TROPMED

Annual Review 2019

Faculty of Tropical Medicine
Mahidol University

Contents

Consultant: Srivicha Krudsood **Coordination & Management:** Pornpimon Adams
Editor: Paul Adams **Writers:** Oiko Tacusalme, Robert Sines
Editorial Staff: Ailada Angatchariya, Pitchapa Vutikes, Sumeth Suebtrakul, Siwaporn Samung, Wijak Anowannaphan and Arada Mahasavin **Graphic Design:** Ronnachai Rarerng, Phaibul Vasanakomut
Photographer: Kamoltip Pomdoung

PRODUCED BY: Publications Unit, Office of Research Services
Faculty of Tropical Medicine, Mahidol University,
420/6 Rajvithi Road, Bangkok 10400, Thailand
Tel.: 66 (0) 2-354-9100-4, 66 (0) 2-306-9100-9; Fax: 66 (0) 2-354-9139;
Web: www.tm.mahidol.ac.th

DEAN'S FOREWORD

I am very proud to reflect upon the progress made in the Faculty over the past year, which will be highlighted and documented in the 2019 Annual Review.

The year 2018 saw numerous significant achievements by the Faculty, as a result of the collaborative efforts of our researchers, educators, service providers, administrators, support staff, collaborators and supporters.

We were ranked as the Mahidol University Faculty with the highest research publication output per staff member, about 3 papers each per year. The Faculty's publication citation rate is the highest in the University.

The Faculty was awarded a Wellcome Trust grant to conduct the *MIST* project, the first *P. vivax* malaria infection study in humans in Thailand. This project should help us fast-track vaccines and novel drug treatments for *P. vivax*.

Assoc. Prof. Dr. Pratap Singhasivanon
Dean, Faculty of Tropical Medicine
Mahidol University

"We were ranked as the Mahidol University Faculty with the highest research publication output per staff member, about 3 papers each per year."

Our Biosafety Laboratory Level 3 (BSL3) became operational, providing us with cutting-edge technologies to research the most virulent and complex viruses and pathogens safely.

The Bangkok School of Tropical Medicine developed two new online courses to commence in 2019. We introduced soft skills and 21st century skills as part of the outcome-based education curricula.

The Hospital for Tropical Diseases was equipped with facilities to provide treatment for increasingly prevalent non-communicable diseases and re-emerging diseases.

Our researchers responded creatively to budgetary limitations by applying successfully for more local and international research grants, using entrepreneurial skills to create a direct positive impact on community health. Translational and innovative research was one of our prime focuses in 2018, and the Faculty allotted funding for researchers for innovative projects with translational potential.

Our research provided a tangible impact on improving public health by influencing the national policy and strategy for malaria elimination and control.

Our strategic plan for 2018-2022 was designed to adapt to a changing world. We will strive for excellence in research, education, good governance, and health and academic services. We will stay true to our following core values: transformation and innovation, open and globally connected, multidisciplinary, embracing creativity and entrepreneurship, and grounded, data-driven decision-making. These core values are the characteristics of "TROPMED" people.

I would like to express my sincere appreciation to our passionate researchers, educators, service providers, and support staff. Your positive, proactive approaches, dedication, creativity, knowledge, and skills, are enabling us to meet the challenges we confront, together.

For a very exciting, productive, rewarding and prosperous 2019.

STRATEGIC PLAN (2018 • 2022)

VISION / To be the World Class Tropical Medicine Research Institute

MISSION / To Strive for Excellence in Research, Education and Health Services in Tropical Medicine

Global and Social Impact
Research

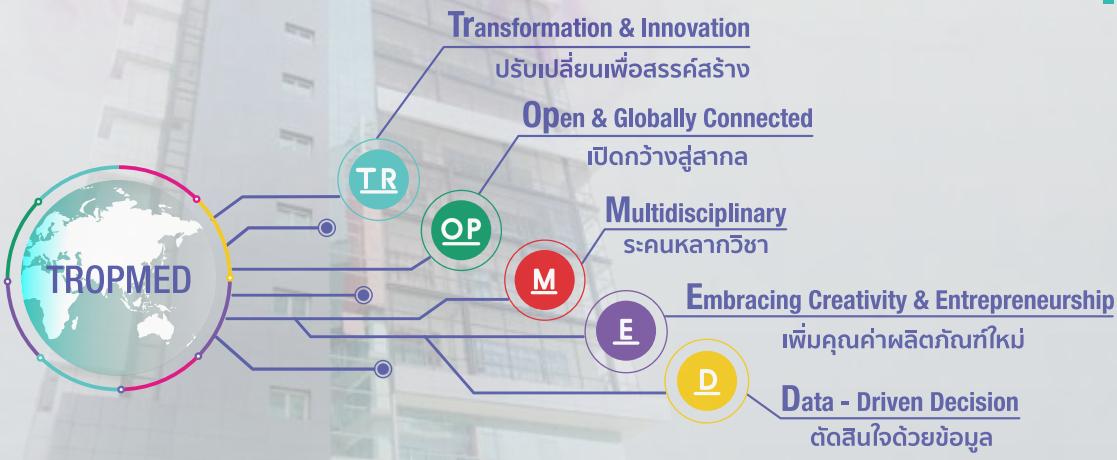
OBE for Globally-Competent Professionals
Education

Leadership
Tropical Health & Academic Services

Sustainable Quality Organization
Good Governance

Faculty of Tropical Medicine, Mahidol University

TropMed Core Values



ADMINISTRATIVE BOARD

1 **Assoc. Prof. Pratap Singhasivanon**
Dean,
Secretary General/Coordinator,
SEAMEO TROPMED Network
Centre Director SEAMEO TROPMED/THAILAND
E-mail: pratap.sin@mahidol.ac.th

2 **Assoc. Prof. Porntip Petmitr**
Deputy Dean for Administration and Finance
E-mail: *porntip.pet@mahidol.ac.th*

3 **Prof. Srivicha Krudsood**
Deputy Dean for Research
E-mail: *srivicha.kru@mahidol.ac.th*

4 **Assoc. Prof. Chamnarn Apiwathnasorn**
Deputy Dean for Information Technology
and Educational Innovation
E-mail: chamnarn.api@mahidol.ac.th

5 **Dr. Wirongrong Chierakul**
Deputy Dean for Quality Development
E-mail: *wirongrong.chi@mahidol.ac.th*

6 **Dr. Surapon Yimsamran**
Deputy Dean for Facilities and Environment
E-mail: *surapon.yim@mahidol.ac.th*

7 Prof. Polrat Wilairatana
Director of Hospital
for Tropical Diseases
E-mail: *polrat.wil@mahidol.ac.th*

8 Assoc. Prof. Waranya Wongwit
Deputy Dean for Education
E-mail: *waranya.won@mahidol.ac.th*

9 Lecturer Dr. Amornrat Aroonnual
Deputy Dean for Student Affairs
and Faculty Welfare
E-mail: *amornrat.aro@mahidol.ac.th*

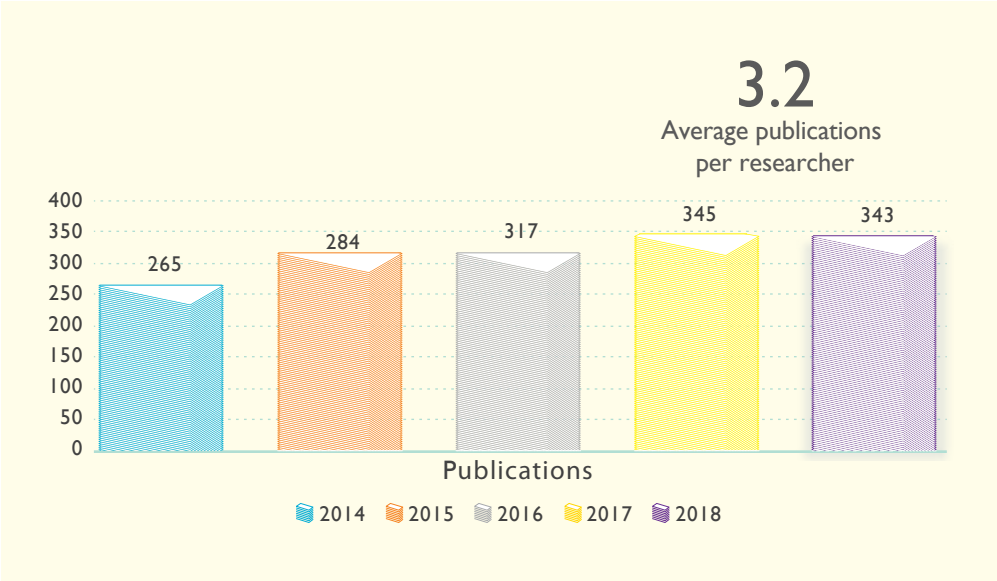
10 Assoc. Prof. Poom Adisakwattana
Assistant Dean for Research
E-mail: *poom.adi@mahidol.ac.th*

11 Asst. Prof. Usa Boonyuen
Assistant Dean for International Relations
E-mail: *usa.boo@mahidol.ac.th*

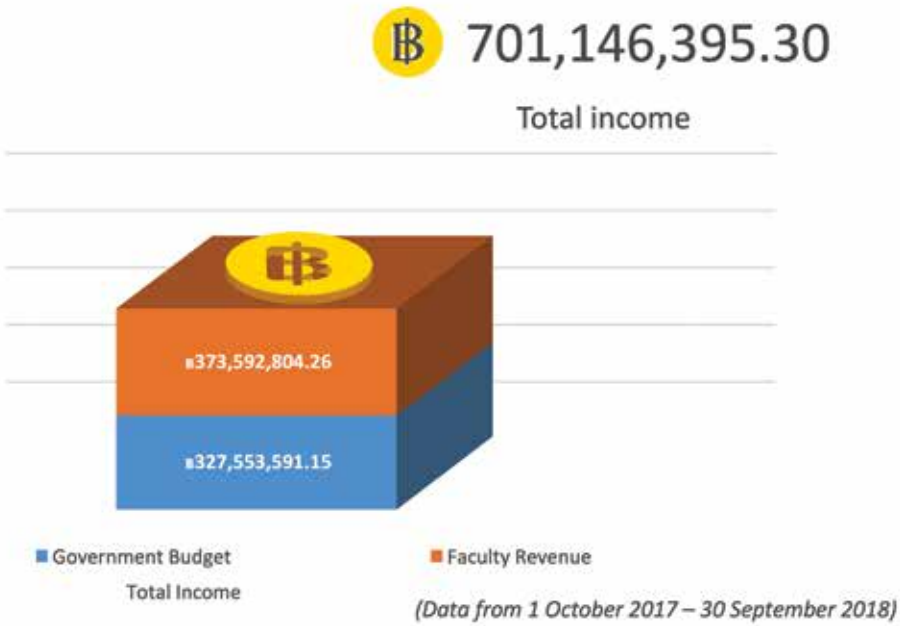
12 Mr. Amnat Khamsiriwatchara
Assistant Dean for Information Technology
E-mail: *amnat.kha@mahidol.ac.th*

STATISTICAL SUMMARY

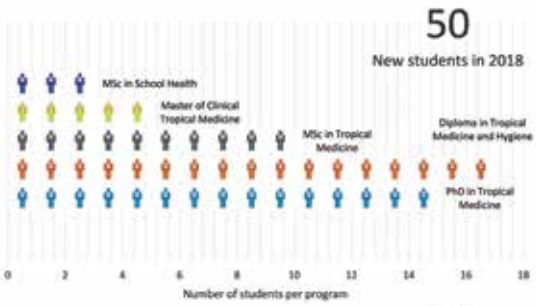
RESEARCH

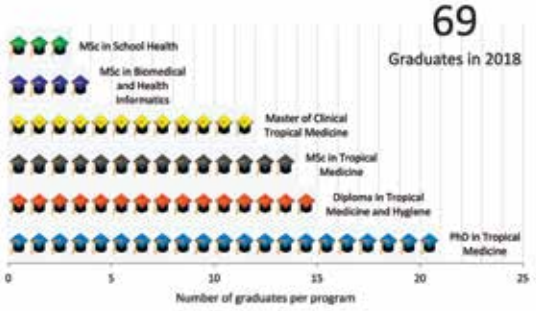


FINANCES

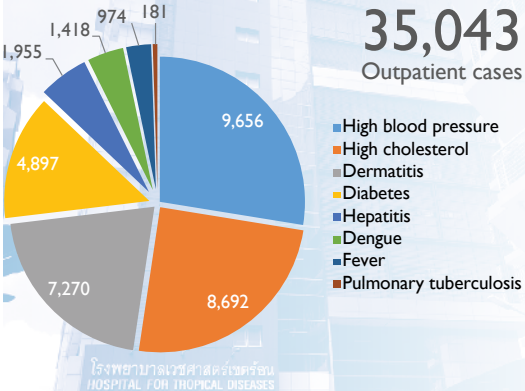


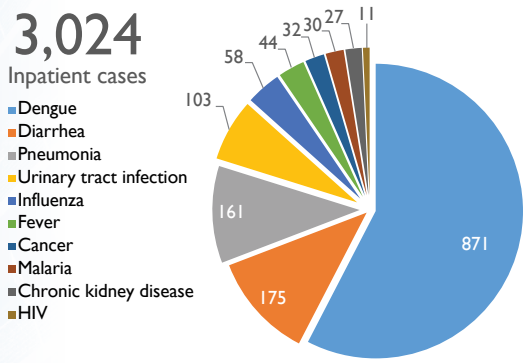
BANGKOK SCHOOL OF TROPICAL MEDICINE



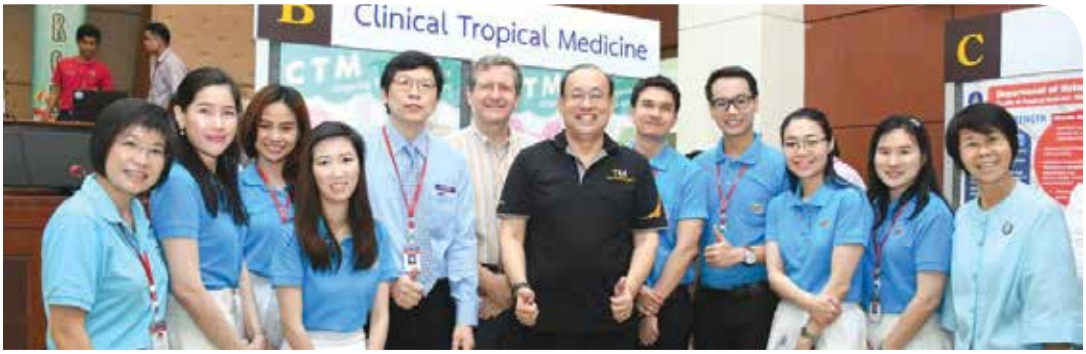


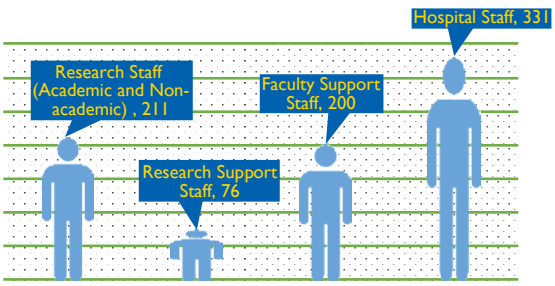
HOSPITAL FOR TROPICAL DISEASES

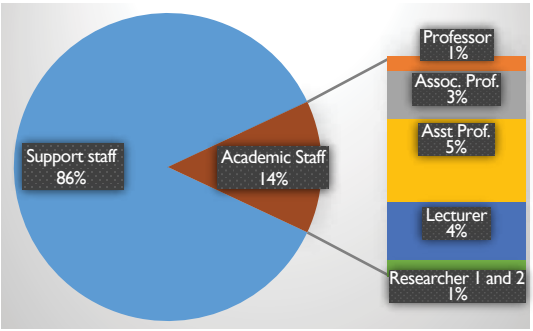




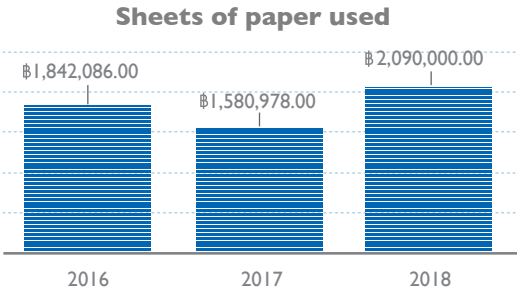
HUMAN RESOURCES

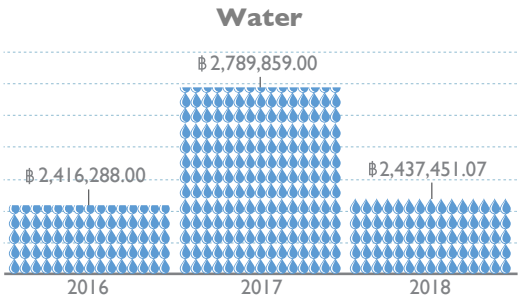


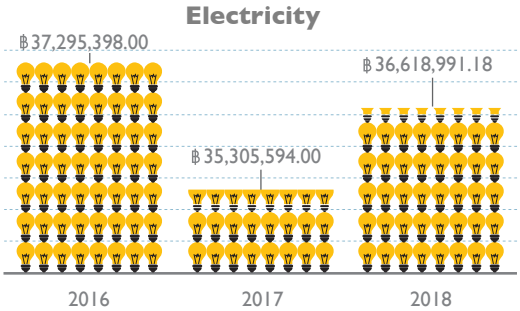




INFRASTRUCTURE AND ENERGY USE REDUCTION







Heads of DEPARTMENT

"When the Faculty was founded in 1960, there were five departments; however, with increased specialization this number has now grown to eleven. Covering a broad range of tropical medicine areas, the departments conduct research, educate students of the Bangkok School of Tropical Medicine, and provide services to both academic and healthcare communities.

The following pages highlight the main research activities of each department, and summarize their work and achievements during 2018."

Prof. Punnee Pitisuttithum
Department of Clinical Tropical Medicine

Assoc. Prof. Paron Dekumyoy
Department of Helminthology

Asst. Prof. Jiraporn Ruangsittichai
Department of Medical Entomology

Asst. Prof. Pornsawan Leaungwutiwong
Department of Microbiology and Immunology

Prof. Mallika Imwong
Department of Molecular Tropical Medicine and Genetics

Asst. Prof. Aongart Mahittikorn
Department of Protozoology

Assoc. Prof. Pongrama Ramasoota
Department of Social and Environmental Medicine

Assoc. Prof. Jaranit Kaewkungwal
Department of Tropical Hygiene

Assoc. Prof. Karunee Kwanbunjan
Department of Tropical Nutrition and Food Science

Asst. Prof. Urai Chaisri
Department of Tropical Pathology

Assoc. Prof. Kriengsak Limkittikul
Department of Tropical Pediatrics

CLINICAL TROPICAL MEDICINE

2018 HIGHLIGHTS

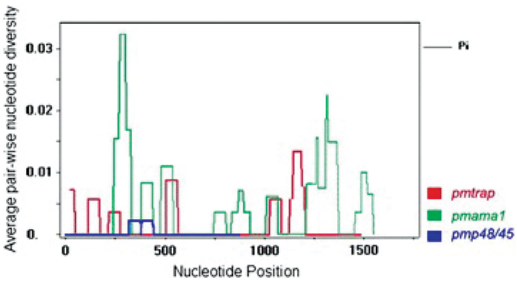
FACTS AND FIGURES

67	2	1	26	14
Publications	Poster presentations	Oral presentation	Academic Staff	Support Staff

RESEARCH HIGHLIGHTS

While fever remains an important cause of hospitalization in Southeast Asia, the common causes of fever in many regions of the Tropics remain unknown. This knowledge is critical for helping doctors decide on the most appropriate treatment in areas where access to diagnostics is difficult, and also for reducing inappropriate antibiotic use, which can contribute to the development of antibiotic-resistant bacteria. To further advance research into this problem, Dr. Wirongrong Chierakul, with other Thai researchers, investigated the causes of fever among hospitalized patients in Chiang Rai, northern Thailand, and assessed whether two specific chemical markers could distinguish bacterial from viral infections. The study revealed that scrub typhus, dengue and leptospirosis were the major causes of fever and that these conditions were not always accurately diagnosed and managed. Researchers found that certain biomarkers, such as C-reactive protein (CRP), are better at differentiating bacterial from viral infections than other biomarkers. These results should help improve the management of febrile patients and aid healthcare workers in the correct use of antibiotics as part of the wider focus on antimicrobial stewardship. The study was published in *PLOS Neglected Tropical Diseases*.

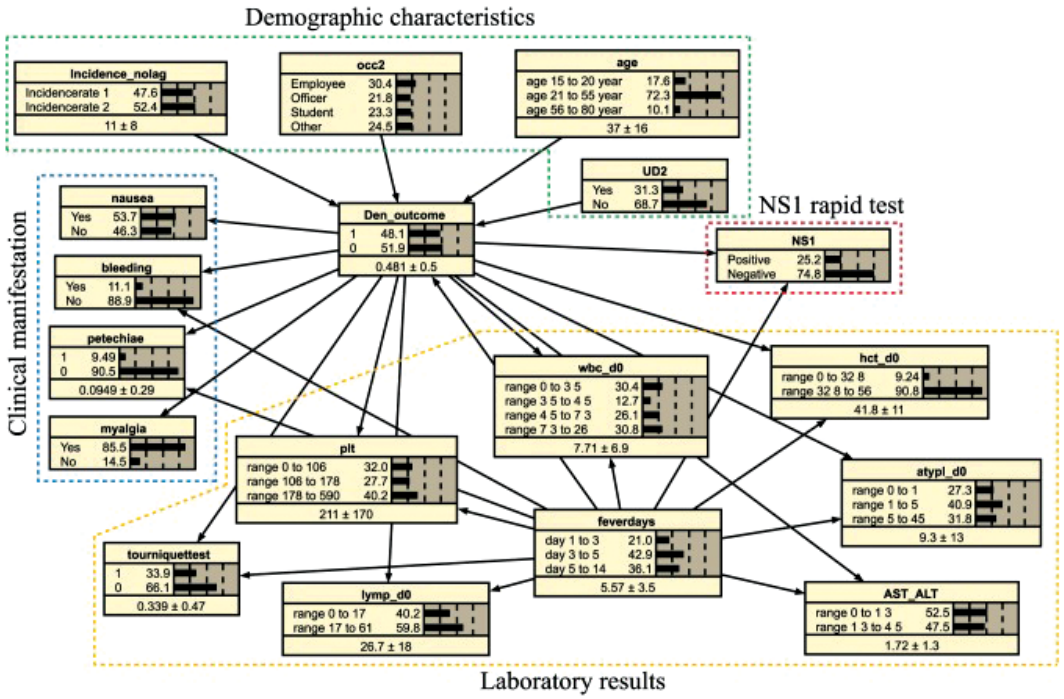
Dr. Wirongrong Chierakul



The temporal spread of scrub typhus and dengue cases for Mueang District, Chiangrai Province

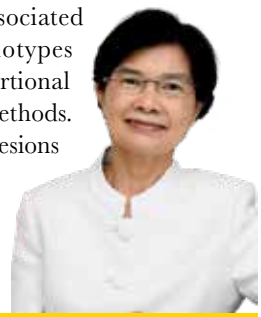
In a recent study to determine the usefulness and reliability of network models, Asst. Prof. Viravarn Luvira, Asst. Prof. Watcharapong Piyaphanee and a collaboration of Thai researchers constructed Bayesian Network (BN) models and used them to predict the probability of dengue infection. Using secondary data collected from a previous study on acute undifferentiated febrile illness (AUFI) patients, the BN models provided solid performance in making dengue diagnosis comparable with physician's diagnosis, and demonstrated that BN models can be applied effectively for dengue diagnosis. The Bayesian network model developed from the study could be useful to assist physicians in diagnosing dengue, particularly in regions where experienced physicians and laboratory confirmation tests are limited. The study was published in *PLOS Neglected Tropical Diseases*.

