

Growing the 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 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 cancer to reduce the high mortality rate of this type of cancer. The Gastric Cancer Center in Santiago was founded in 1977 at the Hospital Paula Jaraquemada (now the Hospital Clinico San Borja Arriaran), and this center has long 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 to the Chilean-Japanese Institute for Digestive Diseases, and it 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 in 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. Lopez of the Clinica Las Condes (CLC), one of the biggest and most advanced hospitals in Chile. Due to the long history between TMDU and Chile, our university was invited to supervise the project. In 2009, the Ministry of Health of Chile, CLC, and TMDU signed a collaboration agreement concerning colorectal cancer screening (Fig. 1), and the Latin American Collaborative Research Center (LACRC) was established at CLC in 2010 (Fig. 2). Over the years, TMDU has continuously sent experts in the fields of pathology, endoscopy, and research to LACRC. Since 2012, the Prevention Project for Neoplasia of Colon and Rectum (PRENEC) has been implemented, using the Japanese method with an immunological fecal occult blood test and colonoscopy.

The Chilean-Japanese Institute for Digestive Diseases at the Hospital San Borja Arriaran is the main place of PRENEC in Santiago. The institute's endoscopy unit has been redesigned for PRENEC, with extensive support from the Japanese Embassy in Chile.

The institute serves as a training center for endoscopy. From October 2013 to March 2020, a total of 26 Latin American doctors have taken a training course in endoscopy, acquiring the skills required for cancer screening (Fig. 3).



Collaboration agreement concerning colorectal cancer screening between the Ministry of Health of Chile, CLC and TMDU



Signing ceremony of the memorandum of understanding between CLC and TMDU for the establishment of LACRC



Colonoscopy training for Latin American doctors

PRENEC, which started in three cities: Santiago, Valparaiso and Punta Arenas, has now expanded to eight major cities: in addition to the above three cities, Coquimbo, Osorno, Valdivia, Concepcion and Antofagasta.

From June 2012 to March 2019, 30860 asymptomatic participants registered with PRENEC. A total of 266 colorectal cancers were detected, and 194 lesions, 73% of which were cured by endoscopic treatment.

PRENEC and supportive activities by TMDU have recognized as essential aspects of Chilean healthcare. In the future, it is expected that PRENEC will be expanded throughout Chile and contribute to the reduction of colorectal cancer mortality.

In December 2017, TMDU's ex-president Takashi Ohyama received the Order of Bernardo O'Higgins from the Government of Chile in appreciation of our contribution to Chile (Fig. 4).



Honoring ceremony of the Order of Bernardo O'Higgins from the Government of Chile for TMDU's ex-president Takashi Ohyama

Spreading Network of TMDU-PRENEC in Latin-America

TMDU has also tried to promote 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 and LACRC doctors 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 been completed and preparations to launch PRENEC's full-scale operation are underway.

Although Ecuador was unable to join the PRENEC network due to the government's intention, colorectal cancer screening has already begun under its own program.

Academic Activities

The results obtained with PRENEC have been reported in various medical journals by Chilean doctors or doctors who were once stationed at LACRC. More reports related to PRENEC results are in progress for future publication.

Endosur, which was an international symposium on digestive disease, has been held in Santiago every two years with TMDU support. Professors from TMDU and LACRC doctors have participated in this symposium and made various presentations (Fig. 5). In addition, LACRC doctors have frequently participated in other international conferences in Chile and in neighboring countries.

TMDU operates the Project Semester Program, appointing medical

students to overseas institutions. Between 2010 - 2014 and 2017 - 2019, two to six medical students from TMDU a year were attached to the laboratories in the University of Chile or CLC, where they conducted advanced research in collaboration with the local doctors.

