (mainly peptides) for Dengue virus, HIV-1, and MERS coronavirus in collaboration with a group in IMSUT.



Confocal
 Microscope



(2) Studies of Host Factors Required for HIV-1 Replication

In IMCAS, host factors associated with HIV-1 replication are being studied, and the molecular epidemiologic studies are underway with HIV-1 prevailing in China by using the method developed in our Chinese Research site. Epidemiologic studies of viral diarrhea are being discussed in cooperation with a hospital in Beijing.



BSL3 Laboratory



(3) Development of New Diagnostic Agents and Preventive-Therapeutic Antibodies for Influenza Virus

In HVRI, we study influenza viruses prevailing in China, predict their epidemic, and develop type-specific diagnostic agents and preventive-therapeutic medicines based on the genetic information on viruses isolated in China.

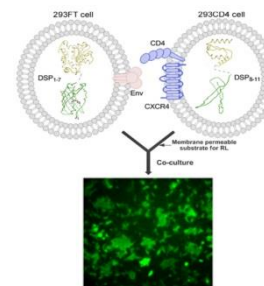


Experimental
 Infection of
 Monkeys



(4) Screening of Chemical Inhibitors of Enveloped Viruses Including Dengue Virus

In IMSUT, the screening method is being developed for chemicals inhibiting cell fusion caused by Dengue virus, HIV-1, or MERS coronavirus, in collaboration with the IBPCAS group. Screening is to be conducted, being supported by Department of Innovative Drug Discovery and Development, AMED.



(5) Construction of the System Collecting Epidemiologic Information on Drug-Resistant Bacteria

The system is being constructed to facilitate the exchange between China and Japan of epidemiologic information on drug-resistant bacteria and resistant genes.

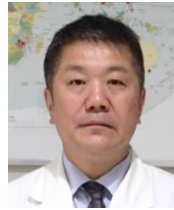
★Beijing Project Office (Activities)

- Support in China of China-Japan joint research
- Strengthening the network between IMSUT and educational/research institutions in Beijing
- Secretariat for Steering Committee and negotiation with Chinese sides
- Collection of information on infections in China; its publication on Web



[Zambia] Hokudai Center for Zoonosis Control in Zambia (HUCZCZ)

【R&D Principal Investigator, Head of the HUCZCZ】



R&D Principal Investigator

- Hokkaido University
- Professor
- Hirofumi SAWA



Head of HUCZCZ

- Hokudai Center for Zoonosis Control in Zambia (HUCZCZ)
- Professor
- Hideaki HIGASHI

【Overview of the HUCZCZ】

- Location: School of Veterinary Medicine, the University of Zambia
- Researchers working in the HUCZCZ
19 Zambians and 10 Japanese, including 2 residents



HUCZCZ in the School of Veterinary Medicine, the University of Zambia



Zambian and Japanese researchers working in the HUCZCZ



Joint symposium between the University of Zambia and the Hokkaido University



BSL-3 facility



Researchers working in the BSL-3 facility

【Research activities using the HUCZCZ】

< Epidemiological research targeting zoonotic diseases >



- Surveillance of arboviruses in mosquitoes in Zambia.
- Detection of viral genome
 - Isolation of viruses



- Surveillance of avian influenza
- Virus isolation from fecal materials from migrating waterfowl in Zambia

< Establishment of diagnostic methods for drug-resistant *Mycobacterium tuberculosis* (*M. Tuberculosis*) >



- Drug susceptibility test of *M. tuberculosis* strains isolated from clinical specimens at the University Teaching Hospital



- Technological transfer of the procedure of molecular diagnosis for *M. tuberculosis* into Zambia
- Fostering of human resources



- Establishment of the library of *M. tuberculosis* strains isolated from clinical specimens



- Identification of multi-drug resistant *M. tuberculosis* from clinical specimens

[INDIA] Activity status at overseas center of Okayama University

[India-Okayama University Research Center]



Institute and representative in charge
Graduate School of Medicine,
Dentistry and Pharmaceutical
Sciences, Okayama
University

Professor Shin-ichi Miyoshi



Overseas research center
Collaborative Research Center
of Okayama University for
Infectious Diseases in India
Director Keinosuke Okamoto

[Current status at the overseas center]

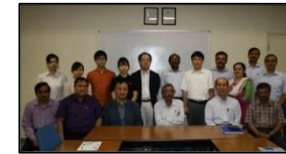
- Host Institute: National Institute of Cholera and Enteric Diseases (NICED) , India
- Japan side: 14 researchers (Resident researcher : 2 researchers)
- India side: 7 researchers



Appearance of NICED building



Laboratory
Meeting between Japanese
and Indian researchers



Researchers and staff



Real time PCR system



Pulsed-Field Gel
Electrophoresis system

[Research Topics]

< Hospital-based active surveillance of diarrheal diseases > Search for novel causative agents of diarrhea by metagenomics



To detect novel causative microorganism, we are using metagenomics to analyze the nucleic acid directly from patients stool sample as they were undetected by our established protocol.