In an effort to further studies in human papillomavirus, Prof. Punnee Pitisuttithum and a large consortium of international researchers contributed to a study



Final Bayesian network model for dengue diagnosis

designed to estimate the proportion of vulvar and vaginal squamous intraepithelial lesions (LSILs and HSILs) in young females attributable to 14 human papillomavirus (HPV) genotypes. A *post-hoc* analysis of prospectively diagnosed vulvar and vaginal LSILs and HSILs among the females enrolled in the placebo arms of two phase 3, randomized HPV vaccine trials, assessed 14 HPV genotypes associated with cervical cancers or anogenital warts using a type-specific multiplex polymerase chain reaction (multiplex PCR) assay. The frequency of lesions associated with specific HPV genotypes was estimated by proportional and other attribution methods. Most vulvar and vaginal lesions were attributable to at least 1 of the 14 HPV genotypes analyzed based on the study. Researchers strongly suggest that effective immunization programs could potentially prevent substantial numbers of HPV-related vulvar and vaginal LSILs and HSILs. The study was published in *Obstetrics & Gynecology*.



Prof. Punnee Pitisuttithum

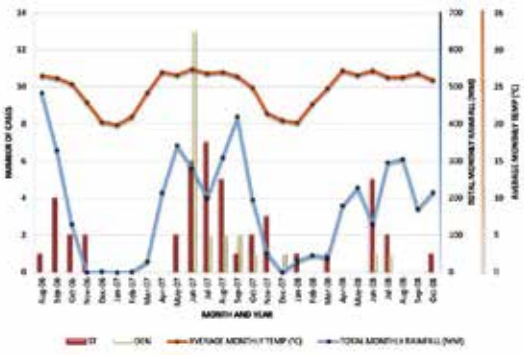
No licensed HIV-1 vaccine exists mainly due to the lack of direct comparability between clinical trials and preclinical studies. In an effort to bring an effective HIV-1 vaccine to market, Prof. Punnee, with a large group of international researchers, evaluated mosaic adenovirus serotype 26 (Ad26)-based HIV-1 vaccine candidates in parallel studies in humans and rhesus monkeys to define the optimal vaccine regimen to advance into clinical efficacy trials. Researchers conducted a multicenter, randomized trial approach where participants were recruited from 12 different clinics in east Africa, South Africa, Thailand, and the USA. A parallel study in rhesus monkeys was also conducted to assess the immunogenicity and protective efficacy of these vaccine regimens against a series of six heterologous and intrarectal challenges with a simian-human

immunodeficiency virus (SHIV). The mosaic Ad26 HIV-1 vaccine induced comparable and robust immune responses in humans and rhesus monkeys as the study helped demonstrate that the vaccine was immunogenic in both study groups, showing substantial protective efficacy in rhesus monkeys. A clinical efficacy trial has been initiated in southern Africa to determine whether this vaccine concept will prevent HIV-1 infection in humans. The study was published in *The Lancet*.

In order to find a better solution to treating a ubiquitous bacterial infection, a Phase II clinical study used to determine the effectiveness and safety of polymyxin B for the treatment of extreme drug-resistant (XDR) Gram-negative bacterial infections in Thai patients was recently conducted by Dr. Thundon Ngamprasertchai in conjunction with other Thai researchers. Overall, a good clinical response rate at the end of treatment was observed in a high majority of cases. Polymyxin B proved to be effective and safe for the treatment of XDR Gram-negative bacterial infections. Based on the research findings, the polymyxin B antibiotic should be considered as an alternative to colistin, which is the primary last-resort treatment antibiotic for those specific infections in Thai adult patients, particularly those at risk of nephrotoxicity. The research was published last year in *Infection and Drug Resistance*.

MALARIA RESEARCH HIGHLIGHTS

In a study published in *Malaria Journal* in 2018, Prof. Sasithon Pukrittayakamee and a group of researchers representing Thailand, Laos and the United Kingdom, examined the genetic diversity of three important antigenic proteins in Thailand, Myanmar and Lao PDR, using conventional polymerase chain reaction (PCR) assay. While studies related to the genetic diversity of these proteins are available for *Plasmodium falciparum* and *Plasmodium vivax*, barely enough information exists regarding *Plasmodium malariae*. The study aimed to demonstrate the genetic variations existing among these three genes in *P. malariae* by analyzing their diversity at nucleotide and protein levels. High mutational diversity was observed in two of the *P. malariae* proteins as compared to 6-cysteine protein in samples isolated from Thailand, Myanmar, and Lao PDR. Taken together, these important new findings suggest that 6-cysteine protein might be a good vaccine candidate against *P. malariae* infection because of its sufficiently low genetic diversity and highly conserved amino acids.



Nucleotide diversity plots of P. malarie proteins isolated from Thailand, Myanmar, and Lao PDR

Dr. Prakaykaew Charunwatthana contributed to an international research study intended to determine whether acetaminophen's capacity to inhibit plasma hemoglobin-mediated oxidation can help severe malaria patients protect their kidneys from damage. The research is significant because acute kidney injury independently predicts mortality in falciparum malaria. Over a two-year period, several patients were randomly assigned to receive acetaminophen or no acetaminophen. Pharmacologic analysis showed that higher exposure to acetaminophen increased the probability of creatinine improvement, which helps show how well the kidneys are removing waste products from the blood. In this proof-of-principle study, acetaminophen showed kidney protection without evidence of safety concerns in patients with severe falciparum malaria, particularly those with prominent intravascular red blood cell

Dr. Prakaykaew Charunwatthana

destruction (hemolysis). The study was published in *Clinical Infectious Diseases*.

In an effort to study the after-effects of widespread experimental drug treatment associated with malaria, Prof. Kesinee Chotivanich and Dr. Borimas Hanboonkunupakarn among a group of international researchers recently evaluated the effectiveness and safety of mass drug administration employing dihydroarteminisin–piperaquine plus a single low dose of primaquine, to study their effects on asymptomatic *P. falciparum* infections in four malaria-endemic villages randomized to early and deferred MDA in southern Savannakhet Province, Lao PDR. Researchers found a significant reduction in *P. falciparum* prevalence and incidence following the MDAs which were safe, well tolerated, feasible, and achieved high population coverage and adherence. MDAs must be integrated in multi-pronged approaches, such as vector control and preventive measures with special focus on specific risk groups, such as mobile, migrant populations and forest-goers for a sustained period to eliminate the remaining parasite reservoirs, based on observation. Findings were published in *Malaria Journal*.

Prof. Kesinee Chotivanich

To further understand the effects of malaria on patients burdened with lung injury, Dr. Natthida Sriboonvorakul, Prof. Sasithon Pukrittayakamee and a team of international researchers studied the relationship between plasma acids, urine acids and renal function in adult patients with acute falciparum malaria which is the deadliest species of parasite that causes malaria in humans. Analysis showed that both plasma and creatinine-adjusted urine concentrations of p-hydroxyphenyllactic acid (pHPLA) were higher in severe malaria patients with acute kidney injury. Both plasma and urine concentrations of pHPLA closely correlate with acute kidney injury in patients with severe falciparum malaria. The research has importance because, in severe falciparum malaria, metabolic acidosis and acute kidney injury (AKI) are independent predictors of fatal outcome in all age groups. This study was also published in *Malaria Journal*.

DEPARTMENTAL HIGHLIGHTS

In a display of high-value research influence in the tropical medicine community, the Department of Clinical Tropical Medicine has three researchers on staff with an h-index at 40 or above. The h-index is a measurement intended to represent both the productivity and impact of a particular scientist or scholar, or a group of scientists or scholars within the context of a specific field of study. Consensus on the index deems that after 20 years of research, an h-index of 20 is good, 40 is outstanding, and 60 is truly exceptional. The advantage of the h-index is that it combines productivity (i.e., number of papers produced) and impact (number of citations) into a single number.

Under "Clinical Tropical Medicine", Prof. Punnee and several staff are also performing extensive research studies on various infectious disease vaccines. Highlights associated with the vaccine work may be found in the Vaccine Trial Center section of the Annual Review. ated with the vaccine work may be found in the Vaccine Trial Center of the Annual Review.

HELMINTHOLOGY

2018 HIGHLIGHTS

FACTS AND FIGURES

14	10	5	6	9
Students	Poster presentations	Oral presentations	Academic Staff	Support Staff

NATIONAL AND INTERNATIONAL COLLABORATIONS

Inspired by Mahidol University's policy to collaborate with foreign experts in academic and research fields, the Department welcomed three visiting Professors from France, China, and the UK.

In addition, the Department collaborated with research groups from Australia, China, Japan, and Spain, including educational collaboration with France, Thailand and other countries on the Erasmus-Capacity Building for Higher Education: LIFE for SEA-ED program (Learning to Investigate by Field Experiment for Southeast Asia Emerging Diseases).

Under national collaborations with Thailand's Ministry of Public Health (MOPH), on opisthorchiasis and bile-duct cancer (cholangiocarcinoma), Assoc. Prof. Paron Dekumyoy was appointed expert by the Department of Communicable Disease Control (CDC), MOPH. Also, Assoc. Prof. Paron Dekumyoy, Assoc. Prof. Dorn Watthanakulpanich, and Asst. Prof. Teera Kusolsuk joined meetings for projects under the auspices of the Department of Health and CDC.

EMPHASIZING RESEARCH

Dr. Paron Dekumyoy published a paper on *Paragonimus heterotremus* recombinant antigen for serodiagnosis, entitled "ELISA based on a recombinant *Paragonimus heterotremus* protein for serodiagnosis of human paragonimiasis in Thailand" in *Parasites & Vectors*. This antigen is one of the recombinant antigens produced from particular helminthes; all recombinant antigens will be studied pursuing the final aim--a rapid test kit--in the future.

PUBLIC PARTICIPATION IN SCIENTIFIC RESEARCH

Citizen science and social media have played a huge role in understanding the distribution of the newly invasive New Guinea flatworm *Platydemus manokwari* (Platyhelminthes: Geoplanidae) in Thailand. Dr. Kittipong Chaisiri and his team at the Department of Helminthology investigated the New Guinea flatworm's potential role as a paratenic host carrying *Angiostrongylus malaysiensis* larvae.

Dr. Kittipong, in collaboration with the Thailand Biodiversity Conservation Group, tapped the public to participate in scientific research that will improve our understanding of the New Guinea flatworm, its potential threat to biodiversity, and its potential impact on human health.

The oldest photographic evidence of Platydemus manokwari occurrence in Thailand (credit: Chayajit Deekrachang, 2010)

Staff and students of the Department at the International Conference for Parasitology (ICOPA), 2018, Daegu, Korea

Using the Siamensis.org Facebook page and Line messaging applications, volunteers were encouraged to send photos of the New Guinea flatworm sighted in their area for identification and reporting. The data gathered from this collaboration between the public and research team enabled the mapping of the presence, distribution, and confirmed the spread of the flatworm in many parts of Thailand. The team also received photographic evidence that suggests the flatworm has been in the country since 2010.

To confirm whether the New Guinea flatworm in Thailand carries Angiostrongylid larvae, Dr. Kittipong's research team obtained lab-confirmed New Guinea flatworm samples provided by the citizen volunteers. Parasitic infection was investigated from the flatworm's tissues, using the artificial tissue digestion technique (pepsin digestion) and microscopic examination. Using molecular methods, the team identified *Angiostrongylus malaysiensis* L3 in 15 of 121 flatworm samples tested (12.4% infection rate).

In 2018, Dr. Kittipong presented the study results at international conferences, such as the 3rd International Symposium of Biodiversity and Health in Southeast Asia, and the Joint International Tropical Medicine Meeting 2018, held in Taiwan and Bangkok, respectively. Dr. Kittipong was also invited to speak at Pint of Science, a local science forum held in Bangkok.

The same year, the study was published in the *Journal of Helminthology*.

HOST-PARASITE INTERACTION

Assoc. Prof. Poom Adisakwattana studied the host-parasite interaction of infection by *Trichinella spiralis*, a parasitic nematode that causes the disease trichinosis. The complications of trichinosis may include inflammation of heart and lungs.

Dr. Poom found a particular protein from the molecules secreted from *Trichinella spiralis*. Prior to the discovery, the role of this protein was unknown until Dr. Poom's lab identified and characterized the functions of this protein. They found that the protein can downregulate inflammation in the host. This protein also inhibits the immune response of the host against infection. Dr. Poom aims to find the mechanism in the helminth that infects the host and reduces the immune response of the host.

This research can potentially lead to the development of a drug or vaccine against the parasite. Moreover, because the protein was found to decrease inflammation in the host from helminth infection, this protein can be a noble therapy against other inflammation complications caused by non-communicable diseases in the future.

Department of Helminthology alumni gathering for New Year and Blessing Ceremony

Department staff at the performance agreement meeting with the Dean

Dr. Poom modelled a method of production of this protein and a patent application for this method is on-going. The ultimate goal of this study is to develop the molecular protein secreted from the helminth and apply for the treatment of inflammation of the host.

Dr. Poom is collaborating with the Institute of Infection and Global Health, University of Liverpool, UK, for this research. The publications are well underway and hoped to be published in journals by Q1 in the following year.

FUTURE HELMINTH RESEARCH

A BIO-Banking center of helminths will be organized as a central resource for collaboration, assistance, and advice for helminthologists. Assoc. Prof. Urusa Thaenkham and Dr. Kittipong Chaisiri aim to develop a DNA barcoding system for helminths to enhance the molecular identification and diagnosis of any objects from the host or environment.

An ongoing research project by Assoc. Prof. Urusa and colleagues has focused on developing a drug from a Thai medical herb for the treatment of gnathostomiasis. This project has been supported by the Agricultural Research Development Agency. The researchers have already proved the safety of the extracts by testing cytotoxicity and animal toxicity (acute and sub-chronic toxicities). The next step is to study the pharmacokinetics and efficacy of the extract for killing *Gnathostoma spinigerum* in infected rats.

Department of Helminthology with the Departments of Medical Entomology and Protozoology at the New Year's Day celebration at the Faculty

Staff and members of the Department of Helminthology

MEDICAL ENTOMOLOGY

2018 HIGHLIGHTS

FACTS AND FIGURES

13	8	1	8	13
Publications	Poster presentations	Oral presentation	Academic Staff	Support Staff

Dept. of Medical Entomology staff and students

PUBLISHED STUDIES

Asst. Prof. Ronald Enrique Morales Vargas recently collaborated with researchers from Japan, Malaysia, and Indonesia in an observational study examining the foraging responses of the yellow-fever mosquito (*Aedes aegypti*) to various colors in equal-choice bioassays using artificial flowers with sugar rewards, since the impacts of artificial flowers on foraging had not previously been explored. The research results indicated that attraction of the mosquito to rewarding artificial flowers in some cases was comparable to live flowering plants. The discovery that both male and female mosquitos can feed on nectar mimics held by artificial flowers opens new avenues for improving sugar-bait technology and for developing new attract-and-kill devices. The study was published in *Acta Tropica* last year.

In a study featured last year in *Tropical Biomedicine*, Asst. Prof. Suchada Sumruayphol, with researchers from Suan Sunandha Rajabhat University, researched effective trapping methods of adult mosquitoes using dried mushroom samples in the wild, with the end goal of helping to reduce the spread of deadly human pathogens, such as Plasmodium species causing malaria. The efficacy

of this strategy was dependent upon the capacity of the trap to attract and retain insects with specific strong mushroom odorants, which are strong attractants for mosquitoes. The efficiency of a resting box baited with five different extracts from local mushrooms used to attract mosquito vectors was tested in Samut Songkhram Province, Thailand. Compared with an unbaited resting box (control), only traps containing high rates of shiitake-mushroom extract captured significantly more mosquitoes. The study findings indicated that shiitake extract can be used as an inexpensive, non-toxic, and locally sourced attractant to increase the efficacy of mosquito control.

As part of another study published in *PLOS One* during 2018, the Department of Medical Entomology applied landmark-based and outline-based geometric morphometric (GM) approaches to differentiate Walchia species of trombiculid mites (chiggers) using scutum (shield) measurements. Chiggers are the main vector of scrub typhus, which is a mite-borne infectious disease widely distributed in the Asia-Pacific region, especially in agricultural areas. Scrub typhus is also a major cause of febrile illness, occurring mainly in northern Thailand. These vectors are very small, making their morphological identification difficult. Based on several chigger specimens characterized by paired genotypic and morphological data, researchers found evidence of genetic polymorphism and morphological plasticity within the genus Walchia. Researchers concluded that the morphologically closely-related trombiculid mite species can be further differentiated by their scutum features alone, using GM approaches. This technique is a promising tool for much-needed characterization studies of chiggers. The entomologists found that geometric morphometrics are useful in supporting or augmenting conventional morphological identification of chiggers, and contribute to improved characterization and validation of genetic mite barcoding, which will substantially facilitate the future identification of mites.

RESEARCH HIGHLIGHTS

The Department of Medical Entomology created a mosquito insectarium for dengue-vaccine trials in 2018. This new insectarium has been named the "Entomological Laboratory for Dengue Virus Infections (ELDVI)". A dengue vector-control project related to Wolbachia infection in mosquitoes was initiated with the development of the new insectarium last year. The insectarium will allow Faculty to implement independent research projects, will provide a critically needed support facility for the ongoing surveillance of mosquitoes, and will offer more insight into mosquito physiology while enhancing opportunities to develop new therapeutic strategies to stop the spread of such infectious agents from multiple angles.

Mosquito larva survey

The Department of Medical Entomology currently has a natural mosquito repellent and a novel mosquito aspirator made from domestic materials in the process of patent submission at the Thailand Department of Intellectual Property (DIP). A small research team from the Department developed the mosquito repellent, which incorporates a specific formula extracted from a combination of three natural essential oils. The repellent is unique, as using multiple oils increases the mosquito-repellent efficacy and protects longer than a typical mosquito repellent using only one oil. Patents for the repellent were submitted to DIP in early 2018 with expected approval in summer 2019.

In another innovative endeavor, Mr. Theerawit Phanphoowong has engineered a unique design for an insect aspirator that is more ergonomic and

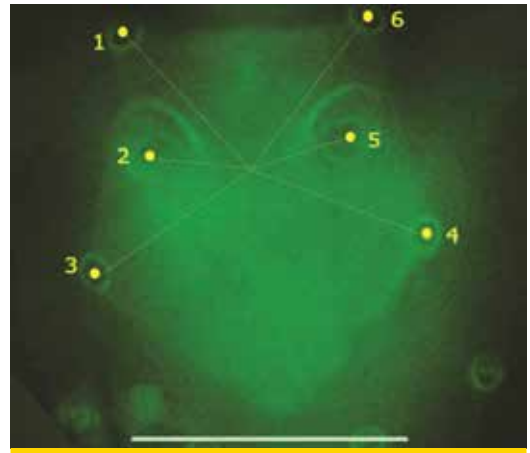
more practical than aspirators currently available in the marketplace. The concept for a newly designed aspirator grew out of the Department's needs for specialized insect research. There is an important need for effective and affordable mosquito sampling methods, and ultimately, the new device can help researchers develop better health intervention strategies. Patents for the new aspirator are currently in process by MU.

In an effort to bring medical research into the 21st century, Dr. Patchara Sriwichai is developing and evaluating a novel mobile application for malaria vector survey and data analysis, which has been utilized, improved and validated over the past year. The mobile application is known as *Survey123* which is used under the ArchGIS system. *Survey123* for ArcGIS is a simple and intuitive form-centric data-gathering solution that replaces unreliable paper-based data collection with a trustworthy digital solution that fits the needs of diverse environments. The modern mobile and cloud-based software solution will assist with various vector control solutions against numerous vector-borne diseases present in the field. *Survey123* data warehousing will also be used as an essential tool in the budget development of the best vector-control methodologies. Overall, the new application should help the Department save time and resources that would otherwise be consumed with traditional data-gathering and analysis methods associated with malaria and other related vector research.

Survey123, the form-centric data collection GIS app

Species identification of chigger mites continues to be a major focus of the Department. In a landmark achievement related to chigger-mite research, Dr. Sungsit Sungvornyothin developed a groundbreaking microscopic methodology for species and related pathogen identification purposes associated with chigger mites. Based on the autofluorescence properties of the chigger-mite exoskeleton, the new method characterizes and identifies external morphology without damaging the internal tissues and microorganisms of the mite. In classical methods, species identification of chigger mites, as well as scrub typhus pathogen detection in the same specimens, is not possible, as each method inhibits dual identification due to the bio-destruction incurred in each process. This is the first time a new microscopic methodology has been developed based on the autofluorescence properties of the chigger mite exoskeleton, in order to characterize and identify external morphology without damaging internal tissues and microorganisms, so the same identified specimens can be used in pathogenic detection. This novel methodology, combined with rational entomological surveys, will provide significant information on epidemiological aspects of scrub typhus that have previously been unknown. In addition, the new methodology will strengthen understanding of chigger-mite taxonomy.

A new concept focusing on the entomological control of scrub typhus vectors envisioned by



Autofluorescence of the chigger mite

Dr. Sungsit Sungvornyothin was proposed to the Bureau of Vector-Borne Diseases, Ministry of Public Health, Thailand by the Department of Medical Entomology, last year. A residual insecticide spraying method has been suggested for application to huts based in agricultural areas, which have been found to be hot-spots for scrub typhus transmission during agricultural activities. Based on striking preliminary research, it has been found that the chigger mite tends to occupy these agriculture-based hut areas regularly, waiting for human hosts. This key observation may have major implications for future scrub-typhus control efforts. Prospective collaborative research plans that will test Dr. Sungsit's hypothesis related to the chigger mite vector are presently in development.

COLLABORATIONS

In a display of strong cross-border relations with other research affiliates, the Department has been actively sharing significant academic knowledge related to chigger-mite biology and ecology with staff from the Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU). LOMWRU is a clinical-research unit in the Microbiology Laboratory of Mahosot Hospital, in Vientiane, Lao PDR, which is mainly funded by the Wellcome Trust (UK). The partnership is designed to provide health workers, government and international organizations in Laos and elsewhere in Asia with key data that will allow them to make evidence-based decisions for individual patients, and for health policy. The exchange of biological and ecological chigger-mite knowledge is of key importance in chigger research, providing essential information for disease epidemiology with significant vector-control implications.

Prof. Jean-Pierre Dujardin, from the Institute of Research for Development (IRD), has been a Visiting Professor at the Department over the past year. Prof. Dujardin conducted a workshop entitled "Online Modern Morphometrics Training Course", sponsored by the French National Research Institute for Sustainable Development (IRD), at the Faculty of Tropical Medicine, Mahidol University, in August 2018. The comprehensive course covered multiple aspects of morphometric studies, including the use of new online morphometric software. The software will assist researchers with species identification as well as other important focus areas of morphometric study which can then be applied to overall research work. Using this innovative approach, Dr. Ronald has been meticulously analyzing different shapes and sizes of various insects over the last few years as the morphometric method represents a more cost effective alternative to the molecular approach. The process also helps demonstrate adaptation and the evolutionary processes of different species.