LACRC Members

LACRC has been staffed by experts from the pathology, endoscopy and molecular biology fields of TMDU. From 2010 to 2020, LACRC has been operated by nine TMDU doctors; as pathologists, Dr. Takashi Ito (April 2010 to March 2012) and Dr. Hiroshi Kawachi (March 2012 to March 2015); as endoscopists, 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 March 2020); and Dr. Maki Kobayashi as a molecular biologist (July 2012 to March 2015).

LACRC is currently operating in the headquarters of TMDU by Prof. Noriyuki Wakabayashi (Vice President), Prof. Masanobu Kitagawa (Department of Comprehensive Pathology), and other staff.

COVID-19 Pandemic in Chile

The pandemic greatly impacted Chile. In March 2020, the first cases of COVID-19 were reported. After that, the number of people infected with COVID-19 increased sharply and quarantines were established locally in various cities and neighborhoods. However, in May 2020, the whole city of Santiago was put under mandatory quarantine due to a further increase in the number of cases and similar measures were extended to most of the largest cities in Chile.

Instead of dispatching doctors to Chile to be stationed on a long-term basis from April 2020 and to support PRENEC and Endosur activities, TMDU planned to dispatch TMDU experts to Chile several times a year but for short periods of 1-2 months. However, PRENEC and other activities have been suspended since mid-March 2020 and have not been reopened yet (at January 2021). All business trips from TMDU have, of course, been postponed.

We hope that the COVID-19 pandemic will pass and that TMDU's activities in Chile will resume as soon as possible.



A commemorative photo with TMDU's professors and LACRC staff in Endosur 2018

Activities for Strengthening Relationships between TMDU and Thai Universities

CU-TMDU Research and Education Collaboration Center, Thailand

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Zoom Discussion Café between TMDU & Affiliated Universities in Thailand!

Coordinated with affiliated universities in and beyond Japan, Discussion Café (DCafé) events are a great opportunity for students from various cultural and educational backgrounds to come together and delve into complex global health issues in English.

With the COVID-19 pandemic precluding international study and overseas travel in general, this time DCafé used the web conferencing system Zoom to network with students overseas with a range of cultural and disciplinary perspectives. As web conferencing effectively removes the barrier of distance, Thailand's Mahidol University, with which we have an Academic Collaboration Agreement, was selected for the first event because of our close student and researcher exchange

relationship (Fig. 1).

On June 9, 2020, the first two-hour DCafé kicked off with 15 TMDU and 15 Mahidol University medical students in their second through sixth years (Fig. 2). After introducing their universities and themselves, the students split into mixed groups of six members each to examine three COVID-19 response topics. Lecturers from both universities listened with interest to the lively student-led group discussions, presentations of results, and general debates.

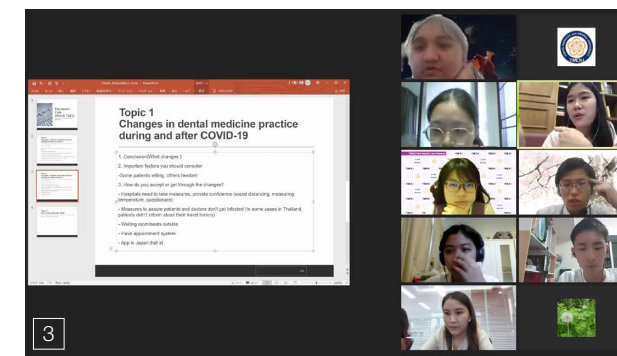
Following the success of this event, the second online DCafé was held on August 26, 2020, between 20 TMDU students from the School of Dentistry, School of Oral Health Care Sciences, School of Medicine, School of Health Care Sciences and 25 dental students from Srinakharinwirot University, with whom we also have a long history of international exchange and an



