Expanding TMDU Network in Latin American Countries: Academic, Educational and Clinical Collaborations

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IN 1968, PROFESSOR Tadashige Murakami, former professor of surgery of TMDU, visited Chile to give a lecture on gastric cancer. This was the start of a long relationship between TMDU and Chile. In the 1970s, the Japan International Cooperation Agency (JICA) launched a project for the early detection of gastric cancers in order to reduce their high mortality rate. The Gastric Cancer Center in Santiago was founded in 1977 at the Hospital Paula Jaraquemada (now the Hospital Clinico San Borja Arriaran), and has long since played a major role in the project. TMDU has dispatched numerous experts there to support the prevention of gastric cancer. The Gastric Cancer Center was later renamed the Chilean-Japanese Institute for Digestive Diseases and still contributes to maintaining the health of the Chilean people.

Colorectal Cancer Screening in Chile, Supported by TMDU

In Chile, mortality from colorectal cancer has been increasing over the last two decades, and thus the need for colorectal cancer screening has grown rapidly. Approval was given in 2009 to start a screening project based on a proposal from Dr. Francisco Lopez of Clinica Las Condes (CLC), one of the largest and most advanced hospitals in Chile. Due to the long history between TMDU and Chile, TMDU was invited to supervise the project. In 2009, the Ministry of Health of Chile, CLC and TMDU signed a collaborative agreement concerning colorectal cancer screening, and the Latin American Collaborative Research Center (LACRC) was established at CLC in 2010. Over the years, TMDU has continuously sent experts in pathology, endoscopy and research to LACRC. Established in 2012, PRENEC (Prevention Project for Neoplasia of Colon and Rectum) uses Japanese medical methods to conduct immunological fecal occult blood tests and colonoscopies.

1 Dr. Yasuno with Chilean surgeons at PRENEC center in Osorno

The Chilean-Japanese Institute for Digestive Diseases at the Hospital San Borja Arriaran is the main facility for PRENEC in Santiago. The institute also serves as a training center for endoscopy. Many Chilean doctors have received training in endoscopy, acquiring the skills necessary for cancer screening. The institute's endoscopy unit has been redesigned for PRENEC, with extensive support from the Japanese Embassy in Chile.

In December 2017, former TMDU Takashi Ohyama received the Order of Bernardo O'Higgins from the Government of Chile in appreciation of TMDU's contributions in Chile.

LACRC Members and University Activities

LACRC is staffed by experts from the pathology, endoscopy and molecular biology divisions of TMDU. As of 2020, nine TMDU doctors have provided leadership to LACRC: Dr. Takashi Ito (April 2010 to March 2012) and Dr. Hiroshi Kawachi (March 2012 to March 2015) as pathologists; Dr. Hiroyuki Uetake (July and August 2010), Dr. Tetsuro Nishikage (January 2011 to January 2012), Dr. Koji Tanaka (January 2012 to April 2013), Dr. Takuya Okada (April 2013 to March 2015), Dr. Masahiro Tsubaki (October 2014 to September 2015) and Dr. Tomoyuki Odagaki (November 2014 to present) as endoscopists; and Dr. Maki Kobayashi as a molecular biologist (July 2012 to March 2015). In November 2017, August 2018 and March 2019, Dr. Masamichi Yasuno visited Chile to supervise colorectal surgery conducted by local surgeons (Fig. 1).

2 Colonoscopy training with colon model
3 Dr. Odagaki performing an endoscopic procedure
4 Meeting with directors from all PRENEC centers

LACRC is currently overseen at TMDU by Prof. Tetsuya Taga (Executive Senior Vice President), Prof. Masanobu Kitagawa (Dean of the Faculty of Medicine, Department of Comprehensive Pathology), Prof. Uetake (Department of Specialized Surgeries) and other staff members.

In Chile, Dr. Odagaki is the current chief of LACRC, and he is engaged in PRENEC as an instructor of colonoscopy to Chilean doctors (Fig. 2). His cutting-edge techniques, including endoscopic resection for superficial cancer, have been in great demand. Many patients are referred to him not only from Santiago, but also from other parts of Chile (Fig. 3). Dr. Odagaki is also a supervisor in the stomach cancer screening project conducted by the Chilean Endoscopic Society.