Prof. Jean-Pierre Dujardin

In an ongoing mutually beneficial collaboration, last year Dr. Ronald was a Visiting Professor at Miyazaki University, Miyazaki, Japan, where he provided teaching and training in the areas of mosquito taxonomy and mosquito-related viruses and bacteria. In exchange, specialists in the area of tick taxonomy and associated virus and bacteria from Miyazaki University provided on-site education and training to faculty members of the FTM.

Dr. Ronald Enrique Morales Vargas

MICROBIOLOGY AND IMMUNOLOGY

2018 HIGHLIGHTS

FACTS AND FIGURES

34	19	10	12	9
Publications	Poster presentations	Oral presentations	Academic Staff	Support Staff

The Department places strong emphasis on research, studying a range of bacterial, fungal and viral pathogens, as well as the human immunological response to these infections. In addition, the Department runs a diagnostic service providing identification of pathogens responsible for a range of diseases, including melioidosis, dengue fever, hepatitis, viral gastroenteritis, influenza, Zika fever, chikungunya, *morphological and molecular analysis* of fungal pathogen and antifungal drug susceptibility tests.

SYLVATIC TRANSMISSION CYCLE OF FLAVIVIRUS

Dr. Kobporn Boonnak was awarded an e-ASIA Joint Research Program (the e-ASIA JRP) Research Cooperation grant in the field of Health Research on the topic of Infectious Diseases. The 3-year project is a collaboration of young and multidisciplinary researchers from Thailand, the USA, and Cambodia. Using monkey blood samples collected in Thailand and Cambodia, the goal of the project is to understand the sylvatic transmission cycle of flavivirus, involving mosquitoes, monkeys, and humans. The project aims to determine the influence of pre-existing immune response in humans and monkeys living in close proximity in subsequent flavivirus infections.

Dr. Kobporn Boonnak

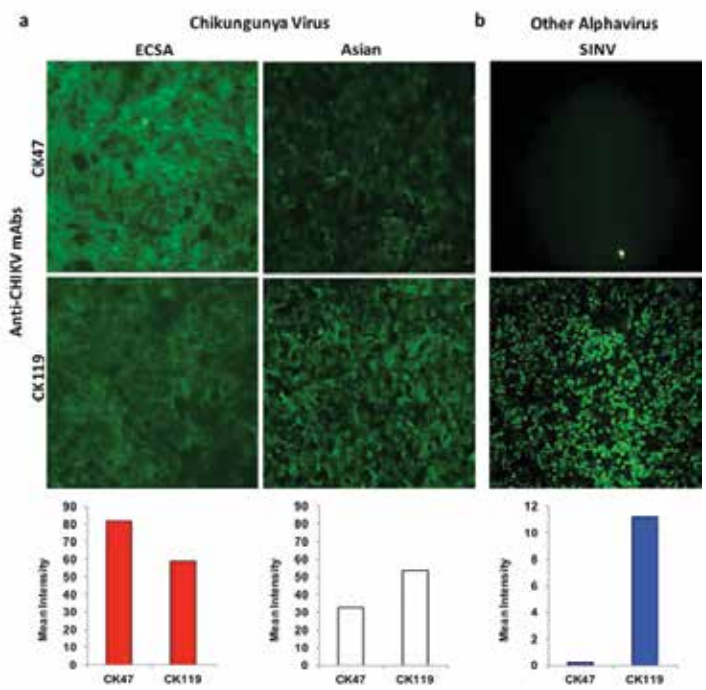
RESPIRATORY VIRUSES

Dr Kobporn Boonnak is involved in a project funded by the National Science and Technology Development Agency (NSTDA) to study severe cases of respiratory viruses, such as influenza virus and respiratory syncytial virus, in Thailand. The study aims to understand the evolution of these viruses and find out how their virulence correlates to disease severity.

CHIKUNGUNYA

Asst. Prof. Pornsawan Leaungwutiwong and PhD student Dr. Aekkachai Tuekprakhon developed a rapid diagnostic immunochromatographic (IC) kit for detection of chikungunya virus (CHIKV) based on broad-spectrum monoclonal antibodies (mAbs) against CHIKV E1 protein. The rapid diagnostic IC kit for

Asst. Prof. Pornsawan Leaungwutiwong



CHIKV detection, which can detect all genotypes of CHIKV, is expected to be of great value for clinical diagnosis and surveillance purposes. The IC kit for CHIKV was successfully patented in Japan in 2018.

Two articles on the development of the CHIKV kit were published in *Scientific Reports* and *PLoS One*, entitled "Variation at position 350 in the Chikungunya virus 6K-E1 protein determines the sensitivity of detection in a rapid E1-antigen test" and "Broad-spectrum monoclonal antibodies against chikungunya virus structural proteins: Promising candidates for antibody-based rapid diagnostic test development", respectively.

FLAVIVIRUSES IN *AEDES* MOSQUITOES

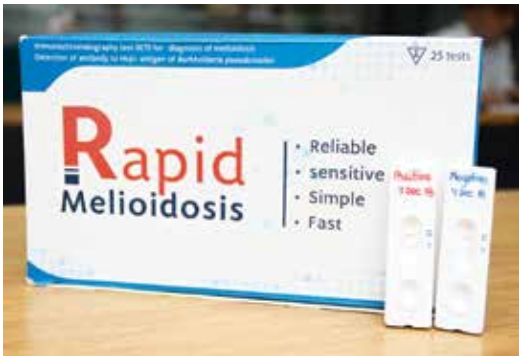
Dr. Pornsawan conducted a retrospective surveillance on the occurrence of flaviviruses in *Aedes* mosquitoes in Phetchabun Province. She tested 1000 mosquito samples archived in 2004-2005 and found four samples positive with dengue serotype 4. The study results improve our understanding of dengue epidemiology in Thailand.

MELIOIDOSIS

Assoc. Prof. Narisara Chantratita investigated the effect of temperature on *Burkholderia pseudomallei* growth, proteomic changes, motility, and resistance to stress environments. The study results show that the bacterium can survive from 25-42 degrees Celsius, with the optimal temperature 37 degrees Celsius, human body temperature. This suggests that the bacteria can multiply rapidly in the human body.

Dr. Narisara also studied the proteins in the bacteria regulated by temperature change. She discovered an antioxidant protein that makes it resistant to oxidative stress and a flagellin protein that makes it motile; these proteins are increased at 37 degrees Celsius. The proteomic expression of the bacteria

Assoc. Prof. Narisara Chantratita



implies that it can adapt and survive in different environmental conditions. This important study was published in *Scientific Reports*, in 2018.

Dr. Narisara's rapid immunochromatography test based on Hcp1 was shown to be a potential point-of-care test for serological diagnosis of melioidosis in hospitals and resource-limited areas. This work was published in *Journal of Clinical Microbiology*, in 2018.

The invention of the rapid immunochromatography test for melioidosis has brought Dr. Narisara a number of awards from Thailand, China, and Singapore.

In 2018, Dr. Narisara was invited to present at several local and international conferences on melioidosis, including the European Melioidosis Congress, held in the United Kingdom.

MOLECULAR TROPICAL MEDICINE AND GENETICS

2018 HIGHLIGHTS

FACTS AND FIGURES

27 Students

36 Publications

10 Academic Staff

8 Support Staff

Research conducted at the Department of Molecular Tropical Medicine and Genetics comprises the study of molecular biology of seasonal and endemic tropical diseases, including malaria, leptospirosis, scrub typhus, tuberculosis, melioidosis, parasitic diseases and cholangiocarcinoma where Department members apply new multidisciplinary technologies for basic and applied research. In 2018, new research trends in the Department focused on entrepreneurship. Development of the Department's recombinant antigen-based diagnostics pipeline featured the advanced progress of several novel products. Recombinant leptospira antigen for IgM ELISA detection reached level 5, based on the technology readiness levels (TRL) scale, while loop-mediated isothermal amplification (LAMP) for scrub typhus detection, high volume quantitative polymerase chain reaction (qPCR) for malaria diagnosis, and matrix-assisted laser desorption/ionization time-of-flight analyzer (MALDI-TOF) biotyper for leptospirosis identification, achieved TRL level 4. In addition, high-throughput technologies, such as epigenomics, transcriptomics and proteomics are ongoing areas of major research in the Department of Molecular Tropical Medicine and Genetics.

Research work accomplished in the area of proteomics was a significant departmental highlight last year as both Asst. Prof. Onrapak Reamtong and Dr. Supachai Topanurak made significant contributions to the field in studies concerned with mass-spectrometry-based proteomics by utilizing several proteomic experimental platforms available in the Department for various types of samples, which include human, parasite, bacteria, fungus, yeast, and virus. Proteomics is the analysis of the entire protein complement of organic material under a technique that provides high accuracy and very important structural information at the molecular level. The field of proteomics is particularly important because most diseases manifest at the level of protein activity. Consequently, proteomics seeks to correlate directly the involvement of specific proteins and their modification status in a given disease state. Such knowledge can provide a fast track towards the identification and development of new drug targets that can be used to diagnose and treat diseases.

SCHISTOSOMIASIS

Schistosomiasis remains a serious global health problem. Schistosomiasis is a tropical disease resulting from infection by trematodes, commonly known as blood flukes, which are parasitic flatworms responsible for a significant group of infections in humans. Schistosomiasis is considered by the WHO

Assist. Prof. Onrapak Reamtong

as the second-most socioeconomically devastating parasitic disease (after malaria), with hundreds of millions of individuals infected worldwide. Because little is known regarding the egg proteins of the *Schistosoma mekongi* trematode, researchers representing the Department of Molecular Tropical Medicine and Genetics led by Asst. Prof. Onrapak collaborated in a study to improve our knowledge in this area using immunoblotting and mass spectrometry-based proteomic approaches to study these proteins and their antigenic properties. Their findings provided new information on the protein composition of *S. mekongi* eggs, as well as the beginnings of a *S. mekongi* immunogen dataset. These new data may help researchers better understand the basic biology of schistosomiasis as well as natural antibody responses against *S. mekongi* egg proteins, both of which may be useful in *S. mekongi* and other Schistosoma diagnostic, vaccine and immunotherapy development. The study was published in *Experimental Parasitology*.

CHOLANGIOCARCINOMA

Cholangiocarcinoma (CCA), commonly known as bile-duct cancer, is prevalent worldwide. However, the highest incidence of CCA has been recorded in northeastern Thailand, where the prevalence of infection with *Opisthorchis viverrini* (OV), a human liver fluke, is higher than other regions of the country. CCA is currently difficult to detect, with the cancer being in the late-stages at the time of initial diagnosis in most cases. However, proteomics offers an unprecedented opportunity to identify new biomarkers and therapeutic targets while providing an understanding of the biochemical pathways involved in pathogenesis. The Department, under Dr. Supachai and a small team of mostly Thai researchers, employed proteomic analysis of bile collected from patients with obstructive jaundice in order to identify potential candidate biomarkers for the Southeast Asian liver fluke commonly associated with CCA. Three potential novel biomarkers for patients with CCA were discovered in the study, which provided new information regarding the detection of liver-fluke infection and associated CCA. These newly discovered protein profiles should prove useful for the development of diagnostic tools for early detection and monitoring of CCA patients with OV infection. The study was published last year in *In vivo*, an international journal of experimental and clinical pathophysiology and drug research.

MALARIA

To support Thai government a national malaria elimination goal of 2024, Asst. Prof. Wang Nguitragool, Asst. Prof. Naowarat Saralamba, Assoc. Prof. Usa Boonyuen, and Prof. Mallika Imwong explored several aspects of molecular biology of human malaria. Asst. Prof. Wang examined the current prevalence of asymptomatic sub-microscopic *Plasmodium* in order to evaluate the parasite reservoir amongst residents from one of the most malaria-endemic regions of Thailand using a highly sensitive molecular method known as light microscopy and loop-mediated isothermal amplification (LAMP). In addition, a clinical trial that will evaluate the ability of ivermectin, a drug used to treat diverse parasite infestations, to interrupt the mosquito reproductive lifecycle through mass administration. Novel vector control tools are urgently needed to accelerate malaria elimination and strengthen antimalarial drug (artemisinin) containment efforts in the Greater Mekong Subregion (GMS). Mass drug administration (MDA) of ivermectin is a new promising tool with previous studies demonstrating that ivermectin MDA can reduce both mosquito and human parameters of malaria transmission in West Africa. Progress of the clinical trial has been hindered by seasonal factors as well as regulatory oversight approval processes. However, recent approval of blood and mosquito surveys at the study site should lead to significant advancement of sample collection and analysis this year which will then be followed by the MDA

Prof. Mallika Imwong

Dr. Supachai Topanurak

of ivermectin. It is hoped that the results of this trial will lead to a new method for reducing malaria transmission and ultimately lead to eradicating malaria in endemic areas.

DEPARTMENTAL HIGHLIGHTS

Last year, three staff members of the Department of Molecular Tropical Medicine and Genetics were awarded Global Connectivity Scholarships for Academic and Supportive Staff Mobility from Mahidol University. Asst. Prof. Onrapak and Asst. Prof. Usa were able to expand their research horizons abroad at the International Center for Biotechnology, Osaka University, Japan, while Dr. Supachai collaborated with the Department of Medicine, Imperial College, London. These scholarships finance valuable research abroad and also foster international partnerships that facilitate important academic exchange. In addition, Asst. Prof. Usa was awarded a Newton Fund grant to finance the research and development of molecular diagnostic assays for G6PD deficiency genetic disorder at the Liverpool School of Tropical Medicine, UK.

UPCOMING RESEARCH

In 2018, Dr. Matthew Phanchana and Dr. Suangsuda Supasai joined the Department as new academic staff. Dr. Matthew focuses on drug discovery for multidrug-resistant anaerobic bacteria and target identification and mechanism of action of the drug artemisinin in *Plasmodium* parasites. In addition, he is developing the molecular diagnosis of tuberculosis. Dr. Suangsuda concentrates on neurobiology and neurotoxicology. Her current research is devoted to investigating the cellular and molecular mechanisms of senescent brain cells, to explore how immunosenescence increases the vulnerability of the aging brain to infection. She is also working on neuropathophysiology resulting from bacterial enteric infection developed in rodent models, to elucidate the relationship between the brain and the gut as well as to learn how to treat the brain from the gut. Due to the addition of these new team members, the Department now has the improved capacity to expand research areas to support the present strategic plans of the Faculty of Tropical Medicine.

PROTOZOOLOGY

2018 HIGHLIGHTS

FACTS AND FIGURES

7	3	5	7	9
Publication	Poster presentation	Students	Academic Staff	Support Staff

RESEARCH HIGHLIGHTS

AMEBIASIS

Last year, PhD students Aulia Rahmi Pawestri and Narumol Khomkhum accomplished breakthrough studies under the supervision of Asst. Prof. Saengduen Moonsom, where the team is seeking specific protein discovery related to the pathogenesis of the parasite *Entamoeba histolytica*, which causes amebiasis. The production of monoclonal antibodies (mAbs) at Dr. Saengduen's laboratory,

Asst. Prof. Saengduen Moonsom

which are specifically aimed at parasite detection, has been a key factor in the team's collective research accomplishments. An important study by Mrs. Pawestri aimed to overcome the problems associated with the inaccurate diagnosis of *Entamoeba histolytica* by developing a sensitive immunological-based antigen detection technique to differentiate *E. histolytica* and *E. moshkovskii*. She found that lab-grown monoclonal antibodies (mAbs) sensitively detected *E. histolytica* and *E. moshkovskii*, while exhibiting no cross-reactivity among species and towards other intestinal protozoa. The end goal of the team is the development of a pan-specific enzyme-linked immunosorbent assay (ELISA) antibody testing that is able to recognize the presence of the parasite *Entamoeba histolytica* with certainty on demand. This exciting innovation is expected to contribute to the accurate differentiation of *Entamoeba* species and reveal the true burden of these parasites and more importantly contribute to an effective management control program for amebiasis in future. In another study that utilized protein identification using liquid chromatography–mass spectrometry (LC-MS/MS), Ms. Narumol studied the characteristics of CXXC-rich proteins related to Ehm2 mAb as these cell membrane proteins have been suggested to be virulent markers of *E. histolytica*. Her study results and sensitivity testing reveal and suggest that CXXC-rich protein in fact plays a critical role in the biology and pathogenesis of *E. histolytica* and also perhaps in *E. moshkovskii*. This groundbreaking

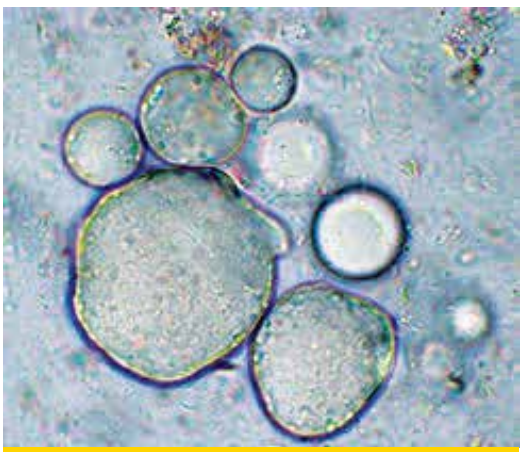
Amoeba under electron microscope

study conducted last year was the first to report the function of CXXC-rich proteins in *E. histolytica* and *E. moshkovskii*, which will further benefit research into the pathogenic dynamics of *Entamoeba*. All of this significant research is in the process of official publication and has been financially supported by the Faculty of Tropical Medicine (FTM), the German Academic Exchange Service and SEAMEO TropMed Network.

PUBLISHED STUDIES

BLASTOCYSOSIS

Several members of the Department of Protozoology along with a team of FTM colleagues recently completed important field research on *Blastocystis*. The objective of one study was to determine the presence and genetic diversity of *Blastocystis* on pig farms in Nakhon Pathom Province, Thailand. The research revealed the possibility of low host specificity of *Blastocystis* subtypes on pig farms in Thailand and suggested that close contact with, or exposure to, pig stools may be a significant source of *Blastocystis* detected in pig handlers. This study was published in *Parasitology International*. In a comparable study, researchers sought to determine *Blastocystis* prevalence and subtype distribution in humans and domestic animals in Ayutthaya Province, Thailand. Based on sample collection, researchers discovered that the overall prevalence of *Blastocystis* in animals was very high as compared with humans. The prevalence of *Blastocystis* in pigs in particular was the highest resulting in the conclusion that livestock may be natural hosts of *Blastocystis* according to test results. The team found that *Blastocystis* subtype 5 was highly prevalent in pigs and humans, with this subtype indicating that close contact with or exposure to animal stools may be a significant source of *Blastocystis* detected in pig handlers as found in the other related study. Poor waste management systems and poor personal hygiene were also found to increase the risk of *Blastocystis* infection. Information specific to *Blastocystis* subtype will increase overall understanding of host-parasite relationships. This work was published in *Infection, Genetics and Evolution*.



Blastocystis

NEOSPORA CANINUM AND *TOXOPLASMA GONDII* INFECTION

In an effort to better understand parasite dynamics in livestock, Ms. Ruenruetai Udonsom along with a team of international researchers aimed to detect seropositivity to *Neospora caninum* and *Toxoplasma gondii* parasites in beef cattle by investigating their presence in areas where testing at two different Thai provinces had been performed five years previously by enzyme-linked immunosorbent assay (ELISA) technique. In addition, risk factors at the animal and herd levels were also evaluated. The study concluded both parasites were still present at the original test sites. Based on the high prevalence of antibodies against subject parasites in beef cattle, it was clear that they represented an important source of infection. Large herd sizes and overcrowding, as well as communal grazing were determined to be the key risk factors of relevant parasite infection in beef cattle. These findings support a better understanding of the prevalence of the two pathogens and will contribute to the design and development of effective control strategies that prevent parasite infection in beef herds. The study was published in the *Thai Journal of Veterinary Medicine*.

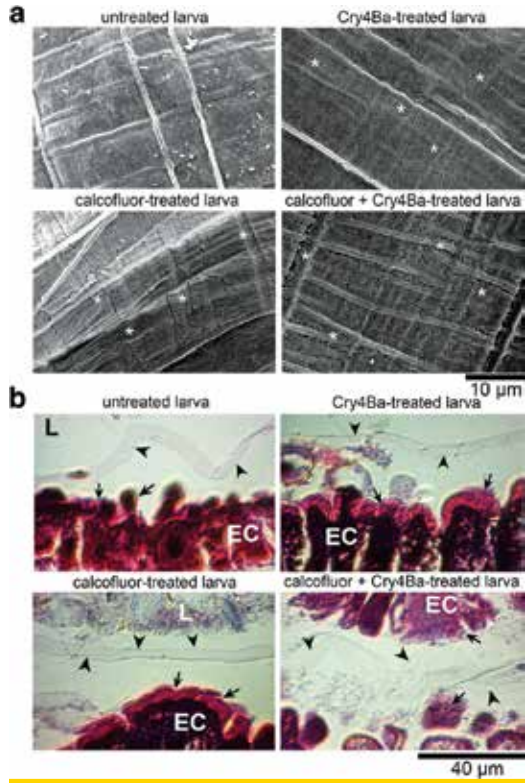
GIARDIASIS

In a study published in *The Southeast Asian Journal of Tropical Medicine and Public Health* last year, Assist. Prof. Supaluk Popruk along with other FTM researchers coordinated in a research effort to determine the efficacy of essential oils from over ten different plants against *Giardia duodenalis*. *G. duodenalis* is a

common zoonotic protozoan causing the diarrheal disease giardiasis, popularly known as beaver fever, an infection of the small intestine. Metronidazole is the drug of choice to treat giardiasis but treatment failure rates are an issue to include side effects such as nausea, headaches and dizziness. The study is important because there is little information about the essential oils of plants found in Thailand used against this parasite. The essential oils of Key Lime (*Citrus aurantiifolia*) were found to be the most effective against *G. duodenalis,* followed by May Chang (*Litsea cubeba)*. The other essential oils had no efficacy against *G. duodenalis*, suggesting that they may contain fewer antigiardial constituents. This work has furthered the understanding of the major active constituents of these essential oils in proving their efficacy and safety for the treatment of *G. duodenalis*.

BIO-INSECTICIDE

Cry toxins have been used worldwide as a bio-insecticide for genetically modified crops because of their environment-friendly properties and killing specificity toward a narrow spectrum of insect larvae. However, due to increased planting of transgenic crops around the world, insect resistance to Cry toxins has increased and has led to their insufficient toxicity in the field. Attempts to improve the efficacy of the Cry toxins have been made by toxin combination, genetic modification, and protein engineering. In a recent study, Asst. Prof. Saengduen Moonsom and other researchers fed mosquito larvae with the chemical Calcofluor and Cry4Ba toxin to investigate the effect of this agent on the toxicity of the mosquitocidal Cry4Ba toxin. The test results demonstrated that Calcofluor had an enhancing effect when co-fed with the Cry4Ba wild-type toxin and that it can function as an enhancing agent for Cry4Ba toxicity by increasing the susceptibility of mosquito larvae resulting in a reduction of both toxin concentration and exposure time. Study results suggested the possible field application of Cry4Ba-toxicity enhancing Calcofluor to improve the efficacy of bio-control of mosquito vectors. The study was published in *Parasites & Vectors*.



Peritrophic membrane topographies of calcofluor and non-calcofluor treated Ae-aegypti larvae

COLLABORATIONS

Asst. Prof. Saengduen Moonsom continues her partnership with Prof. Tomoyoshi Nozaki of the Department of Biomedical Chemistry, Graduate School of Medicine, University of Tokyo, Japan, which began in 2013. Prof. Nozaki has been fulfilling an active mentorship and advisory role to Ms. Narumol by providing specific guidance in the biochemical study of *Entamoeba histolytica* and amebiasis. He also supports a fellowship for short-term research performed by Asst. Prof. Saengduen and Ms Narumol. Prof. Nozaki visited the Department last year as a Visiting Professor providing leading-edge courses on *Entamoeba* isolation and proteomics.