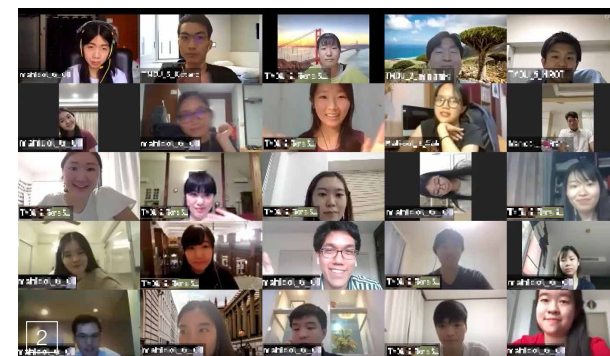
Advisor and student of the JDP with Chulalongkorn University at the TMDU laboratory



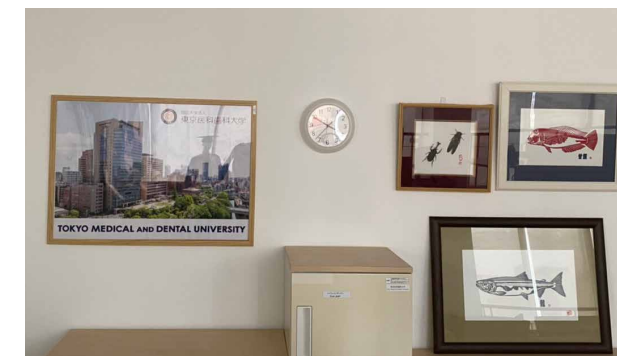
Web conferencing in TMDU x Mahidol University Discussion Café



Group discussion in TMDU x Srinakharinwirot University Discussion Café



Commemorative Photo of TMDU x Mahidol University Discussion Café



Renewed CU-TMDU Research and Education Collaboration Center

Academic Collaboration Agreement.

During the event, students were again split into mixed groups after self-introductions to discuss two COVID-19 related topics: "Changes in dental medicine practice during and after COVID-19" and "Our school life after 2020." Faculties from both universities also joined the event (Fig.3).

These were undoubtedly very stimulating experiences for all the students involved. One participating student challenged herself to form her own opinions based on information from the various aspects presented and discussed during DCafé. Another student explained that, although they found the event difficult, having discussions with a highly diverse range of students was extremely rewarding. These DCafé events also contribute to building connections between students participating from both universities, some of whom continue to keep contact.

Even amidst a global pandemic, the success of this DCafé event, was thanks to advances in telecommunications technology and the long history of exchange between our universities, along with the students' passion and commitment to resolving international issues through cross-cultural collaboration. It was also an extremely valuable experience planning further exchanges with universities in Japan and overseas at a time when face-to-face meetings were prohibited. We hope these DCafé events will be expanded to include participants from all over the world in the near future!

Joint degree program with Chulalongkorn University and CU-TMDU Research and Education Collaboration Center

In the joint degree program with Chulalongkorn University, three students came to Japan in November 2020 and will conduct research at the Departments of Orthodontic Science and Maxillofacial Orthognathics for one year. The timing of coming to Japan was postponed because of COVID-19. So, before coming to Japan, CU supervised the students directly, and TMDU held online meetings with them so that the students could start their research smoothly.

In the CU-TMDU Research and Education Collaboration Center, some furniture was renewed and a TMDU poster was put up for better use. Now the center is used for the monthly teleconference with us or the entrance exam.