TMDU operates the Project Semester Program, appointing medical students to institutions overseas. In 2019, two medical students from TMDU were sent to laboratories at the University of Chile, where they conducted advanced research in collaboration with local doctors.

Public Release of PRENEC Results in Medical Journals

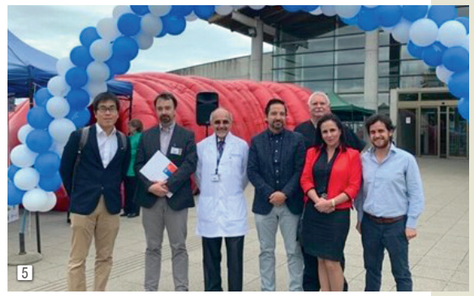
The colorectal cancer screening system of PRENEC has achieved excellent results, detecting many cancer cases. Expert knowledge and technique from TMDU have significantly improved the completion rate of the screening procedures and the detection rate of colorectal cancer. Furthermore, most of the cancers detected by PRENEC were early intramucosal cancers without risk of metastasis, which were treated successfully by endoscopy. These results have been reported in various medical journals by past doctors. More reports related to PRENEC results are in progress for future publication.

In August 2019, Dr. Okada published "Colorectal cancer risk factors in asymptomatic Chilean population a survey of international collaboration between Japan and Chile" in the European Journal of Cancer Prevention. These results suggest that intensive screening of high-risk populations can help improve the detection of colorectal cancer, while higher consumption of cereals or fibers can be effective in preventing its onset.

Expanding TMDU-PRENEC Network in Latin America

PRENEC and supporting activities by TMDU are now recognized as essential aspects of Chilean healthcare. Increasing numbers of participants have enrolled in PRENEC in seven major cities: Santiago, Valparaiso, Punta Arenas, Coquimbo, Osorno, Valdivia and Concepcion (Fig. 4). While the TMDU-PRENEC network is still expanding throughout the country, additional cities and facilities have concluded agreements to join PRENEC in the near future (Fig. 5).

TMDU has also promoted the same screening system in other Latin American counties, in association with JICA and the International Cooperation Agency of Chile (AGCI). In August 2015, the First International Training Course for Colorectal Cancer Screening took place in Santiago. TMDU experts participated in the course as instructors and gave lectures to doctors from Ecuador and Colombia. In 2016 and 2017, the same training course was held in Santiago for medical professionals from Bolivia, Paraguay and Peru. In Paraguay, the PRENEC pilot study has finished and preparation for PRENEC's full-scale launch is underway.



5 Promoting the PRENEC project with a giant colon model

Activities for Strengthening Relationships between TMDU and Thai Universities

CU-TMDU Research and Education Collaboration Center, Thailand

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1. Student Exchange Programs between TMDU and Thai Universities

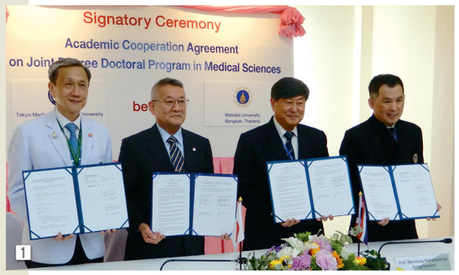
As of May 1, 2019, 40 Thai students are studying in Tokyo Medical and Dental University (TMDU) regular courses. Of the 40 students, two are in the undergraduate course of Faculty of Medicine and 38 belong to the postgraduate course in the Graduate School of Medical and Dental Sciences.

Just half of these students are supported by Japanese government while the others are supported by the Thai government or private expense. After graduation from TMDU, most of the students go back to their country where they promote the health of Thai people through contributions in the research, education and healthcare field.

In addition, TMDU and Thai universities conducted various student exchange programs from January to December in 2019. A total of 42 Thai students came to TMDU (inbound) and 35 TMDU students visited Thailand (outbound) for short-term exchange programs or research projects. Table 1 shows the number of and students from each affiliation.