In 2018, Asst. Prof. Saengduen also collaborated with Prof. Kris Chadee, Cumming School of Medicine, University of Calgary, Alberta, Canada, who specializes in innate immunity of the human

gut and its regulatory mechanisms associated with *Entamoeba histolytica* infections and animal modeling for *E. histolytica* infection. His *in vivo* research and study of *E. histolytica* intestinal infection is of particular interest to the Department of Protozoology. Earlier this year, Prof. Chadee gave a well-received presentation on innate immunity to *E. histolytica* infection at the Faculty of Tropical Medicine. In addition, last year, Ms. Narumol received a student mobility scholarship to conduct exploratory research on *Entamoeba* pathogenesis at the home laboratory of Prof. Chadee.

Asst. Prof. Supaluk Popruk continues to join forces with Prof. Windell L. Rivera of the Institute of Biology at the College of Science, University of the Philippines, Diliman. Prof. Rivera's active and vast research background has enriched and advanced the teaching of parasitology at The Department of Protozoology with training directed towards *Blastocystis*, *E. histolytica* and *Trichomonas vaginalis* expertise. Recent attention of the research partnership has centered on the intestinal parasite *Blastocystis* (including multiple subtypes) and its link to the intestinal microbiota. Practical application of his medical research has contributed towards noteworthy parasitic disease control programs with Prof. Rivera acting as technical consultant and member of various technical working groups.

Assoc. Prof. Aongart Mahittikorn and Prof. Katsuro Hagiwara, Department of Pathobiology, School of Veterinary Medicine, Rakuno Gakuen University, Japan collaborated in the development of a platform for zoonotic infectious diseases common among Japan and Thailand. This important research collaboration focuses directly on the concept of One Health in Zoonosis, which takes a strategic, targeted approach to the control and prevention of infectious diseases at a national level. Assoc. Prof. Aongart also partnered with two other international researchers in a study of the microbial composition and parasitic diversity in wild white-handed gibbons. The researchers sought to identify gibbons' gut microbiota composition (taxonomic and functional) and its central association to parasitic diversity as the precise composition, structure, and role of the gibbon gut microbiota remain unclear relative to certain parasites. The study is expected to be published within 2019-2020.

SOCIAL AND ENVIRONMENTAL MEDICINE

2018 HIGHLIGHTS

FACTS AND FIGURES

19	15	20	8	14
Publications	Poster presentations	Oral presentations	Academic Staff	Support Staff

Department of Social and Environmental Medicine academic staff

BIOTECHNOLOGY

Assoc. Prof. Pongrama Ramasoota, with the Center of Excellence for Antibodies Research (CEAR) team, successfully licensed therapeutic human monoclonal antibodies against dengue virus, to Bharat Serums and Vaccines (BSV) Biosciences Limited, an international drug and vaccine company. The neutralizing human monoclonal antibody (NhuMAbs) developed has 96-100% killing activity against all serotypes of dengue in pre-clinical testing in AG 129 mice. Through the capacity of BSV Limited and the collaboration with CEAR, the license agreement's ultimate goal is to further test and develop the NhuMAbs to reach the global market as an FDA-approved product in 2026, or earlier.

A new rapid test kit for the rapid detection of MPT64 secretion protein of *Mycobacterium tuberculosis* in blood was produced in 2018. This rapid TB test kit has a reading time of 15 minutes with high sensitivity and specificity. The test will be soon available for purchase in selected stores in Thailand. Dr. Pongrama plans to apply for a patent for the test kit.

ENVIRONMENTAL HEALTH

Dr. Athit Phetrak's research focuses on removing and controlling the formation of contaminants and chemicals in drinking water, which can reduce the potential cause of cancers and other diseases. In 2018, Dr. Athit and collaborators in Chulalongkorn University, Mahidol University, and Thammasat University developed iron oxide particles as an effective adsorbent in eliminating heavy metals, such as hexavalent chromium, from water.

Field survey: Household drinking water sampling at Tha Song Yang

A laboratory survey led by Dr. Athit and collaborators, found that drinking water in northern Thailand has a high fluoride concentration, particularly in Tha Song Yang households in Tak Province. The water, which is collected from the mountains due to limited water resources, contains 3.1 ppm level of fluoride, while the safe and suggested level of fluoride in water is only 0.7 ppm. Fluoride, if consumed in excess can cause fluorosis, which affects the teeth and bones. The project also enabled knowledge sharing among the residents about safe water intake.

Assoc. Prof. Kraichat Tantrakarnapa was awarded a 2 million Baht grant by the Thai Government to conduct a haze behavior and forecasting system, including its health effects, in northern Thailand.

In addition, a grant extension has covered the CLMV (Cambodia, Lao PDR, Myanmar, and Vietnam) to develop a forecasting system. Furthermore, a workshop and training in CLMV has been conducted to raise awareness among the relevant organizations and citizens.

Assoc. Prof. Kraichat received an award from Thailand and the United Kingdom to conduct Thailand Air Pollution and Health Impacts (THAPHIA) for the whole country, focusing on Bangkok and Chiang Mai.

Assoc. Prof. Kraichat contributed to research and academic work in Asia countries, such as by organizing an international symposium in Chiang Mai, in collaboration with the Korean Society of Environmental Health and Chiang Mai University, in August 2018.

Asst. Prof. Suwalee Worakhunpiset received a new grant to monitor tuberculosis (TB) from the environment, in Thailand. This research project, funded by the Thai government, is a response to the country's plan to reduce incidence rate of tuberculosis nationwide.Asst. Prof. Suwalee Worakhunpiset conducted a pilot study to determine the potential of *Murdannia loriformis*, *Artemisia vulgaris L.*, and *Aegle marmelos,* to inhibit the transformation of cells into cancer cells, an *in-vitro* study. The results showed all three herbal extracts have the potential to inhibit cell transformation into cancer cells; however, further studies should be conducted to confirm this cell transformation inhibition ability.

SOCIAL MEDICINE

Dr. Suparat Phuanukoonnon leads a social-science component of the International Centers of Excellence for Malaria Research (ICEMR) in South East Asia (2018-2023), funded by the National Institute of Allergy and Infectious Diseases (NIAID/NIH). She has recently received an ICEMR supplementary project grant (400,000 USD), with the aim to evaluate community and health-system readiness for malaria elimination. The project will take place in Thailand and Myanmar, in 2019-2022.

Dr. Suparat also conducted the community infectious diseases evaluation in Thasongyang district, located along Thailand-Myanmar border, such as intestinal infection among pre-school children, weaning practices and nutrition survey, dengue control practices in households and WASH in rural community. All research projects are from the collaborative efforts of Mahidol University, Tokyo University, The Walter and Eliza Hall Institute of Medical Research and University of Melbourne.

MALACOLOGY

Environmental health impact assessment of water reservoir at Srakaew Province led by Assist. Prof. Dr. Yanin Limpanont was conducted in July 2018. In this project, the health impact such as vector-borne diseases, water-borne diseases, and occupational health were assessed by physical examination in villagers, vector and intermediate host survey. The assessment reported health impacts that may be caused by the development project and propose mitigation measures.

AWARDS

On 9 August 2018, the Korean Society of Environmental Health awarded Assoc. Prof. Kraichat Tantrakarnapa an Outstanding Contribution Award to Environment and Health of Asia, to recognize his contribution to education and research in environmental health within Asia.

Dr. Athit received an Outstanding Oral Presentation Award for his presentation "Kinetic adsorption of hazardous methylene blue from aqueous solution on to iron-impregnated powder activated carbon" during the 3rd Environment and Natural Resources International Conference (ENRIC) held 22-23 November 2018, in Chonburi, Thailand.

NEW STUDENT AND STAFF

Mr. Tairyu Sato, an exchange student from Osaka, Japan, Ms. Sirirat Sangkarak, and Ms. Wilarat Puangmanee, joined the Department in 2018.

Community infections diseases evaluation in Tha Song Yang

TROPICAL HYGIENE

2018 HIGHLIGHTS

FACTS AND FIGURES

51	4	7	12	16
Publications	Poster presentations	Oral presentations	Academic Staff	Support Staff

MACHINE LEARNING

MSc. student Mr. Chaitawat Sa-ngamuang, under the supervision of Asst. Prof. Saranath Lawpoolsri Niyom and in collaboration with the Faculty of Information and Communication Technology, Mahidol University, developed Bayesian Network models based on data and profiles of acute febrile illness patients in the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, to diagnose dengue. The impressive diagnostic accuracy of the Bayesian Network model suggests that it can be a useful decision-support system for physicians with limited experience in the diagnosis of dengue situated particularly in localities where laboratory confirmation tests are largely unavailable. The models also address the difficulties associated in differentiating dengue patients from other acute febrile illness patients.

This work was published in *PLoS Neglected Tropical Diseases,* in 2018.

MALARIA SURVEILLANCE

Dr.. Saranath leads the malaria epidemiology group of the ICEMR project in Tha Song Yang District. The team conducts passive and active case detection strategies to identify symptomatic and asymptomatic malaria cases in the area. This routine service involves a mass blood survey and is being performed 3-4 times per year.

Data collected over the 7 years' duration of the project suggested that the malaria incidence rate in Tha Song Yang is low (5%). However, 20% of cases showed evidence of repeating malaria. The team seeks to identify associating factors of repeating infection in the area, including anti-malarial drug resistance, treatment compliance issues, and other concerns that need to be confirmed and explored further.

Malaria blood survey

The research by Dr. Saranath provides important information that supports malaria-elimination efforts in Tha Song Yang.

APPLYING INFORMATION TECHNOLOGY TO MALARIA EPIDEMIOLOGY

In a cohort study for the ICEMR project, Dr. Saranath is collaborating with the University of Bremen, Germany and the Faculty of Information

and Communication Technology, Mahidol University, to develop a mobile application for tracking population movement. The collaboration seeks to understand the movement pattern of the population going to and coming from the Thai-Myanmar border. Through this mobile application, it is hoped to elucidate how population movements are linked to the risk of malaria infection in Tha Song Yang. The data analyzed from this project will help to provide preventive measures against malaria infection in the area. The mobile application will be in its testing stage in 2019.

BIOMEDICAL AND HEALTH INFORMATICS AS AN ONLINE COURSE

The Biomedical and Health Informatics program at the Bangkok School of Tropical Medicine was developed into an online course, allowing prospective students, especially those abroad, to earn their diploma or master's degree program online. Dr. Saranath and the Faculty Committee are pushing for its approval in 2019.

ROLE MODEL TEACHER AWARD

In 2018, Dr. Saranath was awarded a "Role Model Teacher Award" by Mahidol University.

Asst. Prof. Saranath Lawpoolsri

NEW IV ARTESUNATE FORMULATION

Intravenous (IV) artesunate is a strongly recommended treatment for adults and children suffering from severe *falciparum* malaria. The preparation of IV artesunate is deemed difficult and unstable, which is unfortunately often challenging in poor healthcare settings. A new IV artesunate formulation, which is more 'user-friendly' and stable, was evaluated by Dr. Podjanee Jittamala and team in a bioequivalence study to compare the bioavailability of the current and new formulations of IV artesunate. The study found that the new IV artesunate formulation shares similar pharmacokinetic properties with the current IV artesunate and suggests that it can replace the latter in the treatment of severe falciparum malaria.

PRIMAQUINE ASCENDING DOSE REGIMEN FOR G6PD-DEFICIENT PATIENTS

Primaquine is widely recommended for the radical cure of *Plasmodium vivax*, but it is not always administered due to concerns of severe hemolytic anemia in G6PD-deficient patients. Dr. Podjanee, together with the team at Clinical Therapeutic Unit (CTU) and MORU, is administering an ascending dose regimen among healthy G6PD-deficient subjects. This regimen may reduce lethal side effects, such intravascular hemolysis, among these individuals and could therefore be used in situations where G6PD testing is unavailable, such as limited-resource areas.

MDA FOR MALARIA ELIMINATION

In an effort to eliminate *falciparum* malaria in the Greater Mekong Subregion, researchers from the Faculty of Tropical Medicine, AFRIMS, and MORU, are conducting mass drug administration (MDA) of dihydroartemisinin-piperaquine (DHA-PPQ), ivermectin (IVM), primaquine (PQ), and albendazole (ABZ). However, before implementing a large-scale MDA, the effects of these drugs on humans must be evaluated. Dr. Podjanee Jittamala led an open-label study to test the safety, tolerability, potential pharmacokinetic interaction, and mosquito-lethal effects of single-dose DHA-PPQ, IVM and PQ, in healthy subjects.

Dr. Podjanee Jittamala

UNIDENTIFIED ACTIVE METABOLITE IN IVERMECTIN

The evaluation of ivermectin showed that the mosquitocidal effects persist beyond the elimination of the predominant component of the parent compound. This opens up the possibility of either an unidentified active metabolite, or slower elimination of the more active minor component. In either case, this has firmly put ivermectin on center stage as a potential elimination tool.

RTS,S VACCINE: A USEFUL TOOL FOR MALARIA ELIMINATION

The RTS,S malaria vaccine provides short-term drug-independent protection against *falciparum* malaria, and may be a useful tool for malaria-elimination campaigns. Dr. Podjanee and the MORU team have assessed, for the first time, the immunogenicity of RTS,S among Asian adults, and whether concomitant dihydroartemisinin-piperaquine affects it. These studies have now been completed and show good immunogenicity and no significant interactions, thus informing appropriate dosing.

TROPICAL NUTRITION AND FOOD SCIENCE

2018 HIGHLIGHTS

FACTS AND FIGURES

12	1	1	7	8
Publications	Poster presentations	Oral presentation	Academic Staff	Support Staff

The Department of Tropical Nutrition and Food Science is responsible for teaching a portion of the curriculum of the Faculty's international postgraduate programs, including the Master and Doctor of Philosophy in Tropical Medicine programs, Master of Science (School Health), and Diploma in Tropical Medicine and Hygiene (DTM&H). The Department's main mission is to provide a first-rate training program for M.Sc. and Ph.D. students, while researchers in the Department also conduct frontier scientific research in tropical nutrition and food science and distribute the knowledge acquired to the public. In tropical nutrition, they focus on several areas - malnutrition problems, obesity, dislipidemia, coronary heart disease, osteoporosis, and the epigenetic study of nutritional diseases. They also place emphasis on research associated with the effects of genetic and protein changes in individuals based on nutritional status. In addition, the department works with pure natural products derived from Thai medicinal plants that have anti-cancerous, mosquitocidal, anti-HIV, and anti-obesity properties. Regarding food science, the department currently conducts extensive studies on food microbiology and probiotics. Since 1966, the Department has had approximately 400 articles published in prominent international journals and 100 articles featured in both local and national journals. In addition, the Department has produced over 80 Ph.D. and M.Sc. graduates.

TRAINING

Annually, the Department of Tropical Nutrition and Food Science conducts short training courses

Workshop on Methods in Nutritional Assessments and Research

entitled "Methods in Nutritional Assessment and Research", which have been presented for over a decade, resulting in the enriched nutrition-based training of numerous participants over the years. Dr. Karunee Kwanbunjan chairs the academic workshop, which provides comprehensive knowledge in nutrition to teachers, lecturers and nutritionists from both government and private sectors. This three-day workshop is held annually at the Faculty of Tropical Medicine, Mahidol University.

PUBLISHED STUDIES

In Thailand, the prevalence of obesity has been increasing at an alarming rate and in all life stages. Moreover, obesity is positively associated with lower education levels, particularly in rural areas. In an effort to curtail this obesity epidemic, Dr. Karunee and fellow Department of Nutrition and

Food Science researchers examined the effects of an intensive lifestyle modification (ILM) program on reducing weight and metabolic syndrome risk among obese women in rural areas in Thailand, based on a randomized controlled trial. Tailored nutritional counseling, health education and exercise training were included in the lifestyle-modification program that also incorporated behavioral modification techniques. Results from the intervention group showed a statistical reduction in abnormal components of metabolic syndrome compared with the control group. Compatibility of program activities conducted by health professionals who had achieved healthy weight reduction and were accepted as role models was key to achieving effective weight loss and metabolic syndrome risk reduction among obese women in rural areas. The takeaway recommendation was adoption of the ILM program into the conventional practice of local and public healthcare centers. The study was published in the *Journal of Health Research*.

In a study published last year in *BMC Endocrine Disorders*, Dr. Karunee took part in research that assessed whether retinol binding protein 4 (RBP4) and transthyretin (TTR) are associated with insulin resistance, prediabetes and triglyceride levels in rural Thais with high type-2 diabetes mellitus (T2DM) risk. RBP4, a protein secreted by adipocytes (fat cells) and bound in plasma to TTR, has been associated with obesity, the early phase of insulin resistance, metabolic syndrome, and T2DM, which leads to cardiovascular disease. Several studies have reported elevated plasma RBP4 in T2DM subjects with obesity, impaired glucose tolerance, and with nephropathy. Dr. Karunee and fellow Department of Nutrition and Food Science researchers collaborated in an effort to reveal the relationship between RBP4, TTR, triglyceride (TG) and type-2 diabetes risk in rural Thailand. Physical metrics, dietary assessments and blood sample analysis from a large group of Thai volunteers were used to conclude that associations of RBP4 and TTR with hypertriglyceridemia and insulin resistance may have important implications for the risk of heart disease and stroke.

Dr. Karunee also had an investigative role in another study that examined the correlation between waist circumference and indicators of metabolic syndrome and cardiovascular disease among Thai adults. Waist circumference (WC) is a measure of central obesity, which is an established indicator of the risk of chronic disease. The objective of this study was to investigate the applicability of WC and risk of metabolic abnormality among adults living in Thailand, namely, at the umbilicus level (WC-U) and midway between the lowest rib and iliac crest (WC-M). Physical measurements and blood samples along with socioeconomic, health habits, and physical activity data were collected. The results confirmed that both WC-U and WC-M can be used to monitor health status in men and women; however, WC-U was determined as a simpler procedure for community health-risk surveillance and self-monitoring. The study was published in the *Malaysian Journal of Nutrition* last year.

COLLABORATIONS

International academic collaborations and activities are central to the Faculty of Tropical Medicine's key objectives. Through strong international collaborations and activities since its beginning, the FTM has forged several enduring partnerships over the years. In a continuation of this tradition, last year the Department of Tropical Nutrition & Food Science and the Faculty of Food Nutrition Facilities, Münster University of Applied Sciences (MUAS), Germany, entered into a Memorandum of Understanding (MOU) in recognition of the mutual benefits accruing to their academic communities from the establishment of strong international links. The purpose of the Memorandum is to promote beneficial relations through the development of academic collaboration, cooperative training programs and research, exchange of information via academic materials and publications, and staff and student exchanges. Members will be encouraged to consult with each other and develop specific plans for collaboration throughout a five-year partnership period. As Head of Department, Dr. Karunee plans to further collaborations between the Faculty and German universities with a vision to facilitate academic exchange in the future. The

Department also intends to extend their work in food research and subsequently translate their studies into entrepreneurial products.

The increased prevalence of metabolic syndrome (having 3 or more metabolic disorders) like obesity, heart disease, and diabetes, is an emerging and serious public health problem. Visiting Professor Dr. Amandio Vieira, representing the Simon Fraser University, presented a lunch talk in 2018 entitled "Epigenetic perspective on metabolic syndrome: relation to dietary phytochemicals and nutrients" to the FTM as part of a continuing partnership with the Department. As epigenetics – a mediator between genetics and environment – is emerging as a potential candidate to explain the increased prevalence of metabolic diseases, the presentation carried great value for the attendees involved. Dr. Viera also actively consults with several students within the Department of Tropical Nutrition and Food Science, providing assistance with research work and acting as a counselor for academic affairs.

In cooperation with the Department of Public Health, University of Halu Oleo, Indonesia, Dr. Karunee traveled to Indonesia last year as part of her field work in the mentorship of a current student. She also provided support in the development of a research paper exploring nutrition education intervention strategies that can potentially improve the feeding practices and nutritional status of children living in Indonesia. Protein-energy malnutrition (PEM) in children is still high in Indonesia, with many native areas having a high prevalence of this condition. When children are nutritionally stunted at an early age, they risk reduced productivity over time - poor education results in jobs with low earnings. If followed by accelerated weight gain when older, they risk developing obesity and other diet-related non-communicable diseases, leading to a double burden of malnutrition. The study carries importance because proper education and the adoption of sound practices related to nutritional education can help neutralize this growing health problem at an early age.

Dr. Karunee Kwanbunjan and visiting Professor Dr. Amandio Vieira

TROPICAL PATHOLOGY

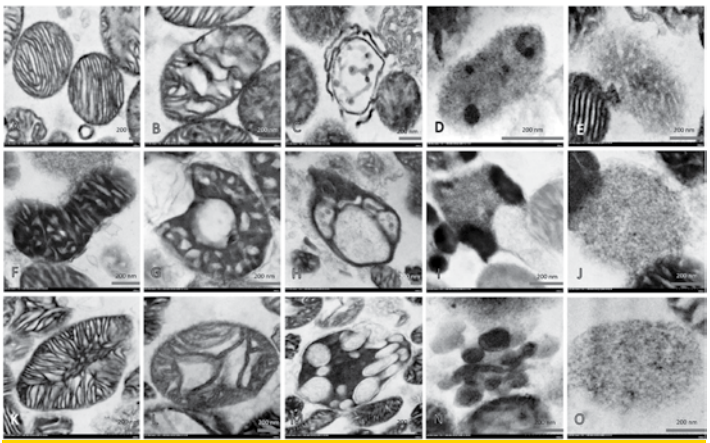
2018 HIGHLIGHTS

FACTS AND FIGURES

4	1	1	4	8
Students	Poster presentations	Oral presentation	Academic Staff	Support Staff

PUBLISHED STUDIES

Last year, Asst. Prof. Sumate Ampawong had nine research articles published in several prominent medical journals. Asst. Prof. Sumate's published work focused mainly on the pathology and pathogenesis of malaria and causal hypercholesterolemic conditions in both *in-vitro* and *in-vivo* electron-microscopy studies. In a 2018 research highlight, Dr. Sumate recently demonstrated that the antioxidant properties of sericin decrease blood cholesterol levels and improve liver mitochondrial architecture. Employing a rodent model, proteomic and electron-microscopy analyses were performed to elucidate the mechanisms underlying the beneficial effects of sericin that help treat high cholesterol. The collective lab results suggest that sericin maintains and improves hepatic mitochondrial architecture through apoptotic, autophagic, energy maintenance and anti-oxidative mitochondrial proteins to alleviate fat accumulation in the liver and promote liver function under hypercholesterolemic conditions. These positive findings highlight sericin as a leading food additive candidate aimed at lowering blood cholesterol. The study was published in *Scientific Reports*. Asst. Prof. Sumate's ongoing research work focuses on the pathology of experimental scedosporiosis and the development of a scedosporiosis rapid detection kit for immunocompromised patients. He is also studying mitochondrial function and its ultrastructure in relation to next-generation sequencing.