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 research project

Overview of the TMDU-NMIMR collaborative research

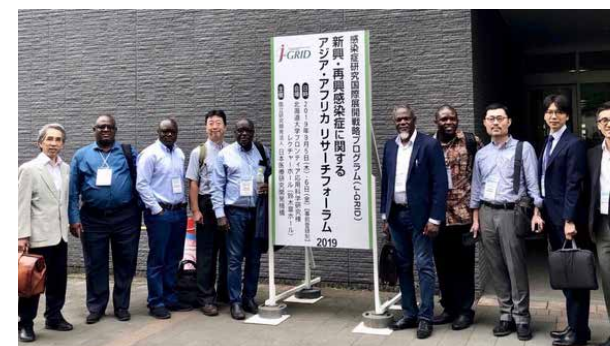
Dr. Hideyo Noguchi, the eminent Japanese microbiologist, died of yellow fever in 1928 in Ghana. In commemoration of Dr. Noguchi's achievements, the Japanese government established the Noguchi Memorial Institute of Medical Research (NMIMR) as a symbolic research facility for medical support for Africa. For the past 40 years, NMIMR has been conducting activities aimed at controlling local infectious diseases through joint research with Japanese research institutes (universities and research institutes). The collaborative research project with NMIMR has been ongoing for 12 years since 2008 through the Japan Initiative for Global Research Network on Infectious Diseases (J-GRID) project in Ghana (1st to 3rd phase), which was supported by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT). Our colleague 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.

In FY2020, our collaborative research was started in the Japan Program for Infectious Diseases Research and Infrastructure for research on emerging and re-emerging infectious diseases with the support of the Japan Agency for Medical Research and Development (AMED). Currently, ten Japanese and fifteen Ghanaian researchers are participating in the project, cooperating on multiple research projects.

The main focus of the AMED 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, our AMED project conducts the following four 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; (3) the identification of antibiotic-resistant bacteria; and (4) the study of life stage and transmission of Buruli-ulcer-causing bacteria. To conduct research more efficiently, TMDU has invited Professor Kazuhiko Katayama of Kitasato University, an expert on viral



Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana



Group photograph of Asian-African Research Forum in 2019 (Sapporo, Japan)

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 vectors of the 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 to virus infection compared to Asian Aedes mosquitos. This result suggests that that strain or subspecies of the mosquito vector probably plays an important role in the outbreaks of dengue fever in West Africa. Our genetic analysis of the rotavirus 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 was found in other geographic areas, such as India and Indonesia. The reemergence of vaccine strains of the rotavirus after the introduction of the vaccine is a global trend of viral genotypes. The carbapenem-resistant bacteria were first found in Ghana in 2017 and then in FY 2018 the NDM-1 gene was then 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 staff moved to this new facility.

At the end of FY2019, a new coronavirus infection (COVID-19) broke out and quickly spread around the world. In Ghana, the border was closed and the lockdown was imposed in Accra City as well as the University of Ghana for six months. As a result, the research activity in NMIMR has been significantly decreased. We hope that the COVID-19 pandemic will be resolved and that research activities and travel will return to normal.

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. They conducted their own research at NMIMR. TMDU accepts young, talented researchers as Ph.D. students under the scholarship program supported by MEXT. In 2020, ten Ph.D. students from the University of Ghana enrolled in TMDU. They joined the parasitology, virology, bacteriology, or biomedical departments in 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 a donation from T.E.N. Ghana MV25.

On November 19th 2020, we received 11 million yen as a donation from T.E.N. Ghana MV25 B.V. for infectious disease research conducted at the Tokyo Medical and Dental University (TMDU)-University of Ghana-Noguchi Memorial Medical Research Institute (NMIMR) Joint Research Center. This donation has continued from last year despite the COVID-19 pandemic.

T.E.N. Ghana MV25 B.V. (MV25), which is funded by Mitsui Ocean Development & Engineering Co. (MODEC), Mitsui & Co., Mitsui O.S.K. Lines, and Marubeni Corporation, operates the Floating Production, Storage & Offloading (FPSO) System off the coast of the Republic of Ghana. FPSO provides marine oil mining, gas production, storage, and shipping. Named after the former President of the country, "FPSO Prof. John Evans Atta Mills," the FPSO is moored at a depth of approximately 1,500 meters and has been producing crude oil and natural gas since 2016. MV25 agrees with the purpose of our AMED project, hopes to contribute to the further strengthening of relations between Japan and Ghana and the development of medical research despite the expansion of COVID-19. We will effectively utilize the donations received and strongly promote local infectious disease control.



Sample collection training from environments by 4th year medical students (Ghana)