Table1 Number of students at each affiliation of TMDU in 2019

TMDU	Regular students from Thailand	Short-term exchange students	
		Inbound	Outbound
Faculty of Medicine	2	10	18
Faculty of Dentistry	0	8	9
Graduate School of Medical and Dental Sciences	38	8	7
Institute of Biomaterials and Bioengineering	0	16	1
Total	40	42	35



1 Signing ceremony of JD program with MU

2. Medical collaboration with Mahidol University

Over the past few years, TMDU and its long-time partner Faculty of Medicine Siriraj Hospital, Mahidol University (MU), have held a series of discussions on launching a new joint degree doctoral program in Medical Sciences. As a result of tireless efforts by both universities, the Joint Degree Doctoral Program in Medical Sciences between TMDU and MU was successfully approved in both Japan and Thailand, by MEXT (Ministry of Education, Culture, Sports, Science and Technology, Japan) in June, and also by the MU Council in July 2019.

On August 7th, TMDU President Yasuyuki Yoshizawa visited MU and concluded the academic cooperation agreement with Acting President Prof. Banchong Mahaisavariya, Prof. Patcharee Lertrit, Dean of Faculty of Graduate Studies, and Prof. Dr. Prasit Watanapa, Dean of Faculty of Medicine Siriraj Hospital.

Both Japan and Thailand have similar medical issues stemming from their super-aging societies and the globalization of medical care, and so both universities expect this program to contribute significantly to solving such issues in the future. Further, this four-year doctoral program is expected to be a part of our ongoing effort "To train medical professionals with a rich international perspective" and strengthen our international competitiveness while at the same time contributing to the nurture of medical professionals throughout the world.

This doctoral program is designed to foster advanced medical personnel involved in the treatment of diseases in a super-aging society, especially multidisciplinary treatment such as cancer treatment. The most distinctive feature of the program is the practical education surgeons can receive due to the advanced research skills and knowledge to train cancer treatment specialists

2 Dental students in JD program and advisers from TMDU and CU
3 Visiting members of Thai Dental Public Health
4 TMDU participants in CU Research Day

available at TMDU, and the abundant clinical research results based on the large number of cases at MU.

Surgeons who have completed this program are expected to work internationally to resolve common issues found throughout Japan and the ASEAN region. Recruiting will begin at both universities from the fall in 2019, and the first students will be enrolled in April 2020.

3. Dental collaboration with Chulalongkorn University

During the four-year implementation of the JD program, the success achieved by TMDU and Chulalongkorn University (CU) has exceeded expectations. This is the first successful case of a JD program in Dentistry in Japan, and provides an excellent role model for other institutions.

Students of the inaugural class, matriculated in 2016, are approaching the final stage of dissertation. Therefore, the methods of guidance on publication and dissertation defense will be a major focus in the coming year.

For the recruitment of future PhD candidates, TMDU and CU hosted booths to introduce the program at the IADR-APR conference held on November 28-30, 2019 in Brisbane, Australia, where one of the JDP students had a poster presentation.

4. Thai Ministry of Public Health team visited TMDU

On August 27-28, 2019, 15 Thai dental public health officers visited TMDU, including Dr. Somkuan Hanpatchaiyakul, Senior Advisor to the Health Technical Office, Ministry of Public Health, Thailand. The purpose of their visit was to learn about elderly dental care and dental hygienists' roles in Japan.

The visitors listened to lectures on the education system and the roles of dental hygienists at School of Oral Health Care Sciences and participated in the training program in the dental hospital and skills laboratory room at TMDU. They also visited the Tokyo Metropolitan Institute of Gerontology to observe health activities for the community elderly. Moreover, they participated and presented in the International Seminar "Public Health Dentistry between Japan and Thailand," which was held at TMDU.

This was an invaluable opportunity to exchange knowledge, techniques and strategy of management of the elderly's health care for both Japan and Thai dentists. We believe their visit will contribute to implement a national policy on elderly dental care programs in Thailand.