< Study on new variant of *Vibrio cholerae* >

To identify a drug target for *V. cholerae* El Tor variant prevailing worldwide, we are studying the relation between genomic changes and enhanced pathogenicity of pandemic strains isolated from patients in India and other area (Yemen, etc.).

< Dynamics of transmission of cholera in epidemic area >

To analyze the transmission dynamics of cholera, we are performing spatio-temporal genomic analysis of *V. cholerae* strains isolated from the patients in Kolkata, India and Dhaka, Bangladesh, along with analysis of *V. cholerae* from environmental water.

< Development of cheap vaccine >

There are many cases of diarrhea throughout the year in India. Infectious Disease hospital situated near NICED reported cases of mortality due to dysentery among patients.

	2005		2006		2007		2008		2009	
	ADM	OTH	ADM	OTH	ADM	OTH	ADM	OTH	ADM	OTH
VIBRIO CHOLERA	235	5	86	134	134	367	103	123	240	100
SHIGELLA	227	30	93	154	112	134	103	123	240	100
DYSENTERY	227	30	93	154	112	134	103	123	240	100
TYPHOID	227	30	93	154	112	134	103	123	240	100
TYPHUS	227	30	93	154	112	134	103	123	240	100
MEASLES	227	30	93	154	112	134	103	123	240	100
RABIES	227	30	93	154	112	134	103	123	240	100
INFLUENZA	227	30	93	154	112	134	103	123	240	100
CHICKEN POX	227	30	93	154	112	134	103	123	240	100
MEASLES	227	30	93	154	112	134	103	123	240	100
RUBELLA	227	30	93	154	112	134	103	123	240	100
TOTAL	26201	702	23245	556	22611	220	12345	453	28636	502

So for diarrheal prevention, we would like to use human antimicrobial peptide after testifying their effects on animal models.

To develop a cheap vaccine for enteroinvasive *Escherichia coli*, we are using heat-killed bacteria cells



< Study on VBNC state of *V. cholerae* >

To develop a specific detection method for VBNC (viable but non-culturable) cells of *V. cholerae* from environmental water at Kolkata, we are studying the molecular mechanism of VBNC state by proteome and transcriptome analysis.



< Involvement of metabolic enzymes in environmental adaptation and pathogenicity >

We will elucidate the mechanistic pathway employed by chitinases for intestinal colonization by *V. cholerae*. This information will be translated towards developing a novel therapeutic intervention different from the existing antibiotics for cholera.

[Indonesia] Activities in Kobe University Research Center

【Representative in charge】



Representative in charge
Institute: Kobe University
Title: Professor
Name: Yasuko Mori



Representative of CRC-ERID
Research center: Collaborative
Research Center for Emerging and
Re-emerging Infectious Diseases
(CRC-ERID)
Title: Appointed Associate Professor
Name: Takako Utsumi (long-term stay)

【Activities in research center】

- Host institution: Institute of Tropical Disease (ITD), Airlangga University, Indonesia
- The number of Japanese researchers: 20 (long-term stay researchers: 3)
- The number of local researchers: 33



Institute of Tropical Disease



Laboratory



Long-term stay researchers and local staff



Sequencer



Next Generation sequencer (MiSeq)



BSL-3 Laboratory

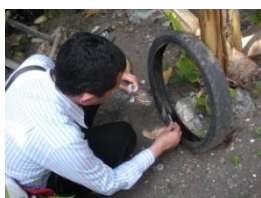
【Research activities】

<Forecast and monitor of emergence of next pandemic virus>



Surveillance of avian influenza viruses in poultry and workers at live-poultry markets to monitor the avian-human transmission.

<Molecular epidemiological and basic studies of dengue viruses>



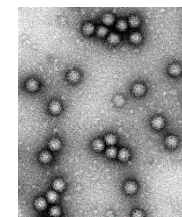
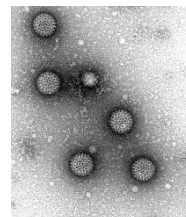
Virus isolation and genotypic study. Basic study to develop new anti-dengue therapeutics and diagnostic methods.

<Molecular epidemiological study of HIV>



Search for new HIV-1 subtypes in Indonesia.
Monitoring of HIV drug resistance.

<Epidemiological study and gene analysis for viral diarrhea>



Epidemiological study and gene analysis for viral diarrhea (Rotavirus and Norovirus).