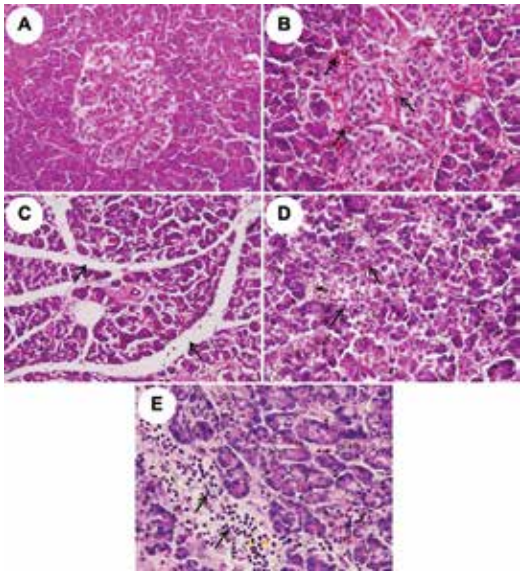
Mitochondrial architecture from heart (A-E), liver (F-J) and kidney (K-O) in hypercholesterolemic rats represents by several forms; normal (A, F, K), swelling (B, G, L), spheroidicity (C, H, M), clumping (D, I, N) and ghost or necrosis (E, J, O)

Increased endothelial cell (EC) permeability in severe *Plasmodium falciparum* malaria contributes to major complications, such as vascular damage in severe malaria. In a cumulative research study published last year in *Scientific Reports*, Assoc. Prof. Parnpen Viriyavejakul and her team explored EC permeability in malaria and evaluated the potential novel use of sphingosine-1-phosphate (S1P) in protecting and restoring EC permeability. S1P was tested and evaluated for its potential

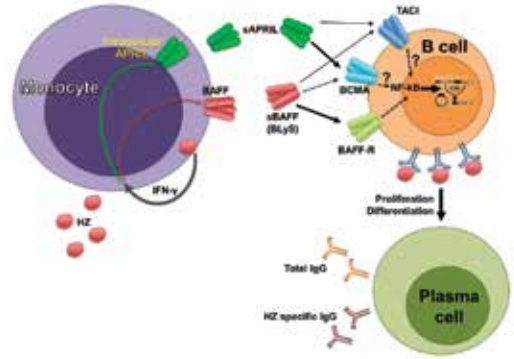
use in maintaining EC integrity and subsequently preventing fluid leakage caused by *P. falciparum* malaria. The effect of S1P on permeability leakage was particularly evident in decreasing leakage in ECs treated with severe *P. falciparum* sera. The therapeutic efficacy and preventive effects of S1P to restore EC permeability exposed to malaria sera were clearly demonstrated in the study. S1P had beneficial effects against damage induced by malaria sera on the EC barrier, in addition to its usefulness as a protective factor. Positive testing results with experimental S1P serve as a proof-of-concept to further explore the benefit of the drug as a promising clinical application to prevent severe malaria complications, such as cerebral and pulmonary edema.

With continuous interest in the pathology and pathogenesis of severe malaria, Prof. Parnpen and Ms. Supattra Glaharn explored the relationship between key factors of pancreatic pathology and blood-sugar levels in *P. falciparum* malaria patients. Their study documented an increase in insulin production and pancreatic endocrine cell size in hypoglycemic patients with *P. falciparum* malaria, which may contribute to the development of hypoglycemia. These findings provide evidence for the potential need to effectively manage this condition seen in malaria infection where clinical hypoglycemia occurs in up to 30% of all severe *P. falciparum* malaria cases. This novel study will be useful for clinicians interested in further understanding and managing the process of hypoglycemia in patients with severe *P. falciparum* malaria. Their research was also published in the highly regarded scientific journal, *Scientific Reports*, in 2018.

Prof. Parnpen Viriyavejakul



Histopathological changes of pancreas in P. falciparum malaria patients



Plasmodium falciparum haemozoin (HZ) induces T independent specific antibody production via BAFF/APRIL signaling pathways

In a cumulative study published last year in *Cytokine*, Assoc. Prof. Yaowapa Maneerat investigated the role of blood-stage *Plasmodium falciparum* hemozoin (HZ) as a T-independent antigen (TI Ag). HZ induces the production of specific Immunoglobulin G (IgG) antibodies to soluble crude *P. falciparum* Ag through the B cell activating factor (BAFF) pathway. However, this study aimed to clarify whether HZ needs a proliferation-inducing ligand (APRIL) signaling

in the TI response. Properties of this specific IgG antibody to *P. falciparum* were evaluated to clarify whether both BAFF and APRIL signaling pathways play dual roles in HZ induction of specific antibody production without T-cell help. Providing additional research support, Ms. Wilanee Dechkajorn investigated the occurrence of B cell activation via the BAFF and APRIL systems in spleen and lymph node tissues of fatal falciparum malaria patients. Collectively, research results raise the possibility that blood-stage *P. falciparum*-derived HZ acts as a TI Ag that drives TI-specific immunity through BAFF, APRIL and other independent complementary signaling pathways. Dr. Yaowapa's research work also covers the immune-system evasion strategies of infective (third) stage *Gnathostoma spinigerum* larvae in gnathostomiasis with *in-vitro* studies focusing on the effect of excretory-secretory products from L3 cultures (*G. spinigerum* ES) on human NK cell activation.

UNPUBLISHED STUDIES

In additional investigative roles under Prof. Parnpen, Ms. Supatra has an ongoing research effort associated with actin proteins. Specifically, the alterations of actin proteins (cytoskeleton) on endothelial cells activated by the sera of malaria patients. Endothelial cells are key cells in the body, whose main purpose are to provide a barrier between the blood and the rest of the body tissues; any negative effects on these particular cells can be critical. In another supporting study, Mr. Chalit Srisook has been leading a research task dedicated to aquaporin expression in the choroid plexus of cerebral malaria. Aquaporins are water channels that control the water balance of an organism and are a vital part of cellular dynamics, as the entry and exit of water from cells is a fundamental process of life. Both studies explore new areas of examination and should provide valuable insight into the field of malaria pathology.

COLLABORATIONS

Last year, the Department of Pathology collaborated with the Faculty of Pharmaceutical Sciences, Chulalongkorn University, and the Faculty of Science and National Laboratory Animal Center, Mahidol University on leading edge research in malaria pathology.

Prof. Stephen A. Ward, Research Centre for Drugs and Diagnostics, Liverpool School of Tropical Medicine, United Kingdom was a Visiting Professor of the Department of Tropical Pathology and presented a lunch talk on anti-Wolbachia drug discovery at FTM last year. For a period of two months, he provided the Department with scientific research consultation and acted as a mentor for several medical research students in the studies of malaria pathogenesis and post-signaling events of severe malaria. Prof. Ward will also be a Visiting Professor and present a lunch talk on antimalarials at FTM in 2019. His expertise in the area of malaria drug development and tropical pharmacology continues to be a high value contribution to FTM.

Assoc. Prof. Parnpen holds a postgraduate orientation

Prof. Stephen A. Ward presenting his 2018 lunch talk

TROPICAL PEDIATRICS

2018 HIGHLIGHTS

FACTS AND FIGURES

11	1	5	10
Publications	Poster presentations	Oral presentations	Academic Staff

PUBLICATIONS

The Department evaluated the immunogenicity and safety of an inactivated chromatographically purified Vero-cell-derived Japanese encephalitis vaccine (CVI-JE, Beijing P-3 strain) in 152 Thai children. The study concluded that CVI-JE is safe and immunogenic. It resulted in 100% seroconversion and provided high geometric mean titers after the primary doses and booster vaccination. This significant study was published in *Human Vaccines & Immunotherapeutics* journal.

An article published in *The Southeast Asian Journal of Tropical Medicine and Public Health* relates the work of the Department in the development and validation of the Mahidol dengue clinical score (MDCS) as a screening diagnostic tool for dengue infection in Thai children in a dengue-endemic area. With its feasible diagnostic value, MDCS can be used to provide management and clinical diagnosis in dengue-endemic areas where laboratory diagnosis is often expensive or unavailable.

Assoc. Prof. Kriengsak Limkittikul was involved in a four-year safety follow-up study of tetravalent dengue vaccine efficacy randomized controlled trials in Asia and Latin America. This globally collaborative work was published in *Clinical Microbiology and Infection* journal.

Data being collected for a dengue vaccine trial

PRESENTATION

Asst. Prof. Weerawan Hattasingh presented a poster entitled "Application of opsonophagocytic killing assay (OPKA) for assessment of functional antibody among children with pneumococcal vaccine" at the Joint International Tropical Medicine Meeting (JITMM), 12-14 December 2018, at the Amari Watergate Hotel, Bangkok, Thailand.

Physical examination in dengue vaccine trial

ACTIVITIES

Survey studies and vaccine trials were the main research activities of the Department in 2018. A Zika survey study was conducted in Amphawa District, Samut Songkram Province, Thailand. Dengue and meningococcal vaccine trials were performed in Chachoengsao Province and at the Faculty of Tropical Medicine, Mahidol University in Bangkok, respectively.

The Department participated in several candidate dengue vaccine clinical trials (phase 2B and phase 3). The vaccine clinical trial results could provide extremely valuable vaccine safety and efficacy information, essential for policy-makers and doctors in making decisions on the use and administration of vaccines in the future.

COLLABORATIONS

The Department partnered with several national and international institute, such as the National Science and Technology Development Agency (NSTDA) to further study the prevalence and diagnosis of Zika; King Mongkut's University of Technology Thonburi (KMUTT) for research related to diagnostic tools for dengue infection; the Faculty of Pharmacy, Mahidol University, to study the host genetic factor for dengue severity; and the Global Dengue & Aedes-Transmitted Diseases Consortium, to further understand the epidemiology of dengue. The Department also collaborated with several vaccine companies on research related to vaccine clinical trials

NEW APPOINTMENTS

Assoc. Prof. Kriengsak Limkittikul succeeded Assoc. Prof. Chukiat Sirivichayakul as Head of the Department in October 2018. Dr. Salin Sirinam joined the Department as lecturer

Heads of CENTERS OF EXCELLENCE

Mr. Amnat Khamsiriwatchara
Center of Excellence forBiomedical and Public Health Informatics (BIOPHICS)

Assoc. Prof. Pongrama Ramasoota
Center of Excellence for Antibody Research (CEAR)

Asst. Prof. Thanat Chookajorn
Genomics and Evolutionary Medicine Unit (GEM)

Dr. Jetsumon Prachumsri
Mahidol Vivax Research Unit (MVRU)

Prof. Srivicha Krudsood
Clinical Malaria Research Unit (CMRU)

Prof. Punnee Pitisuttithum
Vaccine Trial Centre (VTC)

Dr. Rapatbhorn Patrapuvich
Drug Research Unit for Malaria (DRUM)

"The Faculty has 7 Centers of Excellence – the Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS), the Vaccine Trial Center (VTC), the Center of Excellence for Antibody Research (CEAR) and the Center of Excellence for Malaria Research. The Center of Excellence for Malaria Research is divided into 3 sub-units--the Mahidol Vivax Research Unit (MVRU), the Genomics and Evolutionary Medicine Unit (GEM), and the Clinical Malaria Research Unit (CMRU). In 2018, the Drug Research Unit for Malaria (DRUM) was established as the 7th unit of the Faculty's Centers of Excellence. On the following pages, there are more details about each center and unit, including their areas of focus and recent achievements."

CENTER OF EXCELLENCE FOR BIOMEDICAL AND PUBLIC HEALTH INFORMATICS (BIOPHICS)

2018 HIGHLIGHTS

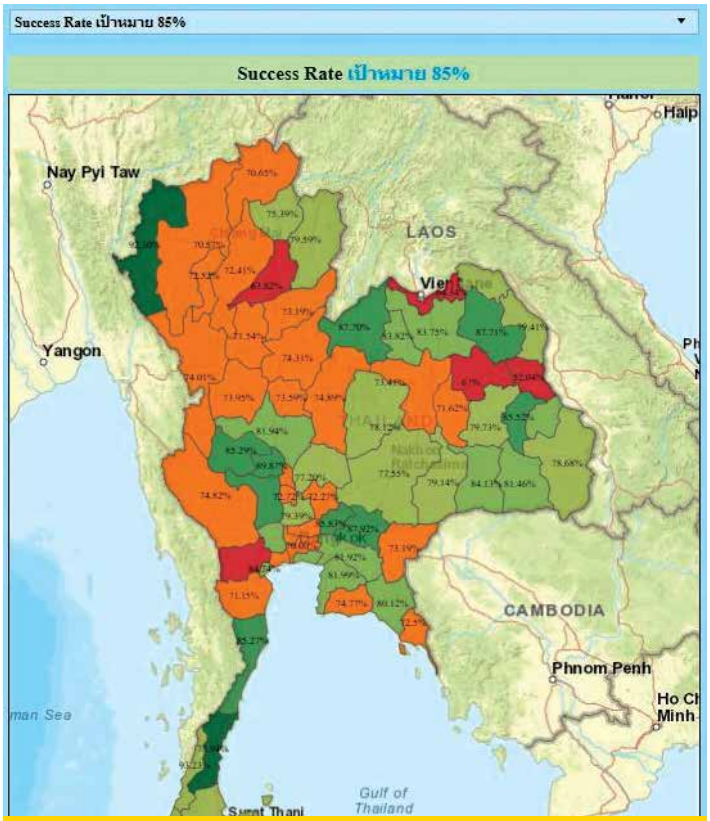
TB CASE MANAGEMENT SYSTEM

In 2018, BIOPHICS implemented the largest tuberculosis (TB) case-management system in the country.

BIOPHICS, in cooperation with the Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health (MOPH), Thailand, implemented an integrated web-based surveillance and case-management system for TB incidence in Thailand.

The TB case-management system comprises an online database that gathers, stores, monitors, analyzes, and reports data collected from over 1,200 TB hospitals and clinics nationwide. It now functions as the central network for the management of TB in Thailand.

The system, due to its massive coverage, is able to map the numbers of TB cases in every clinic, and show which geographical areas have the highest and lowest numbers of TB cases in Thailand. The system can show TB-patient treatment success rates, the number of on-going treatments, mortality rates, and other important data, including the incidence of drug-resistant TB cases.



Dashboard of the TB case-management system

BIOPHICS team site visit and data monitoring in Tha Song Yang District, Tak Province

BIOPHICS equipped the system with new features, including a referral and data transfer system, by which clinics can refer a patient to another clinic with better facilities or requisite expertise for patient treatment and care. Through the system, clinics can transfer the patients' profile and medical history to the recipient clinic or hospital, allowing doctors to manage the patient treat most efficiently. Since the data for all TB cases are stored in one database, transferred patients are not required to re-register in hospitals frequently.

The TB case-management system's real-time operation and accurate interpretation of data from TB cases in Thailand can provide critical decision-making information to support the country's TB control and eradication strategy.

Mr Amnat Khamsiriwatchara hopes to hand over the TB case management system to MOPH for exclusive administration. He also wishes that other TB-burden countries may adopt the system to inform their own future TB-management policy and strategy development.

COLLABORATION

BIOPHICS has provided data-management and statistical support for the Mahidol Vivax Research Unit's (MVRU) malaria epidemiological study at Tha Song Yang, Tak Province, Thailand.

TRAINING AND WORKSHOPS

BIOPHICS held several workshops and seminars in 2018. The "Statistical analysis plan and practices for clinical research studies" and "Ethical principles in good clinical research protocols and practices meetings" were held at the VIE Hotel, Bangkok on 18-20 July 2018 and 16-17 July 2018, respectively.

AWARD

The Malaria surveillance system developed by BIOPHICS received a Public Sector Excellence Award from the Thai government. This prestigious accolade exemplifies the high quality of BIOPHICS' services and products.

CENTER OF EXCELLENCE FOR ANTIBODY RESEARCH (CEAR)

2018 HIGHLIGHTS

CEAR is focused on the use of monoclonal antibodies as therapeutic agents against a wide range of infectious diseases. The Center is equipped with state-of-the-art facilities, including apparatus necessary for biosensor, flow cytometry, viral culture, and real-time PCR. In 2018, CEAR's therapeutic human monoclonal antibody was licensed to an international drug and vaccine company.

THERAPEUTIC HUMAN MONOCLONAL ANTIBODIES AGAINST DENGUE VIRUS

The year 2018 saw a groundbreaking achievement in innovative and translational research at the CEAR, and the Faculty of Tropical Medicine, Mahidol University. Therapeutic human monoclonal antibodies against dengue virus, developed by Dr. Pongrama Ramasoota and Dr. Pannamthip Pitaksajjakul, with their CEAR team and Japanese collaborators, were licensed to Bharat Serums and Vaccines (BSV) Biosciences. BSV Biosciences is an international drug and vaccine company located in the USA and India.

The patented neutralizing human monoclonal antibody (NhuMAbs) has shown 96-100% killing activity against all serotypes of dengue in pre-clinical testing in mice and monkeys. It has since passed safety and toxicity tests, as well. To further drug development, a large amount of NhuMAbs is needed for clinical trials. With funding from the National Research Council of Thailand, Dr. Pongrama started industrial-scale production of NhuMAbs by stable expressed Chinese hamster ovary (CHO) cells, under good manufacturing practices (GMP) conditions. The large amount of expressed NhuMAbs will subsequently be used for clinical trials. BSV Biosciences will provide financial support of 250 million Baht for the entire clinical-trial phases of product testing. BSV Biosciences will also pay milestone payments and royalty fees to Mahidol University.

CEAR Easy Test for TB

Dr. John Kaundinya, President of BSV Biosciences Inc., signed a contract for the production and testing of therapeutic MAbs.

Through the capacity of BSV Biosciences and its collaboration with CEAR, the license agreement aims to complete the last phase of clinical trials in 2023, with the main goal of reaching the global market as an FDA approved product in 2026, or earlier. BSV Biosciences will support the production and marketing of the therapeutic product.

RAPID TEST KIT FOR TB

A new rapid test kit for detecting the MPT64 secretion protein of Mycobacterium tuberculosis in blood was produced in 2018. This rapid TB test kit has a reading time of 15 minutes with high sensitivity and specificity. The test will soon be available for purchase in selected stores in Thailand. Dr. Pongrama accordingly plans to apply for a patent for the test kit.

PUBLICATION

The Center published six papers in peer-reviewed and respected international journals. One example is an article entitled, "Oxidized carbon black: preparation, characterization and application in antibody delivery across cell membrane" which was published in *Scientific Reports.*

NEW RESEARCHER

Dr. Punpichaya Fungwithaya joined CEAR as a researcher.

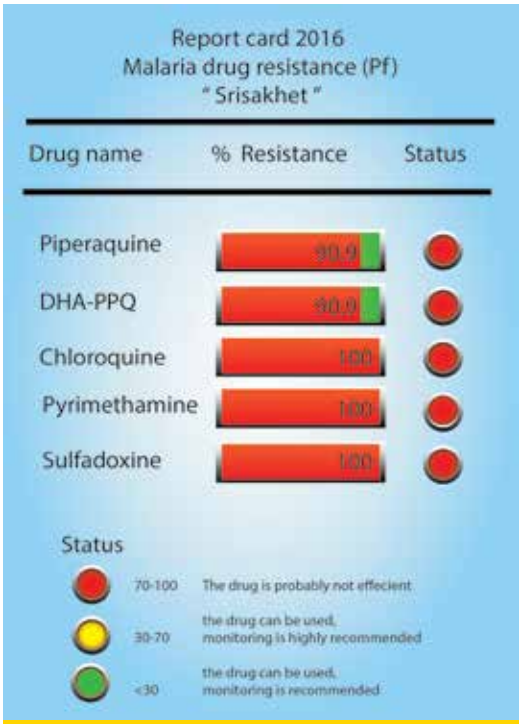
GENOMICS AND EVOLUTIONARY MEDICINE UNIT (GEM)

2018 HIGHLIGHTS

REPORT CARD

By combining genomic technology, bioinformatics, and big data management, the Genomics and Evolutionary Medicine Unit (GEM), in collaboration with the Thai Ministry of Public Health (MOPH), Wellcome Sanger Institute, Big Data Institute at Oxford University, and Mahidol-Oxford Tropical Medicine Research Unit (MORU), aims to observe and report the genomic epidemiology of malaria drug resistance situation in the Greater Mekong Subregion (GMS), covering Cambodia, Laos, Myanmar, Vietnam, and Thailand.

The surveillance project, funded by the Bill and Melinda Gates Foundation, involves blood-spot collection from malaria patients, whole genome sequencing, understanding large-scale genomic data, and translating the genomic data obtained into a simple report card for user-friendly data interpretation. The report card summarizes malaria drug resistance conditions in a country. Through the project, the team intends to develop a new paradigm of how epidemiologic data can be further used in tackling malaria elimination and control.



An example of the report card

The report card indicates every malaria drug used in a certain geographical area. The percent or level of resistance of the falciparum parasite against each drug is categorized by colors green, yellow, and red. Green means the drug is still effective against the parasite and can be used in the area, yellow means the drug can be still used but needs strict sensitivity monitoring, and red means the drug no longer works, or the parasite in the area has become fully resistant to the drug.

As antimalarial drug resistance becomes one of the greatest challenges in malaria control and elimination, the report card, as simple as it may seem, holds valuable data that can be utilized by policy makers, such as the Thai MOPH as an important factor in decision making and strategy for malaria control and elimination programs in the region. This is an example of the operational research that Dr Thanat and the team have been working on passionately.

The project puts GEM, along with its authoritative collaborating institutes, at the forefront of combatting malaria drug resistance, and the treatment and care of malaria patients.

SOCIAL IMPACT

As part of the malaria surveillance project, the GEM Unit, in cooperation with MOPH, held training sessions for malaria-clinic workers in various regions of Thailand on how to collect blood samples more efficiently. The malaria clinics provide the team with blood-spot samples from malaria patients. The training has also provided an opportunity for GEM to introduce the purpose of the project and to share how the surveillance project can affect their work positively. The team provides malaria-clinic workers with data that demonstrates the progress of malaria treatment in their area.

DRUG DEVELOPMENT

GEM's work on drug discovery made further achievements by narrowing drug candidates from hundreds down to twelve potential compounds that are hoped to proceed to animal testing. The Unit will enter a more challenging phase of drug development with the goal of narrowing the remainder to three compounds. By understanding the modes of action of the compounds, Dr Thanat aims to learn how to target novel mechanisms that can affect artemisinin sensitivity.

TRAINING

The Unit and Wellcome Genome Campus co-organized a five-day laboratory-based course that provided participants with a working knowledge of, and practical experience in, cutting-edge Plasmodium experimental-genetics techniques; from designing gene-targeting vectors and creating transgenic parasites, to genotyping and phenotyping the resulting strains. The course, which was attended by 16 participants from Asia and Australasia, included seminars by global experts and guest speakers. The course was held 22-27 April 2018 at the Faculty of Tropical Medicine, Mahidol University.

Dr Thanat held a one-day pre-meeting course for JITMM2018 entitled "The Power of Big Data in Genomic Epidemiology of Malaria Drug Resistance" on 11 December 2018 at the Faculty of Tropical Medicine, Mahidol University. The pre-meeting course included experts in genomics and bioinformatics, and was attended by 15 health practitioners and researchers from MOPH and JITMM participants.

Dr.Thanat Chookajorn presents at the JITMM pre-meeting course entitled "The Power of Big Data in Genomic Epidemiology of Malaria Drug Resistance"

MAHIDOL VIVAX RESEARCH UNIT (MVRU)

2018 HIGHLIGHTS

MASS ADMINISTRATION OF PRIMAQUINE

Mass blood survey

The MVRU, in collaboration with Assoc. Prof. Jaranit Kaewkungwal and his team from the Department of Tropical Hygiene, received a supplemental grant under the International Centers of Excellence for Malaria Research (ICEMR) program, to evaluate the effectiveness of mass primaquine preventive treatment (MPPT) for malaria elimination in Thailand and Myanmar. The ultimate goal of this project is to accelerate malaria elimination in the Greater Mekong region. This study will initially evaluate primaquine MDA performed with 4,000 people in Thailand and Myanmar, and, given positive results, will later be expanded to a population of 100,000. The team will also be performing G6PD testing for malaria patients and endemic residents, since primaquine can be fatal for individuals with G6PD deficiency.