5. Research Day program

On February 13, 2019, three TMDU postgraduate students visited CU and participated in the Research Day program and presented their research topics orally in front of a packed audience. This is a special program for dental students to present their research activities as part of a competition. Since 2013, TMDU has sent students to participate in this program. Ms. Akane Wada and Mr. Takahiko Yamada won the first and third prize and received an award from Dr. Suchit Poolthong (Dean, Faculty of dentistry CU). Assoc. Prof. Shigenori Nagai (Dept. of Molecular Immunology) also participated in the CU Research Day and contributed as a special lecturer, evaluator of the oral session and chair of the poster session.

6. Appointment of visiting scholars in Thailand

TMDU appointed the following four Thai doctors and dentists as visiting scholars in 2019.
Dr. Thiravud Khuhaprema: Visiting Professor
Dr. Prasit Watanapa: Visiting Professor
Dr. Atiphan Pimkhaokham: Visiting Associate Professor
Dr. Issareeya Ekprachayakoon: Visiting Assistant Professor

5 Visiting Professor Thiravud Khuhaprema (left) and President Yoshizawa (right)

Research Partnership between TMDU and Noguchi Memorial Institute for Medical Research, University of Ghana

Ghana-Tokyo Medical and Dental University Research Collaboration Center

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Leader of TMDU-AMED/JGRID Project in Ghana

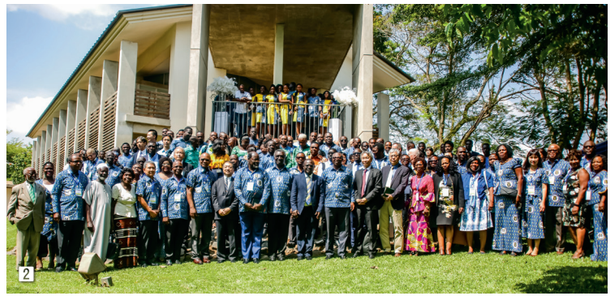
Overview of the TMDU-AMED/J-GRID Project

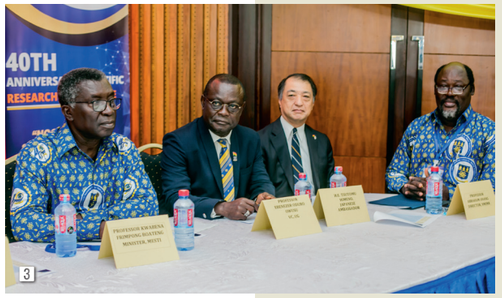
The Japanese Initiative for Global Research Network on Infectious Diseases (J-GRID) program has been carried out between TMDU and the Noguchi Memorial Institute for Medical Research (NMIMR) since 2008. The first and second terms of the J-GRID program, which were supported by the Japanese Ministry of Education, Culture, Sports and Technology (MEXT), were completed at the end of Japanese FY2014. The third term of the project started in FY2015 under the support of the Japan Agency for Medical Research and Development (AMED). Dr. Takaya Hayashi, project lecturer at TMDU, joined the project from FY2017 and started to work with research fellows in NMIMR. Dr. Yen Hai Doan, project lecturer at TMDU, also joined the project from FY2019.

Currently, ten Japanese and twelve Ghanaian researchers participate in the project, cooperating on multiple research projects. The main focus of the AMED/J-GRID project is to promote innovative research collaboration with researcher counterparts for collecting information about pathogens in endemic areas, evaluating vaccine efficacy, and identifying the drug resistance of pathogens. Under this concept, the TMDU AMED/J-GRID project conducts the following three research projects: (1) the surveillance and isolation of dengue viruses prevalent in Ghana; (2) the genetic analysis of rotavirus, which is the causative agent of acute diarrhea; and (3) the identification of carbapenem-resistant bacteria. To conduct research more efficiently, TMDU invited Kitasato University Professor Kazuhiko Katayama, who is an expert in rota virus research to build an "all-Japan collaboration team."