<Epidemiological study and gene analysis for AMR and cholera>



Epidemiological study and gene analysis for *Vibrio cholera*.
Surveillance and gene analysis for AMR (antimicrobial resistance), and establishment of hospital infection control system using JANIS.

[Philippines] Research Activity of Tohoku University

【Representative Research Project and Head of Collaboration Center】



Representative of Research Project
Department of Virology,
Tohoku University Graduate School of
Medicine
Title : Professor
Name : Hitoshi Oshitani, MD, PhD, MPH



Head of Collaborative Research Center
Tohoku-RITM Collaborating
Research Center on Emerging and
Reemerging Infectious Diseases
Title : Assistant Professor
Name : Emiko Nakagawa, PhD

【Efforts of Collaborating Research Center】

- Counterpart of host country: Research Institute for Tropical Medicine (RITM)
- Number of Japanese researchers : 8 (permanently stationed in the Philippines: 1)
- Number of researchers in host country : 26



Research Institute for
Tropical Medicine (RITM)



Tohoku-RITM Collaborative
Research Team



Real-time PCR



Molecular Biology Laboratory - 1



Virus isolation Laboratory



Molecular Biology Laboratory - 2

【Research Topics】

<Molecular epidemiology of enteric viruses for elucidation of antigenicity and transmission mechanism, and development of diagnostic system>



Cohort study is conducted to reveal the actual situation and significance of the norovirus and sapovirus infections in the communities in the Philippines.
(Photo : Field staff in La Paz, Tarlac)

<Molecular epidemiology of mosquito-transmitted infectious diseases>

Dengue is endemic in all over the Philippines. Recently, chikungunya infections are reported also nation-wide. To elucidate the situation of mosquito-borne viral infections in the country, we establish a genetic information database of viruses circulating in the Philippines in collaboration with national surveillance team.

<Molecular epidemiology of antimicrobial-resistant bacteria and development of rapid diagnostic system>

Molecular epidemiology of carbapenem-resistant Enterobacteriaceae (CRE) and extended spectrum beta-lactamase (ESBL)-producing organisms is conducted to identify the major drug-resistant strains in the country. We also develop rapid diagnostic system for the monitoring of antimicrobial-resistant bacteria.



<Clinical and epidemiological study of childhood pneumonia, and development of biologicals for treatment and diagnosis>

Respiratory syncytial virus (RSV) is a leading cause of severe respiratory infections among young children. Cohort study is conducted to obtain comprehensive understanding of the epidemiology, transmission dynamics and risk factors for severe pneumonia, which aims to provide evidence-based medicine for effective measures against respiratory infections.

<Establishment of a research base>

We established a research base, which runs state-of-the-art clinical and epidemiological studies. The research base can be used to gather clinical, epidemiological and genomic information on various infectious diseases in the Philippines and Japan. Such information can be shared not only to local but also to the global medical community. The base also offers training opportunities in field epidemiology researches, clinical researches and global outbreak responses to Japanese researchers and medical professionals.

[Republic of Ghana] Activity report of the research center for J-GIRD project of Tokyo medical and dental University (TMDU).

【Project Leader & Director】



Project leader
Shiroh Iwanaga, Ph.D.
Professor of TMDU.



Director
Mitsuko Ohashi, Ph.D.
Project Associate Professor and
Director of the research center for
J-GRID project of TMDU.

【Activity of the Research Center】

- Collaborative research institute : Noguchi Memorial Institute for Medical research (NMIMR)
- Japanese researchers : 15 members (Resident staff: 1)
- Ghanaian researchers : 21 members



NMIMR



P3 laboratory
in NMIMR



Japanese and Ghanaian member



90th Anniversary Symposium of
Dr. Hideyo Noguchi's Arrival in Ghana

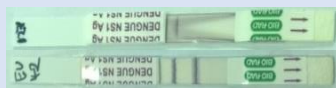


Meeting for field-work

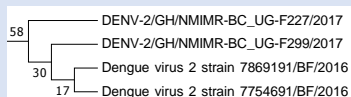
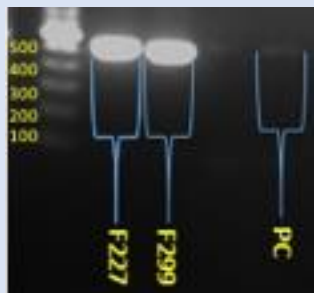
【Research Projects】

<Molecular epidemiology of DENV and CHIKV in West Africa>

Genetic analysis of DENV and CHIKV

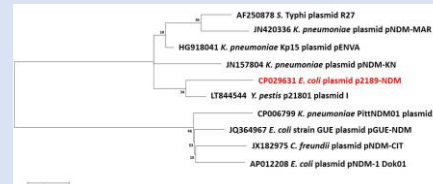
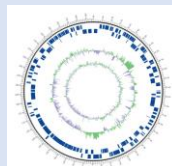


Using serum specimens from patients with fever of unknown origin, we survey the presence of DENV or CHIKV by various tests to clarify the actual epidemic situation, and try to isolate and characterize the viruses in comparison to strains found in other endemic regions such as Asia.