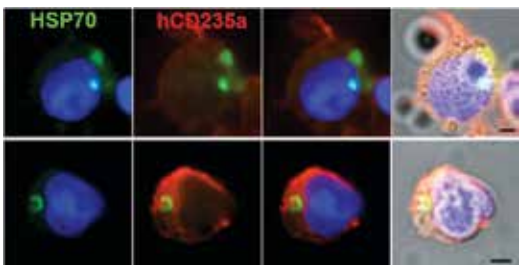
MASS ADMINISTRATION OF IVERMECTIN

As an additional effort to help eliminate malaria in Thailand, the MVRU will conduct a cluster randomized trial to evaluate the effectiveness of a mass delivery of ivermectin in southern Thailand. Ivermectin, an anti-helminthic drug, is recognized as a potentially effective tool for malaria elimination because of its mosquitocidal effects. This year, the team is evaluating the baseline malaria transmission dynamics at the study site, to select clusters for trial in 2020.

LIVER STAGE CULTURE

Exciting updates and findings on liver stage culture were seen in 2018. Using genetic engineering, the team identified a number of host immunoregulatory genes that suppress *P. vivax*. Using genetic engineering to knock out those regulators, MVRU has produced new hepatic cell lines that support increased *P. vivax* infection and are suitable for drug screening. MVRU plans to apply for a patent for these new cell lines.

YOUNG BLOOD: FROM ACADEME TO ENTREPRENEURSHIP



Dr. Wanlapa Roobsoong and team successfully pitched her first business project of 1.5 million baht from the National Innovation Agency (NIA). This Young Blood project aims to produce and further develop immortalized Young Blood cells as ready-to-use reticulocyte-like cells. Young red blood cells are required for in vitro culture of *P. vivax*, which is crucial for drug and vaccine development. The use of induced pluripotent stem cell (iPS) technology has essentially enabled the production of unlimited supplies of reticulocyte-like cells for research. With the product's translational potential and research demand, distribution to the global market is foreseen. Dr. Roobsoong is collaborating with MiCAN Technologies in Japan for the production and distribution of Young Blood, while MVRU will test and validate the product in *P. vivax* culture.

The MVRU in collaboration with MORU, won a grant from the Wellcome Trust to build capacity for a malaria infection study in Thailand (MIST).

MALARIA INFECTION STUDY IN THAILAND (MIST)

This year, Dr. Jetsumon Prachumsri, in collaboration with Mahidol Oxford Tropical Medicine Research Unit (MORU), won a grant from the Wellcome Trust to build capacity for a malaria infection study in Thailand *(MIST)*. The project aims to establish a human-challenge model for *P. vivax* for future vaccine and drug testing. This study will also be a unique platform to allow a better understanding of *P. vivax* malaria and how the human immune system responds to malaria infection. Once the model is established, it will be a premier resource in an endemic country for the evaluation of new interventions. The study team believes this model will enable the pace of vaccine and drug development for *P. vivax* malaria to be improved. This will be the first ever human infection study for *P. vivax* in Asia.

CO-CHAIR ASTMH INTERNATIONAL COMMITTEE

The American Society of Tropical Medicine and Hygiene (ASTMH) appointed Dr. Jetsumon Prachumsri Co-Chair of the ASTMH International Committee. The goal of the Committee is to increase members from outside the US, especially from countries where several tropical diseases are endemic. The Committee increased funding for travel awards to allow more non-US researchers to present their research at the ASTMH Conference.

ICEMR ANNUAL MEETING 2018

The Southeast Asia International Center of Excellence in Malaria Research hosted the ICEMR Annual Meeting 2018 during 13-16 May 2018 at Le Méridien Chiang Mai Hotel, Chiang Mai, Thailand. The meeting was joined by more than 100 participants from ICEMR-affiliated consortia around the world.

CLINICAL MALARIA RESEARCH UNIT (CMRU)

2018 HIGHLIGHTS

VIVAX MALARIA ELIMINATION: A REAL POSSIBILITY

The World Health Organization's (WHO) Global Technical Strategy for Malaria has set a goal for global malaria elimination by 2025. The current global malaria situation shows ever-decreasing cases of falciparum malaria. However, vivax malaria, due to the biological and social challenges it presents, remains a bottleneck to the attainment of this goal. The only available drug for the radical cure of vivax malaria is primaquine, which requires a 14-day treatment regimen. Unfortunately, many patients find it difficult to comply with the lengthy treatment routine. Primaquine also has limitations for patients with G6PD deficiency, due to concerns about potential severe side effects.

Prof. Srivicha Krudsood is a collaborator with Medicines for Malaria Venture (MMV) and GlaxoSmithKline (GSK) in the development of the drug tafenoquine, a 3-day-dose radical cure for vivax malaria. Compared with the 14-day treatment regimen with primaquine, the 3-day dose of tafenoquine will bring major improvements in patient compliance and the clinical management of vivax malaria.

Prof. Srivicha is cooperating with Thailand's national malaria policy-makers on malaria treatment policy, and determining whether tafenoquine can be implemented on a national scale. Testing and screening G6PD-deficient patients in Thailand is part of the broader scope of the study, as tafenoquine shares the same limitations as primaquine regarding G6PD-deficient patients.

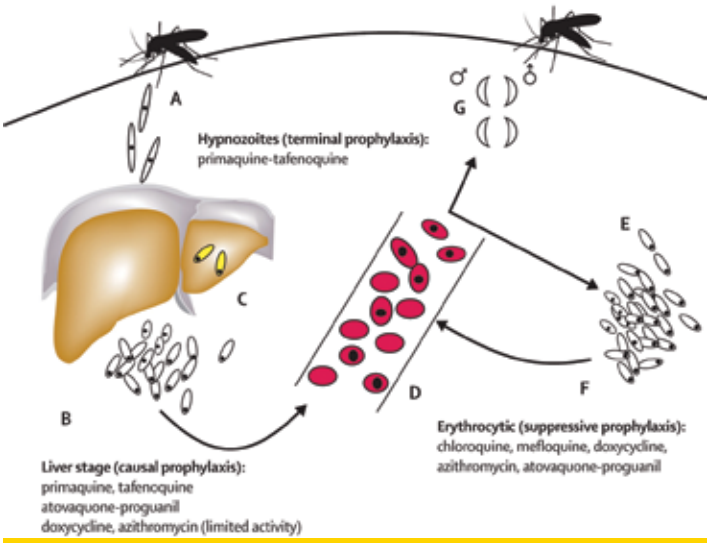


Photo credit: newdrugapprovals.org

Tafenoquine was approved by the US Food and Drug Administration and the Australian Therapeutic Goods Administration in July and September 2018, respectively.

Although tafenoquine is not yet available in the global market, the drug is recognized among malariologists as a hope for malaria elimination, especially for vivax malaria. Prof. Srivicha believes that, with 3-day-dose tafenoquine, the goal of malaria elimination by 2025 is achievable.

Attendees and instructors at the 16th international training on the management of malaria

SOCIAL IMPACT

CMRU acts as a consultant to many hospitals in Thailand for the clinical management of malaria. This routine service informs and influences the Thai national malaria policy.

The Unit holds an annual international training program on the management of malaria. It was held for the 16th year on 27-31 August 2018 at the Faculty of Tropical Medicine, Mahidol University. The training was attended by 24 participants from Japan, Cambodia, Sri Lanka, and the United Kingdom. The training covered topics such as updates on malaria, diagnosis, treatment, management, prevention, and control.

PROF. SRIVICHA KRUDSOOD AS DEPUTY DEAN FOR RESEARCH

Entrepreneurship

Entrepreneurship is a subset of translational research, which is one of the major research focuses of the Faculty in 2018 and ensuing years.

Faculty researchers are strongly encouraged to develop their research into marketable products. The Faculty granted seed money to selected researchers that work on innovative research. A number of significant activities regarding entrepreneurship were held in the Faculty during 2018.

Experienced entrepreneurs were invited to hold seminars and lunch talks in the Faculty to familiarize and teach entrepreneurship to other researchers. A faculty-wide "research market" was held to highlight the innovative products of each unit and department.

Future research

This year saw the opening of the Biosafety Laboratory Level 3 (BSL3). The BSL3 will provide the Faculty with modern tools and cutting-edge technologies that are capable of tackling the most virulent, complex, and difficult viruses and pathogens that can cause serious threats to global health.

A shift on the tropical disease landscape saw a decrease in tropical disease-related cases, including samples and specimens. To preserve tropical-disease specimens, the Faculty will archive all tropical-disease samples in the Faculty. The archiving facilities will comprise a museum and a laboratory.

A policy committee for archiving specimens was formed in 2018. This committee will lead the archiving of blood and mosquito samples, and other specimens in a laboratory to be used in future research.

Ageing society

Thailand is trending towards an ageing society in coming years. The Faculty sees a potential upsurge of opportunistic infections among elderly and immunocompromised hosts. The Faculty is preparing for this trend by transcending research areas and improving facilities to provide excellent care for the ageing society in the future.

VACCINE TRIAL CENTRE (VTC)

2018 HIGHLIGHTS

Vaccine Trial Centre (VTC) staff

PUBLISHED RESEARCH

Vaccine shortages remain an ongoing threat to the control of vaccine-preventable diseases. As part of a comprehensive international analytical study highlighting selected hot topics in the area of vaccinology, Prof. Punnee Pitisuttithum documented the progress made to date in dengue vaccine development. Research in this area is critical because the incidence of dengue has increased dramatically with more than half of the world's population currently at risk of dengue infection. In the past, the only options to control or prevent dengue virus transmission were through interventions directed at the vector. However, problems regarding widespread implementation, sustainability and cost, remain. Thus, immunization remains an important tool to reduce dengue disease burden, morbidity, and mortality. Among the candidate dengue vaccines currently in development, the most advanced is Dengvaxia, developed by Sanofi Pasteur, which is the only licensed vaccine for dengue. While access to an effective dengue vaccine is most desirable, many countries remain cautious to the introduction of Dengvaxia due to perceived riskiness associated with the vaccine. However, this dengue vaccine remains efficacious for at least five years, reducing the risk of hospitalization from infection. Further development of candidate vaccines for dengue are very much needed to achieve licensure and widespread adoption aimed at dengue control in the coming years. Research was published in the *Journal of Clinical Pharmacology*.

It has been reported that vaccination with the tetravalent dengue vaccine (CYD-TDV; Dengvaxia) may interfere with the diagnosis of dengue based on immunoglobulin M (IgM) and immunoglobulin G (IgG) assessments. The current immunological definitions of dengue infection based on IgM and IgG serology are inadequate in vaccinated individuals and need to be reevaluated urgently as the dengue vaccine is now available in several endemic countries. To address this mounting global concern, Prof. Punnee and a group of international researchers undertook an analysis of febrile episodes that occurred during the active surveillance phase of two CYD-TDV efficacy studies involving children across ten countries in Asia and Latin America. Overall predictive values reflected a low probability of correctly confirming probable dengue in a population, including vaccinated groups. Analysis verified that caution is advised when interpreting IgM and IgG data obtained during routine surveillance in those vaccinated with CYD-TDV, as those readings can lead to the misdiagnosis of probable dengue, igniting an urgent need for new dengue-specific diagnostic procedures not affected by vaccine-induced immunity as part of dengue case management and surveillance operations. The study was published in *Clinical Infectious Diseases* last year.

Vaccination programs may represent the most effective prevention strategies in countries without organized screening programs for life-threatening human papillomavirus (HPV) related cancers. This is particularly relevant to Asia, where comprehensive, organized screening programs have not been widely implemented. To further vaccination development in this area, Prof. Punnee and members of a global study team provided a comprehensive review of the 9-valent human papillomavirus vaccine (9vHPV) describing efficacy, immune response, and safety in Asian participants from two international studies. The research team demonstrated that 9vHPV vaccine prevented HPV-related persistent infection with 90% or more efficacy across countries observed. At month seven, nearly 100% of the study participants seroconverted for each HPV type making disease detection in blood tests possible for the related antibody. Global epidemiological data also indicated that the 9-valent HPV vaccine also extends coverage to types of HPV which are next most commonly associated with cervical cancer. The 9vHPV vaccine was proven to be effective and well-tolerated based on clinical studies with Asian participants, which was consistent with findings in the global clinical program. Data strongly supports widespread 9vHPV vaccination programs in Asia. Findings gathered from

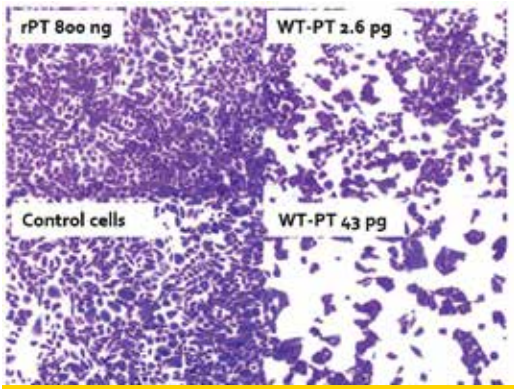
Dengvaxia - the world's first licensed vaccine that protects against dengue

this assessment will provide valuable insight for the implementation of vaccination programs and HPV-related disease prevention. The study was published in the *Journal of Infectious Diseases*.

Over 30 years after the discovery of HIV as the causative agent of acquired immunodeficiency syndrome (AIDS), HIV/AIDS continues to be a significant challenge for global public health; the development of a safe and effective HIV vaccine remains a high research priority. CD4 T-cells are white blood cells that play an important role in the immune system and are central to host immunity by providing help signals to other components of the immune system. Their protective role has been documented for various pathogenic infections, including HIV, but they are also major target cells for HIV infection. Other clinical trials testing candidate HIV vaccines previously reported that human adenovirus serotype 5 (Ad5)-specific CD4 T-cells induced by Ad5 vaccination are susceptible to HIV underscoring the necessity to investigate HIV susceptibility of viral vector-specific CD4 T-cells in HIV vaccination. Prof. Punnee, among a team of international researchers, further investigated the HIV susceptibility of vector-specific CD4 T-cells induced by ALVAC, a canary pox viral vector, in one trial as compared to Ad5 vector-specific CD4 T-cells in another trial. Compared to Ad5 vector, the ALVAC-specific CD4 T-cells are more resistant to HIV infection, providing evidence for distinct HIV susceptibility of CD4 T-cell populations induced by different HIV vaccine vectors. Collectively, the data provided strong evidence for distinct HIV susceptibility of CD4 T-cells induced by different vaccine vectors, which highlights the importance of better evaluating anti-vector responses in HIV vaccination while also providing new insights into the understanding of host immunity in HIV vaccination. The study that was published in *PLOS Pathogens* last year.

Following the rise in whooping cough disease in many countries, there is renewed interest in new-generation pertussis vaccines containing genetically inactivated pertussis toxoid; a pertussis toxin inactivated by hydrogen peroxide. BioNet-Asia and Mahidol University are co-developing a third generation, recombinant acellular pertussis vaccine. The organizations are collaborating to push towards broad licensing and eventual mass adoption and application of the vaccine in the future. In this pursuit, last year Prof. Punnee and her collaborators further assessed the safety and immunogenicity of a recombinant acellular pertussis vaccine containing genetically inactivated pertussis toxin and filamentous hemagglutinin in two different studies. The positive test results of these trials led to the licensure of new acellular pertussis vaccines in Thailand. The availability of recombinant monovalent pertussis vaccines that induce high antibody responses provides the medical community and consumers with the opportunity to vaccinate against pertussis when immunisation against diphtheria and tetanus is not required or undesired. Additional evaluations are underway to pave the way for licensure of this acellular pertussis vaccine in other countries, as well. Both studies were funded by BioNet-Asia and published in *Lancet Infectious Diseases*.

OUTPUT SUMMARY



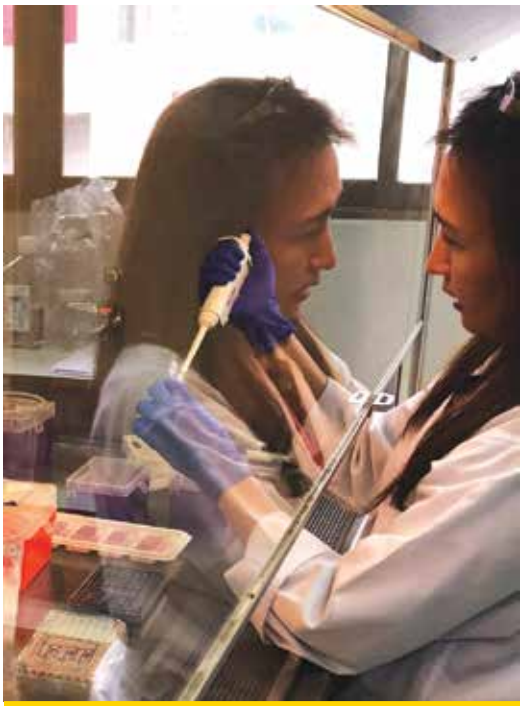
Positive results of PTgen as demonstrated on amino acids

In 2018, the Vaccine Trial Center remained a prolific center of research with the publication of over 50 titles that were mostly featured in highly respected medical journals carrying high impact factors, such as *Lancet Infectious Diseases* and *PLOS Medicine*. Collectively, the research papers covered a wide range of important focus areas and demonstrated major impacts on advances in tropical disease vaccine research.

DRUG RESEARCH UNIT FOR MALARIA (DRUM)

2018 HIGHLIGHTS

One of the greatest challenges facing malaria control is the spread and intensification of parasite resistance to antimalarial drugs. The availability of limited numbers of effective drugs has led to increasing difficulties in the development of antimalarial drug policies and adequate disease management. As a result, malaria has imposed a major burden on global health. The Drug Research Unit for Malaria (DRUM) currently has five different core test models under their malaria drug development research program: blood stage, liver stage, hypnozoite stage, drug resistance and high-throughput models. Since the Unit was formed in 2017, it has focused keenly on liver stages and *Plasmodium vivax* hypnozoites in particular. Eradication of *P. vivax* malaria is difficult because of the ability of the hypnozoite, the dormant liver-stage form, to cause relapse in patients. Due to the scarcity of robust study models to date for liver-stage malaria parasites, significant research into the hypnozoite phase has been lacking. As a result, prime research projects at DRUM have concentrated on this area, because of the knowledge deficiency, and because hypnozoite research is becoming increasingly recognized as a key driver of antimalarial drug discovery.



Dr. Rapatbhorn at DRUM

RESEARCH HIGHLIGHTS

A recent exciting accomplishment at DRUM is the development of a new *in vitro* model for *P. vivax* hypnozoite formation and enrichment that offers a significant breakthrough in the characterization of hypnozoite biology and the discovery of anti-relapse interventions. With their *in vitro* hepatocyte model as their foundation, the Unit's research will make a substantial contribution to new drug development and help them understand drug sensitivity as well as the drug resistance of liver cells. This project is supported by a NIH US-Japan Cooperative Medical Sciences Program Collaborative Awards initiative, where new or expanded infectious-disease and immunology-focused biomedical research collaborations between researchers in Japan, the Asia-Pacific region, and U.S. investigators and

institutions, are fostered. Comprehensive details regarding the *in vitro P. vivax* hypnozoite model are in preparation for publication.

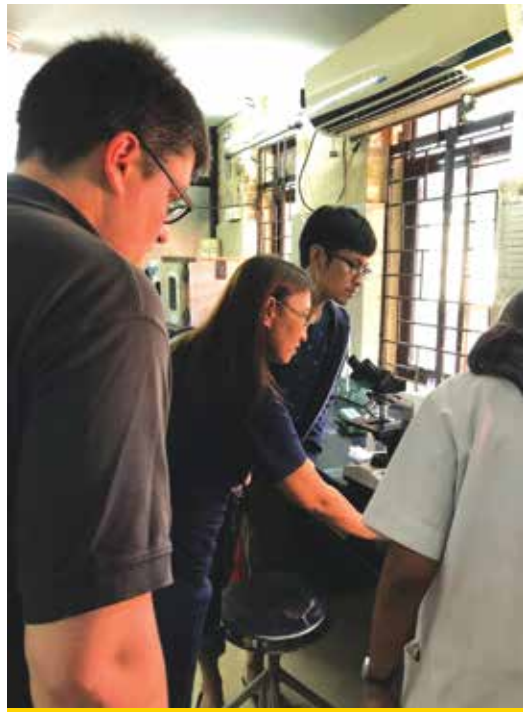
Throughout history, nature has played a significant role in the discovery of lead compounds for the treatment of malaria with many natural products exhibiting antimalarial activity. Numerous plant species have been identified as having antimalarial properties which have led to the development of many successful antimalarial therapies consisting substantially of natural products and related derivatives. Based on this knowledge, last year DRUM in partnership with the Excellent Center for Drug Discovery (ECDD) started high-throughput screening of Thai natural compounds for antimalarial activity. Initially, the compounds were screened against blood-stage forms of *Plasmodium falciparum* malaria parasites. Testing of the compounds against liver-stage forms of malaria parasites using their new robust liver-stage model is also in the works within the Unit. Some natural molecules are also being investigated in the lab for their potential as antimalarial drugs. Based on the historically high success rate among natural products, the diversity of chemicals found in nature continues to be an important source of molecular templates in the Unit's search for new antimalarial drugs.

In an effort to find a new mechanism for analyzing human *P. vivax* hypnozoites, Dr. Rapatbhorn Patrapuvich and a team of Mahidol University researchers established a novel immortalized hepatocyte-like cell line (imHC) that can serve as a robust system for analyzing human *P. vivax* liver-stage parasites, particularly hypnozoites. Observed high drug metabolic activity and potent responses in liver-stage parasites to the anti-relapse drug, primaquine, highlight the potential use of this imHC model for anti-liver-stage screening. Consequently, this new cell line will facilitate a better understanding of parasite biology and potentially offer an alternative, robust model for screening drugs against liver-stage parasites. The study was published in *Malaria Journal* in 2018.

High throughput screening of antimalarial compounds

COLLABORATIONS

In a major effort to advance the Unit's malaria research, DRUM has initiated a major collaboration with Goa Medical College and Hospital and the National Institute of Malaria Research in Goa, India under the US National Institutes of Health-sponsored Malaria Evolution in South Asia-International Center of Excellence for Malaria Research (MESA-ICEMR). DRUM supports the MESA-ICEMR program by establishing methods for the study of sporozoite production in Indian mosquitoes and liver-stage infections with Indian sporozoites. DRUM also helps establish drug assays at multiple stages of malaria-parasite development in order to evaluate susceptibility and resistance to control measures. Thus, Dr. Patrapuvich travels to India on a quarterly basis to conduct malaria research which should greatly benefit the DRUM program. DRUM also actively works in collaboration with the Rathod group at the Department of Chemistry, University of Washington in Seattle, USA, where Prof. Rathod is an expert in malaria drug discovery and has provided mentorship and counsel to Dr. Rapatbhorn in the establishment of DRUM. The main purpose of the group's associated joint research activity at present is to study the evolution of drug-resistant malaria parasites. In addition, during 2018, DRUM established several new important partnerships with research institutes/programs, such as BIOTEC, NSTDA Thailand, Phramongkutklao College of Medicine, Kasetsart University, Mahasarakham University, Rangsit University, Armed Forces Research Institute of Medical Sciences (AFRIMS), University of South Florida, Walter Reed Army Institute of Research, and Liverpool School of Tropical Medicine, UK.