In 2019, we successfully determined the genome sequence of the dengue type 2 virus from Ghanaian patients. In addition, we collected the Aedes mosquitoes, which are the vector of dengue virus, and have succeeded in maintaining mosquito colonies in Japan. The artificial feeding experiments using those mosquito colonies and dengue virus isolated from South-East Asia showed that African Aedes mosquitoes exhibited resistance against virus infection compared to Asian Aedes mosquitos. This result suggested that that strain or subspecies of mosquito vector probably plays an important role in outbreak of dengue fever in West Africa. Our genetic analysis of the rota virus showed that the vaccine strain disappeared from the field sites after the introduction of the vaccine, but reemerged in 2018. Global surveillance in 2019 showed that similar reemergence of vaccine strains were found in other geographic areas, such as India and Indonesia. The reemergence of vaccine strains of the rota virus after the introduction of the vaccine is a global trend of rotavirus genotypes. The carbapenem-resistant bacteria was first found in Ghana in 2017, and then in FY 2018 the NDM-1 gene was identified as the drug resistant gene. In FY2019, we continued to survey novel drug resistance from specimens obtained from two field sites. A new research building named Noguchi Advanced Research Laboratories began operation. This building has several P3 laboratories and new equipment for infectious disease research. In FY2019, researchers and laboratory staffs moved to this new facility.

1 Noguchi Memorial Institute for Medical Research (NMIMR)





2 Group photograph of 40th Anniversary Symposium of NMIMR
3 Professor Kwabena Frimpong Boateng (Minister of Environment, Science, Technology and Innovation, Republic of Ghana, Left), Professor Ebenezer Oduro Owusu (Vice-chancellor of University of Ghana, Left-Center), Mr. Tsutomu Himeno (Japanese Ambassador of Ghana, Right-Center), Professor Abraham Kwabena Anang (Director of NMIMR).

Important Collaboration between TMDU and NMIMR, University of Ghana, in the Development of Human Resources

Collaboration between TMDU and NMIMR plays an important role in the development of human resources in Japan and Ghana. TMDU runs an educational program for medical students who want to gain experience at medical institutions overseas. Under this program, undergraduate students stay to carry out their research projects for a few months at NMIMR. For example, three students visited NMIMR in 2019. The visiting students worked with young Ghanaian scientists in the laboratory and field. One student belonged to the Department of Virology and the other two belonged to the Department of Parasitology. They conducted their own research at NMIMR. TMDU accepts young, talented researchers as Ph.D. students under the scholarship program supported by MEXT. In 2019, three Ph.D. students from NMIMR entered the doctoral course at TMDU. They joined the Parasitology Department of Medicine at TMDU and started a "new research life. " They are expected to bridge TMDU and NMIMR moving forward, contributing to collaboration between the two institutions.

TMDU received the donation from T.E.N. Ghana MV25

T.E.N. Ghana MV25 (MV25) was established based on investment by MODEC Inc., Mitsui& Co., Ltd., Mitsui O.S.K. Lines, Ltd., and Marubeni Corporation. MV25 carries out a charter business for FPSO and has produced crude oil and natural gas since 2016. MV25 provided a monetary donation of US$250,000 to the TMDU AMED/J-GRID Project. This donation not only contributed to the effective progress of the research project, but also to bridging research between Japan and Ghana. This donation will strengthen the relationship between our two countries and contribute to advances in medical research in Ghana.

40th Anniversary Symposium of NMIMR

NMIMR was established in 1979, and now in 2019 it is celebrating its 40th anniversary, on which behalf an international symposium was held on 28th-29th of November. In addition to many scientists, Professor Kwabena Frimpong Boateng, the Minister of Environment, Science, Technology and Innovation; Professor Enbeneser Oduto Owusu, the vice-chancellor of University of Ghana; and Mr. Tsutomu Himeno, Japanese ambassador to the Republic of Ghana, were invited as guests.

In the symposium, Prof. George E. Armah, Dr. Anthony Ablordey, Dr. Samuel Dadzi who are TMDU AMED/J-GRID members, presented recent research results about diarrhea caused by rota virus infection, pathogenic bacteria, and mosquito vector for dengue virus transmission. On behalf of TMDU, Dr. Hayashi and Dr. Doan offered their support for this anniversary symposium.

4 TMDU staff members in 40th Anniversary Symposium.