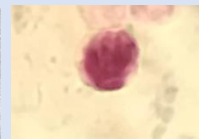
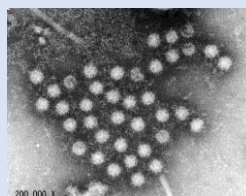
< Studies for diarrheal disease control in West Africa >

Epidemiological and mechanistic analyses of multidrug-resistant bacteria



Our research activities include epidemiology of gram-negative bacilli resistant to third-generation cephalosporins or carbapenems and molecular analysis of their resistance mechanism.

Genetic analysis of childhood diarrhea-causing agents in Ghana



Using samples from childhood diarrhea diagnosed in selected facilities in Ghana, we identify the causing agents, and further perform genome-sequencing and phylogenetic analysis. Our goal is to establish epidemiological and genetic evidence of diarrhea-causing pathogens in Ghana together with comparative analysis with other countries.

[Myanmar] Activity Status of Infectious Diseases Research Center of Niigata University in Myanmar (IDRC)

【Project Leader ▪ Director】



Project Leader

Division of International Health (Public Health), Graduate School of Medical and Dental Science, Niigata University
Professor Reiko Saito



Director

Infectious Diseases Research Center of Niigata University in Myanmar ▪ Specially Appointed Prof., Graduate School of Medical and Dental Science, Niigata University

【Outline of our research】

<Epidemiology of Influenza and Other Respiratory Virus Infections >

A long-term study at NU showed that the peak for influenza prevalence was during the rainy season in Myanmar, and new strains such as A/H3N2 emerged earlier than in Japan. Because of this, NU has been regarded as a leading institute for WHO selection virus for the seasonal influenza vaccine.

In July 2017, NHL detected the severe cases of influenza A/H1N1pdm09 in Myanmar and MoHS declared the high level of alert to the influenza outbreaks in the country. The overall number of severe pneumonia cases and fatalities reached 1,198 and 38 respectively. NU contributed to the mitigation of this outbreak by donating, sharing information, and providing technical support.

We intend to strengthen the surveillance of influenza and other respiratory viruses. We also contribute to the evaluation of existing vaccines and the development of the new vaccines by

【Activity Status】

- IDRC location : National Health Laboratory (NHL) , Yangon
- Japanese Researchers : 24 members
(Myanmar stationed researchers : 2 members)
- Myanmar Researchers : 14 members
- Homepage address : <http://www.med.niigata-u.ac.jp/idm/>



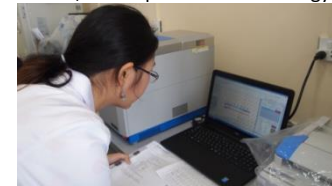
Exterior of NHL



IDRC Laboratory at NHL

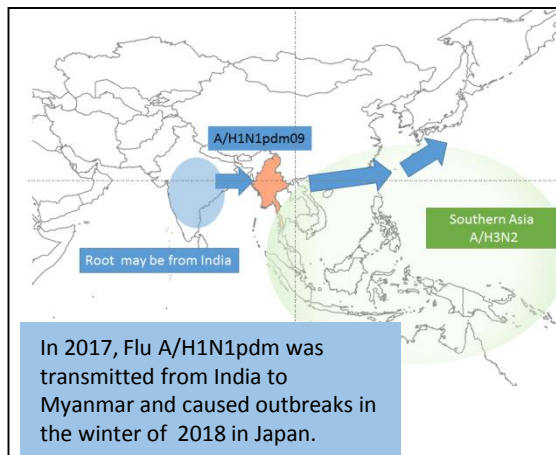


Influenza Center, The department of Virology / NHL



Analysis of Flu virus by Real-Time PCR

analyzing the antigenic changes with virology, sharing information, and providing virus strains for WHO and the National Institute of Infectious Diseases, Japan. Moreover, we aim to evaluate the risks for viruses entering Japan by creating maps of genotype distribution (GIS: Geographic Information System) using the analysis of viral gene evolution.



<Research of Severe Pneumonia in Children>

We aim to identify microbes isolated from respiratory and blood specimens of patients, and detect them by isolation and molecular biological methods.

We compare microorganisms between Asian countries' and Japanese to propose judicious use of antimicrobials through our surveys. We also aim to focus on vaccination coverage of children attending to medical institutions and evaluate the effectiveness of vaccines.



Kick-off meeting of Severe Pneumonia in Children (May 2017, Yangon)