Dr. Rapatbhorn and team at Goa Medical College and Hospital in Goa, India

LOOKING FORWARD

In the future, it is hoped that Dr. Patrapuvich can develop DRUM into a central hub for malaria drug research and increase its visibility within the tropical-disease community. Under her leadership, she hopes to mentor and further the development of Unit researchers, and encourage them to take a more significant role in research collaborations abroad, which should help advance the discovery of breakthrough innovations in malaria drug treatment.

COLLABORATIONS

"International academic collaboration is central to the work of the Faculty. Currently, six international organizations or units are hosted, covering a range of research and activity areas. The following pages describe the work of each collaboration and their highlights and impacts in 2018."

Prof. Tatsuo Shioda
Mahidol-Osaka Center for Infectious Diseases (MOCID)

Prof. Nicholas Day
Mahidol Oxford Tropical Medicine Research Unit

Prof. Leo Braack
Malaria Consortium

Dr. Eileen Dunne
Silom Community Clinic at TropMed

Assoc. Prof. Pratap Singhasivanon
Southeast Asian Ministers of Education Organization (SEAMEO) Tropical Medicine and Public Health (TropMed) Network

MAHIDOL-OSAKA CENTER FOR INFECTIOUS DISEASES (MOCID)

2018 HIGHLIGHTS

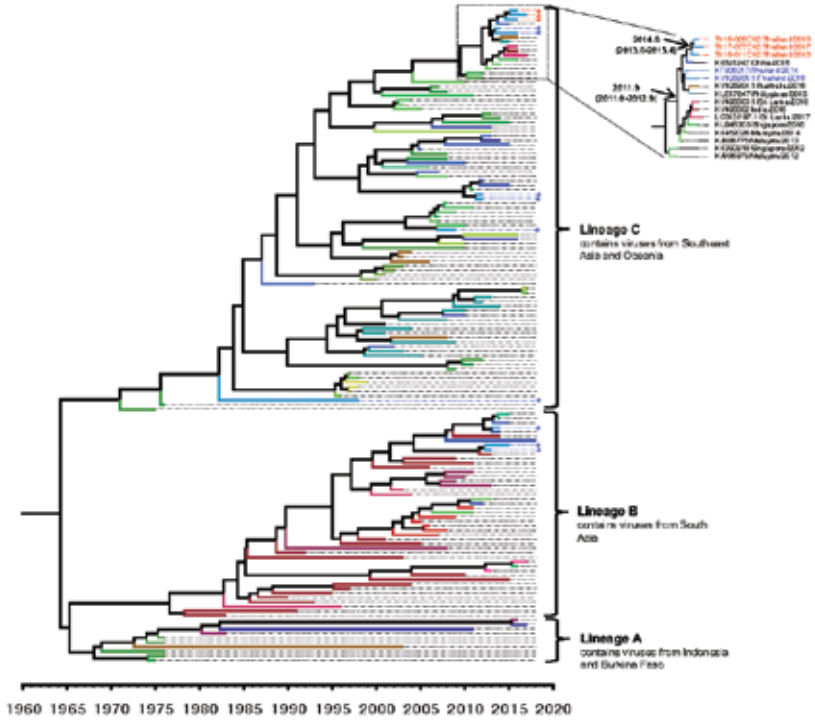
The Mahidol-Osaka Center for Infectious Diseases (MOCID) was established by the Faculty of Tropical Medicine, Mahidol University (FTM-MU) and the Research Institute for Microbial Diseases, Osaka University (RIMD-OU). The FTM-MU and RIMD-OU focus on basic laboratory research fields while the partnership aims to synergize the infectious disease research of collaborating members from both organizations. MOCID was primarily established to efficiently host the outputs of collaborating members from the FTM-MU and RIMD-OU. Studies, discoveries and information obtained by the collaboration, including patent applications, are released for publication under co-authorship.

A researcher and med students from Osaka University visiting MOCID for infectious diseases research

PUBLISHED STUDIES

DENGUE

Dengue is a prolific mosquito-borne disease that has spread to over 100 countries and causes various clinical symptoms, including dengue fever and severe dengue. Dengue fever is caused by the dengue virus (DENV), and comprises 4 serotypes; each serotype is divided into distinct genotypes. Thailand happens to be an endemic area where all 4 DENV serotypes coexist. To understand the current genotype distribution of native DENVs, researcher Juthamas Phadungsombat of MOCID and a small international team of researchers enrolled 100 "fever with dengue-like symptoms" cases at the Bamrasnaradura Infectious Diseases Institute (BIDI) in Thailand. Next Generation Sequencing of the viruses obtained revealed that DENVs in Thailand have increased in genotypic diversity, suggesting that the DENV genotypic change observed in other Asian countries might also be taking place in Thailand. The team was able to show that the cosmopolitan genotype of dengue virus type 2 (DENV-2) has recently surfaced as a genotype co-circulating with the Asian-I genotype, at least in the local area (adjacent to the capital city, Bangkok) served by BIDI. Researchers involved in the study are curious to observe whether the DENV-2



A time scaled phylogenetic tree showing the introduction time of DENV-2 genotype cosmopolitan to Thailand

cosmopolitan genotype will replace the current local genotype (Asian-I) and whether cosmopolitan might cause a new outbreak in Thailand, given that their data also showed evidence of dengue genotype shift. The study was published last year in *PLOS One*.

CHIKUNGUNYA

As there is no preventive medication or vaccine against chikungunya, the virus will be an important research area for several departments of the Faculty of Tropical Medicine. Chikungunya virus (CHIKV), a mosquito-borne pathogen, consists of three genotypes. Previously developed by MOCID, a novel rapid immunochromatographic (IC) test detecting CHIKV E1-antigen showed high sensitivity to East-Central South African (ECSA) genotype viruses, but poor performance against the Asian genotype virus that is spreading in the American continents. To understand the basis for the inferior performance of this IC test against the Asian-genotype virus, MOCID researchers, with a small team of international researchers, re-examined anti-CHIKV monoclonal antibodies (mAbs) used in the test for their interaction with E1-antigen of the three CHIKV genotypes, to explore possible reasons for the decreased sensitivity against the Asian-genotype. The researchers found that the reactivity of one monoclonal antibody (mAb) for Asian-genotype virus was lower than that for ECSA virus. Collective study results confidently indicated that amino acid residue at a precise sequence position (350) of the CHIKV 6K-E1 protein is a key factor affecting the low performance of the novel IC assay. As a result of these findings, MOCID has added to its cumulative knowledge in this area and has successfully progressed chikungunya virus antigen detection based on the findings revealed by the study. This research was published last year in *Scientific Reports*.

MOCID was also recently part of significant research work that focused on the development of

broadly reacting monoclonal antibodies against three genotypes of chikungunya virus (CHIKV). In response to the continuing global spread of CHIKV, a diagnostic tool that can accurately detect CHIKV in a simple and inexpensive way is of high importance. Effective diagnosis is one of the keys to disease control, but to date, no antibody-based rapid immunochromatographic (IC) platform for CHIKV is commercially available. Thus, the application of the monoclonal antibodies (mAbs) for CHIKV detection is expected to be of great value for clinical diagnosis and disease surveillance. A previous rapid IC test detecting CHIKV proteins showed promising performance for detecting one particular associated genotype, but unfortunately the test exhibited lower capacity to detect other related genotypes. To address this shortcoming, several MOCID researchers set out to generate a new panel of broad-spectrum anti-CHIKV mAbs using hybridoma technology, which is a method for producing large numbers of identical antibodies by the injection of a specific antigen into mice. Monoclonal antibodies developed by the team were specific to CHIKV and lacked cross-reactivity to closely related alphaviruses and flaviviruses (dengue and Zika virus). MOCID researchers have applied for a patent of these novel antibodies against the chikungunya virus with the Thai Department of Intellectual Property (DIP), as these tools represent great improvements for clinical diagnosis and surveillance of CHIKV infection. The study was published last year in *PLOS One*.

COLLABORATIONS

MOCID researchers started to collaborate actively with the Department of Protozoology in 2018, based on a student exchange program between Mahidol and Osaka universities. Interdepartmental exchange of research in the areas of *Blastocystis* sp. subtyping will be a core focus area between the two parties. The new partnership intends to expand the overall knowledge base between the two groups with respect to collective areas of study and solutions development within each department. MOCID also relies on the active assistance of Center of Excellence for Antibody Research (CEAR) at the FTM, where their support contributes to an integral part of MOCID's infectious-disease research efforts. MOCID is grateful to the Bamrasnaradura Infectious Diseases Institute (BIDI), Thailand for contributions made to dengue research and to Dr. Marco Yung-Cheng Lin, Department of Medical Research, Mackay Memorial Hospital, New Taipei, Taiwan for supervision of molecular phylogenetic analysis, as both entities helped advance their infectious disease research successfully last year, in particular.

AWARDS

Mr. Aekkachai Tuekprakhon, Ph.D. of MOCID received the first prize for the top 'Young Investigator Presentation' at the Joint International Tropical Medicine Meeting (JITMM) in 2018. Eligible applicants for this noteworthy award must be current Master's or Ph.D. students, or recent graduates. The top five abstracts are selected for oral presentation on the basis of scientific merit. Mr. Tuekprakhon received a certificate of recognition and 5,000 Baht for his first place finish. MOCID researcher Dr. Hisham Ahmed Imad also received a 'Young Investigator Presentation' award at JITMM 2018. Aekkachai Tuekprakhon, Ph.D. and Dr. Hisham Ahmed Imad receiving awards for Young Investigator Presentation at JITMM 2018

Young Investigator Presentation Awards at JITMM 2018

MAHIDOL OXFORD TROPICAL MEDICINE RESEARCH UNIT (MORU)

2018 HIGHLIGHTS

The MORU Tropical Health Network continues to make good progress on the objectives and themes set out in the 2015-2020 renewal application. In 2018, the Unit published 234 peer-reviewed publications (5% of these in Wellcome Open Research). Since the last renewal in 2015, they have published 832 papers, which represents 32% of all the papers published in our 39-year history.

EPIDEMIOLOGY AND DIAGNOSTICS

MORU continued to study the etiologies and outcomes of febrile illness and sepsis in Southeast Asia, in 2018 demonstrating the high mortality from community-acquired bacteremia, assessing the utility of qSOFA score as a predictor of outcome in LMICs, and demonstrating in fever studies the high prevalence of rickettsial infections across the region.

MORU assisted national malaria control programs, WHO, and the Asia Pacific Leaders Malaria Alliance (APLMA) in mapping malaria across the region, modelling interventions for malaria control and elimination, and providing genomic epidemiology on the parasites. This has also involved mapping travel patterns and the location of villages, using innovative technologies.

MORU developed and evaluated a variety of diagnostic methodologies for a range of infectious diseases, including malaria, melioidosis and scrub typhus.

MALARIA ELIMINATION

A series of large trials on the use of targeted mass drug administration (MDA) as a tool for malaria elimination in the region has been completed with sites in Myanmar, Cambodia, Laos and Vietnam. These studies show good efficacy and acceptable

A doctor examines a patient at Shwe KoKo Clinic, in Myawaddy Township, Myanmar, where the Shoklo Malaria Research Unit (SMRU) provides the local population with diagnosis and treatment services for TB, TB/HIV co-infection and multi-drug resistant TB (MDR)© MORU 2019, Gerhard Jörén

Malaria testing at the Shoklo Malaria Research Unit on the Thai-Myanmar border—SMRU provides quality health care to refugees and migrant workers, combining research and humanitarian services. © MORU 2019, Gerhard Jörén

safety for dihydroartemisinin-piperaquine with or without low-dose primaquine, and the importance of community engagement to achieve high population coverage. Social science studies were conducted to understand factors motivating target populations for malaria-control activities to participate.

MORU described the dynamics of asymptomatic parasitemia over time, crucial for defining the contribution of the asymptomatic reservoir to malaria transmission in low-transmission settings and informing policy makers.

Studies were completed assessing the safety and benefit of ivermectin in malaria control, understanding the effect of population level MDA on vector infectivity, and understanding the aspects of housing which protect against vector entrance.

A large healthy volunteer study showed that the RTS,S/AS01 vaccine was well tolerated and immunogenic, and had no interactions with DHA-piperaquine. Modelling has shown that vaccination with RTS,S is a potentially useful adjunct to MDA in elimination campaigns.

A systematic review of the risk of sudden unexplained death after dihydroartemisinin-piperaquine exposure was completed. It demonstrated the safety of this drug combination and informed the WHO treatment guidelines.

TRANSLATION POTENTIAL

Triple artemisinin combination therapies are currently used to prevent the emergence and spread of drug resistant malaria. A large multicenter multi-country trial (TRAC2) finished recruiting in 2018, and preliminary results show that they are reasonably well tolerated and effective against multi-drug-resistant malaria.

CRP testing was shown to be effective at reducing antibiotic usage in the treatment of febrile illness. With partners, MORU plans to develop and test rapid tests which combine CRP with disease-specific tests (such as malaria, dengue, and scrub typhus). A modelling exercise has shown that this approach would be cost-effective.

Dihydroartemisinin-piperaquine was evaluated as a seasonal chemoprevention in young children in Burkina Faso. The MORU pharmacology department conducted the bioanalysis and described the PK/PD properties of piperaquine using modelling and simulation, showing that young children need a relatively higher dosage than adults. Increased piperaquine dosage and extended coverage during the high transmission season could have a substantial impact on the incidence of malaria.

The renoprotective effects of paracetamol were evaluated in patients with severe and moderately severe falciparum malaria in a randomized, controlled, open-label trial. Pharmacokinetic-pharmacodynamic analysis showed that higher exposure to paracetamol increased the probability of creatinine improvement, and therefore, the renoprotective effect of paracetamol.

MALARIA CONSORTIUM

2018 HIGHLIGHTS

RESEARCH HIGHLIGHTS

The *Aedes aegypti* mosquito is the primary vector for the transmission of dengue fever, chikungunya, Zika fever, other yellow fever viruses, and additional disease agents. As a consequence, it is targeted with insecticide treatments where outbreaks have occurred, mainly in the tropics and sub-tropics. In a study published last year in the *Asia-Pacific Journal of Public Health*, Dr. Hii of the Malaria Consortium was instrumental in the assessment and characterization of insecticide resistance status of the *Aedes aegypti* mosquito from rural and urban locations in Cambodia. Specifically, susceptibility to temephos, permethrin, and deltamethrin, was evaluated in accordance with World Health Organization (WHO) guidelines. Collective results from multiple sites proved particularly alarming for dengue vector control employing the most commonly used public health insecticides, as widespread resistance may compromise the entomological impact of larval control operations. In the event of an epidemic in Southeast Asia, these insecticides may no longer be effective. The study highly recommends the development of innovative vector-control tools, which are very much needed to replace ineffective pesticides currently deployed in Cambodia.

High coverage of effective malaria control initiatives – such as the use of treated mosquito nets, and, to a lesser degree, indoor residual spraying – in the Greater Mekong Subregion (GMS), has resulted in sharp decreases of malaria in countries where national programs have successfully deployed these tools. However, the persistence of malaria transmission has moved from villages to farm plots and forests, with secondary vectors, as observed in Vietnam. This remaining, low-level transmission has been termed 'residual malaria transmission' (RMT). In an effort to address RMT, last year Dr. Jeffrey Hii and co-investigators developed a mixed-methods package, comprising epidemiology, entomology, socio-anthropological and GIS tools, for quantifying the magnitude of RMT and outdoor biting along the Thai-Myanmar border and in central Vietnam. This project seeks to better understand the scale and causes of RMT, using multiple approaches so that appropriate interventions can be adopted to eliminate it. In such places, the deployment of long-lasting insecticidal nets (LLINs) requires new approaches, while other vector control tools are also needed. Translating the mixed methods may assist in the development of a toolkit and protocols for RMT measurement that can be applied to other settings. Scientific evidence acquired from this comprehensive RMT study to date was presented at four international forums over the course of 2018.

As the Principal Investigator of two different studies published last year, Dr. Jeffrey Hii's research was integral to the adoption of new national policy outcomes associated with malaria and dengue elimination in disease-affected countries. The study of residual malaria transmission (RMT) in two Mekong countries has led to important policy implications for malaria elimination with the Special Programme for Research and Training in Tropical Diseases (TDR) supporting the implementation of research and development plans for malaria-affected

countries to implement and also the deployment of new approaches based on the local context of transmission for preventing and controlling malaria. One of the public-health benefits is a package of recommendations and guidance options for the development of targeted malaria-control tools. Another study produced data based on dengue knowledge, attitudes and practices (KAP) and their impact on community-based vector control in rural Cambodia, which contributed to a stronger evidence-base of cost-effective, achievable, sustainable and environmentally-friendly vector control interventions that will assist dengue-affected countries in deciding where to deploy resources.

Dr. Jeffrey Hii in discussion with colleagues at the annual general meeting of the Asia Pacific Malaria Elimination Network (APMEN) Vector Control Working Group (VCWG), September 2018

In addition, Dr. Hii successfully assessed the efficacy of transfluthrin spatial repellent last year, in the laboratory, semi-field, and at rubber-plantation settings, with the aim of deploying new approaches for preventing and controlling outdoor malaria vectors. Transfluthrin is a fast-acting synthetic insecticide with low persistence, generally used for mosquito control. Research into the effectiveness of this specific spatial repellent is especially important to mobile migrant workers, forest goers, police and military personnel, who are often unprotected while working outdoors. Study results and other related research documentation is currently in preparation for dissemination and uptake.

DEPARTMENTAL HIGHLIGHTS

As part of the Joint International Tropical Medicine Meeting (JITMM) in 2018, the Malaria Consortium organized a symposium on 'Accelerating access to existing new and old technologies for vector-borne disease elimination in Asia-Pacific'. Dr. James Tibenderana from the Malaria Consortium, and Jason Nash representing Bayer, chaired the symposium. Speakers from the World Mosquito Program in Yogyakarta, Bayer, and the Malaria Consortium, took part in the presentation. The symposium provided an opportunity to exchange scientific findings and lessons learned in malaria-elimination and mosquito-borne neglected tropical diseases (NTDs) in the Asia-Pacific region. The symposium also provided an opportunity to strengthen collaboration between regions, as well as between public, private and non-governmental organizations with a shared common goal of controlling and eliminating vector-borne diseases.

The continuing partnership between the Malaria Consortium and Mahidol University saw two new students receive the Dr. Sylvia Meek Scholarship in Entomology last year. Shobiechah Aldillah Wulandhari of Indonesia, and Kiattiyos

Dr. James Tibenderana and Jason Nash chairing a symposium at the JITMM

Ruengthamchariya of Thailand, were awarded the scholarship at the Wai Khru Day Ceremony at the university by Malaria Consortium's Global Technical Director, Dr. James Tibenderana. The Dr. Sylvia Meek Scholarship was set up in 2016 to support students from across the world to study entomology at universities in Nigeria, South Africa, and Thailand. The students embarked on a two year Masters program in entomology at Mahidol University, joining five previous scholars who have undertaken studies in similar programs at Mahidol, the University of Nigeria, Nsukka and University of Pretoria, South Africa.

In personnel news, both Dr. Jeffrey Hii, Senior Vector Control Specialist and Tiff Dahmash, Technical Specialist left the Malaria Consortium last year, while new members Prof. Leo Braack, Senior Vector Control Specialist, and Dr. Htin Kyaw Thu, Technical Specialist, joined the organization recently. Both new team members are based at the Malaria Consortium office at the Faculty of Tropical Medicine.

As a result of mutual past success and the continuation of medical research progress into the future, the Malaria Consortium and the Faculty of Tropical Medicine recently agreed to extend their current ten-year MOU and ongoing professional relationship for a further ten years. Malaria Consortium leadership is excited about this opportunity to sustain an important collaboration with the Faculty of Tropical Medicine, Mahidol University for several years to come.

Dr. James Tibenderana (C) with Shobiechah Aldillah Wulandhari (L) and Kiattiyos Ruengthamchariya (R), the new Meek scholars

SILOM COMMUNITY CLINIC AT TROPMED

2018 HIGHLIGHTS

In addition to functioning as a dynamic clinical trial unit for HIV and STD prevention, Silom Community Clinic @TropMed (SCC @TropMed) was also active in the publishing department in 2018. A total of 13 research studies were published in high-value scientific and medical journals, such as *PLOS One* and *The Lancet*, among others. The majority of the publications concentrated on MSM- and HIV-centric research. Three featured studies are summarized in this Annual Review.

PUBLISHED STUDIES

Seeking casual sex partners on the internet and methamphetamine use have been described as risk factors for HIV infection for men who have sex with men (MSM). However, the interplay between these factors has not been analyzed in totality. In a diverse research study published in *The Lancet* last year, SCC affiliates took part in an observational study of Thai MSM aimed at determining the associations between these specific influences using survival model analysis to evaluate these influences for incident methamphetamine use and HIV infection. The results showed that, for MSM in Bangkok, casual sex partner recruitment on the internet, methamphetamine use, and sexually transmitted infections play important roles in sustaining the HIV epidemic. HIV incidence was high among MSM who reported methamphetamine use for sexual pleasure. Risk factors for both methamphetamine use and HIV incidence were younger age, finding casual sex partners on the internet, and chemsex party attendance. In addition, the internet has become a very popular tool for finding new acquaintances, including new sex partners, by MSM in Bangkok and elsewhere, as it is especially utilized by young same-sex-oriented or -interested men. The study concluded that virtual HIV prevention education, drug-use harm reduction, and biomedical HIV prevention methods, could help to reduce or revert the HIV epidemic among MSM in Bangkok.

Neisseria gonorrhoeae (NG) is a common, global sexually transmitted infection that can have serious complications. There is increasing concern about the development of antimicrobial-resistant NG to the main drugs recommended for primary NG infection treatment. As a result, the monitoring of patterns of resistance and risk factors are crucial for detecting and monitoring antimicrobial resistance (AMR). In collaboration with the World Health Organization (WHO), the U.S. Centers for Disease Control and Prevention (CDC), and the Thailand Department of Disease Control (DDC), Ministry of Public Health (MoPH), the first Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP) was officially implemented in 2015. Since then, the director of the SCC, Dr. Eileen F. Dunne, has been very instrumental in the formation and progress of this new global surveillance program based in Thailand, which is designed to collect standardized data used to monitor trends of global antimicrobial-resistant NG infection. Data collection efforts at Silom Community Clinic have involved the assessment of men with urethritis, including demographic and behavioral details linked to laboratory data. All data collected from the first EGASP site in Thailand will be used to inform future treatment guidelines in Thailand and the SEA region. The expansion of EGASP to different global settings will augment the ability to detect antimicrobial-resistant NG and initiate timely prevention and control steps globally. The

first data sets from EGASP were published in *PLOS One* last year.

High HIV incidence has been reported among young men who have sex with men (YMSM) in North America and Western Europe, but there are limited data for Southeast Asia. Young people remain at the center of the HIV epidemic across the world, accounting for 30% of all new global HIV infections, with YMSM now driving the HIV epidemic in Thailand. SCC researchers assessed and determined HIV incidence and risk factors among a large group of YMSM living in Bangkok, Thailand, from 2006 to 2014, who enrolled in a group study at Silom Community Clinic, where participants were interviewed, tested and counseled. Based on the findings, the HIV incidence rate was found to be 7.4% per 100 persons studied on average, a rate that is much higher than reported for other key populations in Thailand. High-risk behaviors and/or combined with illegal drug use were significantly associated with HIV incidence among YMSM. As preventative measures against HIV, specialists recommend that health clinics meet the specific needs of YMSM and should be available with services that include counseling, testing and treatment, including referrals, delivered in a way that provides easy access, confidential services, and a supportive environment free from discrimination. Prophylactic measures, in conjunction with education and awareness through specific policies and programs, are needed to reach this population in order to reduce new HIV infections in YMSM and reach the HIV-prevention goals set by Thailand and the region. Observations were published in *AIDS and Behavior* in 2018.

ONGOING CLINICAL TRIAL

The Silom Community Clinic @TropMed is one of 43 clinical-research sites across seven countries (Argentina, Brazil, Peru, South Africa, Thailand, the U.S., and Vietnam) conducting a study (HPTN 083) of an injectable pre-exposure prophylaxis (PrEP) for HIV prevention. HPTN 083 is a large-scale clinical trial that is part of the NIH-DAIDS-funded HIV Prevention Trials Network (HPTN). The study is evaluating long-acting injectable cabotegravir (CAB LA) compared to daily oral PrEP to prevent HIV and is designed to establish the safety and efficacy of CAB LA for PrEP in HIV-uninfected men who have sex with men (MSM) and among transgender women (TGW). More than 200 eligible participants - HIV-uninfected men and transgender women who have sex with men (MSM and TGW) - enrolled in the study at SCC @TropMed, which is currently the clinical research site in Asia with the highest number of enrollments on average per week and is expected to achieve the new enrollment target of 208 participants by end April 2019. Results from the ongoing trials are expected sometime in 2021.

HPTN 083 Study promotion with outreach team in August 2018

COLLABORATIONS

The Silom Community Clinic program partners with a number of collaborators, including the Thailand Ministry of Public Health (MoPH), Bangkok Metropolitan Administration (BMA), Rainbow Sky Association Thailand (RSAT), Service Workers in Group Foundation (SWING), APCOM, Gay BKK, AIDS Healthcare Foundation (AHF), Sisters Foundation and The Planned Parenthood Association of Thailand (PPAT). The Multiple-sexuality person Community Advisory Board (M-CAB) meeting has been held on a quarterly basis at SCC with the main objective to advocate for policy and monitor the progress of HIV/AIDS prevention, healthcare and research for persons with multiple sexuality. The M-CAB members have been selected by community representatives, which currently consist of over 20 partners from five sector levels, including government, private business, community-based organizations, medical research institutes

and public media in Thailand. The M-CAB builds and fosters partnerships between SCC researchers and local community, voices concerns from the community and study participants, and suggests strategies to address ethical and operational aspects of study development, which include recruitment, implementation and retention of community engagement strategies for research. To ensure all M-CAB members are equipped with the proper tools to carry out CAB responsibilities effectively, the SCC has regularly organized semi-annual research training that will assist these members in building and increasing their capacity towards HIV/AIDS prevention.

VIP VISITORS TO SCC

Last year, the SCC welcomed representatives from the U.S. Department of Health and Human Services (DHHS) on two different occasions. In late 2018, high-level representatives from the U.S. Centers for Disease Control and Prevention (CDC) - the main federal agency that conducts and supports public health activities in the U.S. - were given a tour of on-site operations. The delegates were led by Dr. Robert R. Redfield, Director of CDC and Administrator, Agency for Toxic Substances and Disease Registry (ATSDR). The CDC delegates visited the clinical research site to review the progress of important scientific work, including ongoing NIH-supported clinical trials in Bangkok, Thailand, which are conducted by the HIV/STD Research Program, Division of HIV/AIDS Prevention. On another visit last year, the SCC welcomed delegates from the Division of HIV/AIDS and Prevention (DHAP), U.S. Centers for Disease Control and Prevention (CDC) and Emory University on their biennial site visit to Thailand. The delegates were led by Dr. Eugene McCray, Director of the Division of HIV/AIDS and Prevention, and Dr. Carlos Del Rio, Professor of Epidemiology, Rollins School of Public Health, Emory University. During the site visit, guests reviewed comprehensive program operations and research progress. New planned research activities were also discussed.

CDC officials visiting the SCC@TropMed

AWARDS

In recognition of the outstanding work accomplished at the Silom Community Clinic, several team members were recognized and awarded various accolades throughout 2018. Among them, Dr. Chaiwat Ungsedhapand received an official Honor Award. Ms. Dararat Worrajittanon and Ms. Supawadee Na-pompet each received Embassy Employee of the Month recognition and Ms. Punneeporn Wasinrapee was the recipient of the Mission Time-Off Award. The SCC was also bestowed a Group Eagle Award and Certificate of Appreciation for effective collaboration and teamwork by providing critical and early data on men who have sex with men in support of the Bangkok MSM Cohort Study, a study initiated to understand and investigate the HIV epidemic in YMSM in Bangkok, Thailand.

U.S. Embassy Bangkok recognizes SCC Staff

SOUTHEAST ASIAN MINISTERS OF EDUCATION ORGANIZATION TROPICAL MEDICINE NETWORK (SEAMEO TROPMED NETWORK)

2018 HIGHLIGHTS

SCHOLARSHIPS

In 2018, SEAMEO TROPMED Network awarded 19 scholarships to health professionals in SEAMEO Member Countries to pursue Diploma, Masters, and PhD programs offered by TROPMED Malaysia, TROPMED Philippines and TROPMED Thailand.

CONFERENCES, MEETINGS, AND FORUMS

The 57th SEAMEO TROPMED Network Governing Board Meeting was convened 29-30 August 2018 in Nay Phi Taw, Myanmar, and was presided over by Professor Thet Khaing Win, Permanent Secretary, Ministry of Health and Sports of Myanmar.

The Partners Meeting "Learning to Investigate by Field Experiment for Southeast Asian Emerging Diseases (LIFE for SEA ED) Project co-funded by the Erasmus+ Program of the European Union, was held in Bangkok, 2-4 April 2018. The partners included Sorbonne University of Paris, Universidade Nova de Lisboa, Portugal, University of Primorska, Slovenia, three universities in Thailand- Mahidol, Chulalongkorn and Prince of Songkla, and SEAMEO TROPMED network, which is the co-coordinator of the project.

SPECIAL PROJECTS

Thailand One Health University Network (THOHUN) was professionally evaluated. The evaluation included all activities covering the years 2013-2017 of the national Coordinating Office and 20 faculties in 8 member universities in four project sites--Bangkok, Chiang Mai, Songkla, and Khon Kaen provinces. Review of the Current Expertise and Curricula of three Universities in Thailand in relation to Applied Medical Entomology, Vector-borne parasitic and Viral Diseases, Ecology and Environment, Epidemiology, Data management and GIS. The review covered 9 postgraduate academic programs, and 68 course syllabi.

NEW COLLABORATIONS

As Deputy Coordinator of the Network, Dr Sandra Tempongko is proud to be part of an organization that has stayed relevant throughout its over 50 years' existence.

SEAMEO TROMPED Network and DAAD Meeting to discuss implementation of three-year DAAD scholarship funding.

A three-year Memorandum of Understanding was signed with the International Society of Geriatric Oncology (SIOG), a multidisciplinary society, including physicians in the fields of oncology and geriatrics, and allied health professionals with over 1700 community members in 40 countries.

SEAMEO TROPMED NETWORK IMPACT

The overall impact of the SEAMEO TROPMED network is its contribution to health human resource development through the following strategies: (i) provision of scholarships for postgraduate degree programs; (ii) conduct of training courses; (iii) provision of technical assistance to Member countries; (iv) organizing platforms for discussion of emerging issues; and (v) provision of opportunities for scientific publication through the Network's journal.

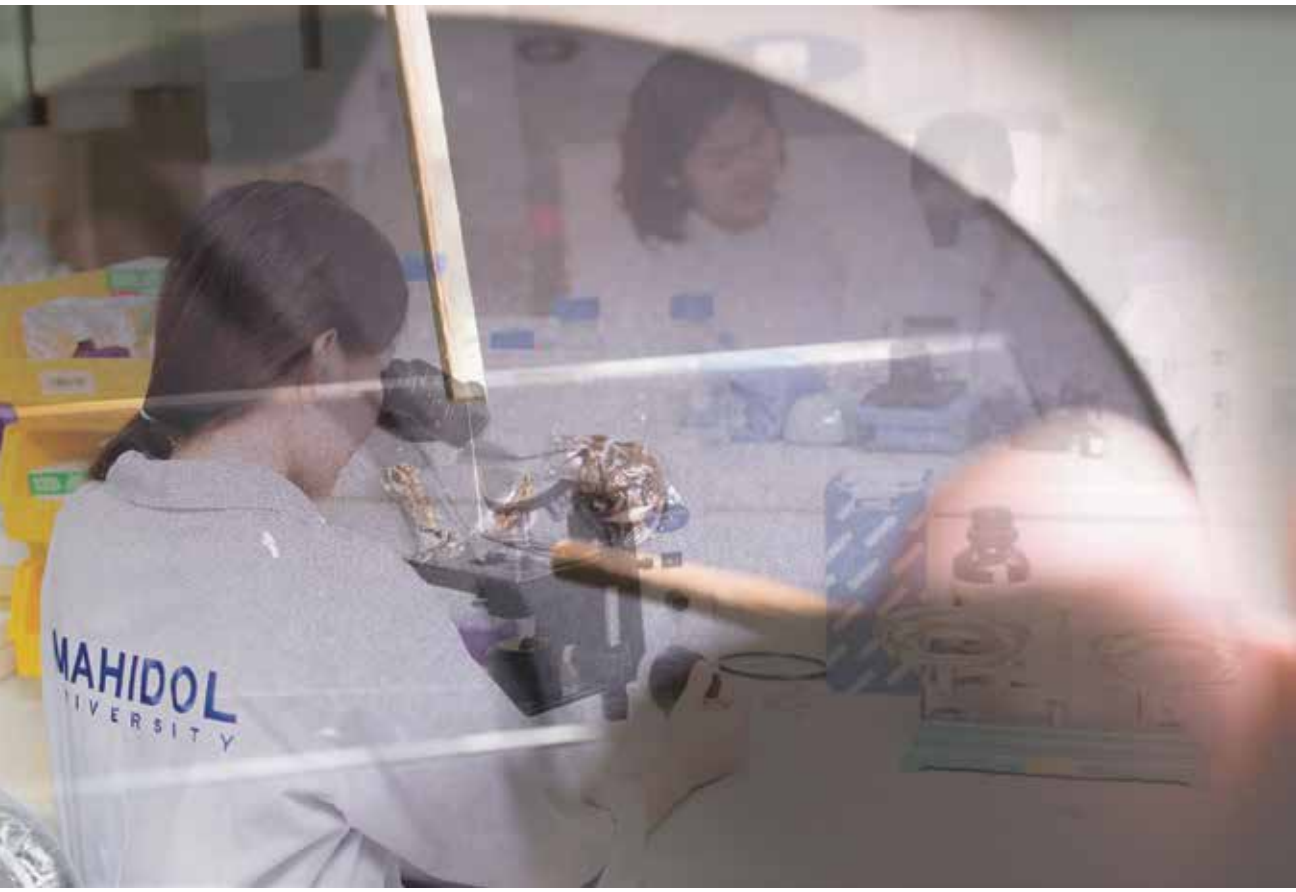
In addition, SEAMEO TROPMED Network contributes to enhancing the implementation of school health programs and services in the different Ministries of Education in the region.

CHALLENGES

The changing public health landscape and the new roles that the health professionals of today need to assume, require different sets of competencies. Thus, for the Network, the biggest challenge is how to ensure that the approaches and strategies of the Network will enable it to contribute to meeting the needs of health professionals. Technical or hard skills alone are not enough to address the challenges posed by the public health landscape now. Health and health-related professionals need to develop the soft skills that will enable them to be more efficient and effective in the performance of their different roles and the implementation of their functions.

In-House Management Meeting of SEAMEO TROPMED Network participated by Directors and focal persons of the three TROPMED Regional Centers and officials of the Network Office.

FTM INNOVATION AND TRANSLATION



INNOVATION AND TRANSLATION: FROM RESEARCH TO PRODUCTS

ANTIBODY-BASED RAPID DIAGNOSTIC IMMUNOCHROMATOGRAPHIC TEST FOR CHIKUNGUNYA VIRUS DETECTION

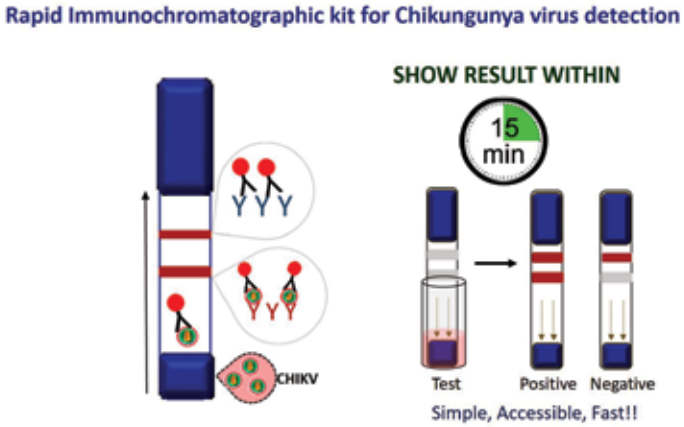
Innovator:
Asst. Prof. Pornsawan Leaungwutiwong

The last cases of chikungunya in Thailand were reported in 1996. But in 2008 and 2018, numerous confirmed chikungunya outbreaks were reported, mainly from the four southernmost provinces of Thailand, suggesting that chikungunya virus (CHIKV) is re-emerging in the country.

Diagnosis of chikungunya fever is always seen as complicated as it shares similar symptoms with dengue fever and Zika virus infection. Its specific clinical symptom is a prolonged arthritis that burdens a patient for months, or even years for more severe cases. There are no specific drugs for the treatment of chikungunya, but an efficient diagnosis of chikungunya is important to inform appropriate patient care.

The real-time PCR assay is currently considered the "gold standard" diagnostic method for chikungunya, but is seen to possess many disadvantages in settings where the virus is endemic. An accessible rapid diagnostic immunochromatographic (IC) test for chikungunya virus detection, based on the E1 protein, has previously been developed. Unfortunately, it can only detect two of the three CHIKV genotypes. It can detect the East/Central/South African (ECSA) and West African (WA) genotypes, but not the Asian genotype.

This is the obstacle that Asst. Prof. Pornsawan Leaungwutiwong, Dr. Aekkachai Tuekprakhon, and collaborators from Mahidol Osaka Center for Infectious Diseases (MOCID) were able to overcome in 2018.



To address the bottleneck in the previous test, Dr. Pornsawan and collaborators produced a broad-spectrum mouse anti-CHIKV monoclonal antibodies (mAbs) targeting CHIKV E1 and capsid proteins. The developed antibody-based rapid diagnostic IC test for CHIKV detection can detect all of its three genotypes, indicating that it can be of great value in clinical diagnosis and surveillance.

Currently, the IC is in its prototype stage and was granted a Japanese patent in 2018. The IC test can provide results within 15 minutes; the team will further evaluate the sensitivity and specificity of the test to all CHIKV genotypes in 2019. This project is supported by Tanaka Scientific Limited, Osaka University, and Mahidol University. A Japanese company offered to support the marketing and production of the test kit after the evaluation of test's sensitivity and specificity proves effective to all CHIKV genotypes. Dr. Pornsawan believes the commercialization of the test is promising.

Dr. Pornsawan hopes for the IC test for CHIKV to reach its translational potential. In future, she sees the product being the first option in diagnosing CHIKV in patients in areas where it is endemic, and where laboratory diagnostic methods are often unavailable.

RAPID IMMUNOCHROMATOGRAPHY TEST FOR MELIOIDOSIS

Innovator:
Assoc. Prof. Narisara Chantratita

Dr. Narisara Chantratita's primary research area is melioidosis, an infectious disease caused by the bacterium *Burkholderia pseudomallei*. In her research, she tries to further understand the microbiology of this bacterium and the virulence factors that causes the disease. She is also especially interested in the development of improved methods of diagnosis and treatment for this neglected tropical disease. Her work focuses on northeast Thailand, where the mortality rate for melioidosis patients is ~40%.

The clinical diagnosis of melioidosis is often difficult, as it mimics the symptoms of other diseases. Laboratory diagnostic tests for melioidosis are currently available, but all similarly are slow in providing test results and their sensitivity is unimpressive (≈60%). In addition, the laboratories where the tests can be conducted are largely unavailable in primary hospitals in Thailand, especially in the northeast where the disease is endemic. This results in melioidosis being under-diagnosed, under-reported, and untreated.

"How can you treat melioidosis if you cannot diagnose it more efficiently?" This is the challenge that sparked Dr. Narisara's determination to create a much-improved version of the current diagnostic methods for melioidosis.

In collaboration with researchers from the Faculty of Tropical Medicine, Mahidol University, Khon Kaen University, the University of Nevada, Reno School of Medicine, USA, and Mahidol-Oxford Tropical Medicine Research Unit, Dr. Narisara has developed a rapid immunochromatography test (ICT) for melioidosis using hemolysin-coregulated protein 1 (Hcp1) as target antigen. The test can detect the antigen in patient's blood, read results in 15 minutes, and provide 88% sensitivity and 86-92% specificity, as confirmed by blood samples from 487 melioidosis patients at four hospitals in northeast Thailand.

Compared with the existing diagnostic methods for melioidosis, such as the indirect hemagglutination assay (IHA), which provides only 69.5% sensitivity and 67.6 specificity for Thais, this new ICT offers significantly improved results.

Dr. Narisara successfully patented this rapid melioidosis test in 2017, with venture entrepreneurship commencing in 2018. The ICT product is now available in the market and currently costs 250 Baht per test

or 6,250 baht per box of 25 tests. The product is also available as a Latex Agglutination test for bacterial identification and costs 6,500 for 250 tests. The Hcp1-ICT is now available for purchase at the Faculty of Tropical Medicine, Mahidol University.

Currently, the government and private hospitals in Thailand are testing and evaluating the ICT. This project is a collaboration with Med Tech Solution Company, supported by the National Innovation Agency, Ministry of Science and Technology, Thailand.

The simplicity, reliability, and affordability of the rapid Hcp1-ICT for melioidosis indicates that it can be a potential point-of-care test and may be used to replace IHA for screening melioidosis in hospitals and resource-limited areas.

Dr. Narisara hopes to extend the product to highly melioidosis-endemic countries in Asia, Australia, and other tropical countries where the disease is neglected. Dr. Narisara also welcomes investors to support the marketing and production of the rapid ICT for melioidosis.

THERAPEUTIC HUMAN MONOCLONAL ANTIBODY AGAINST DENGUE VIRUS

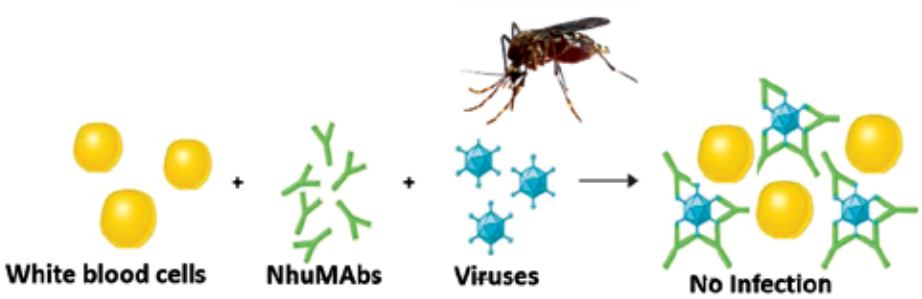
Innovator:
Assoc. Prof. Pongrama Ramasoota

Nearly 10 years ago, Dr. Pongrama and his team started human antibody research projects to treat dengue fever.

About 3.9 billion people live in dengue-endemic countries. Approximately 100 million dengue symptomatic dengue cases are recorded every year, with 30,000 people dying from severe dengue. Despite the serious threat dengue imposes upon endemic countries, no specific drug or therapeutic product is yet available against the dengue virus. Dr. Pongrama has sought to solve this problem by developing a therapeutic product against all dengue virus serotypes.

The year 2018 saw a groundbreaking achievement in innovative and translational research at the Center of Excellence for Antibody Research (CEAR) and the Faculty of Tropical Medicine, Mahidol University. Therapeutic human monoclonal antibodies against Dengue virus developed by Dr. Pongrama Ramasoota and Dr. Pannamthip Pitaksajjakul, with their CEAR team and Japanese collaborators, were licensed to Bharat Serums and Vaccines (BSV) Biosciences. BSV Biosciences is an international drug and vaccine company located in the USA and India.

The patented neutralizing human monoclonal antibody (NhuMAbs) has 96-100% killing activity against all serotypes of dengue in pre-clinical testing in mice and monkeys. It has since passed safety and toxicity tests, as well. To further drug development, a large amount of NhuMAbs is needed for clinical trials. Through the funding from National Research Council of Thailand, Dr. Pongrama started industrial-scale production of NhuMAbs by stable expressed Chinese hamster ovary (CHO) cells, under good manufacturing practices (GMP) conditions. The large amount of expressed NhuMAbs will subsequently be used for clinical trials. BSV Biosciences will provide financial support of 250 million Baht for the entire clinical-trial phases of product testing. BSV Biosciences will also pay milestone payments and royalty fees to Mahidol University.



Through the capacity of BSV Biosciences and its collaboration with CEAR, the license agreement aims to complete the last phase of clinical trials in 2023, with the main goal of reaching the global market as an FDA approved product in 2026, or earlier. BSV Biosciences will support the production and marketing of the therapeutic product.

Dr. Pongrama estimated that production costs will be 1,500 Baht per dose, and will sell in the market for 5,000 baht per dose. If 1% of 100 million dengue cases use the new drug, the product will generate 3 billion Baht in profit per year.

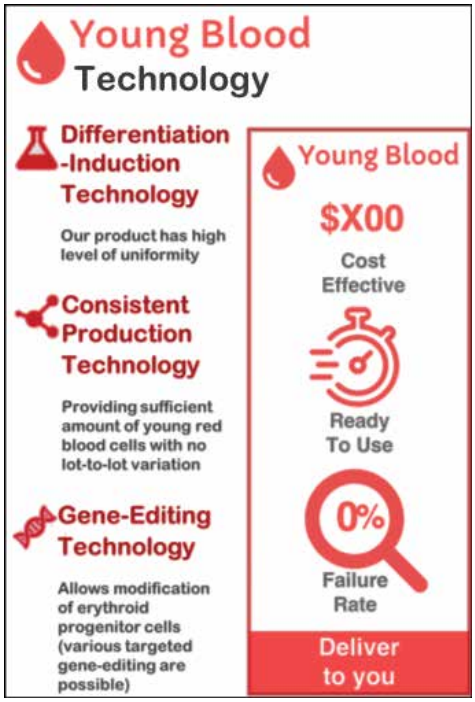
Dr. Pongrama wishes his product to be a hallmark of treatment against dengue fever in the future. He aims for the product to be accessible and available to people affected by dengue, especially in endemic countries.

YOUNG BLOOD

Innovator:
Dr. Wanlapa Roobsoong

Reticulocyte cells, or young red blood cells (RBC), are essential for continuous *in-vitro* culture of *P.vivax*. The *in-vitro* culture of *P.vivax* accelerates the development of drugs and vaccines against vivax malaria. Unfortunately, a stable supply of reticulocytes is difficult to obtain, as adult humans have only 2% reticulocytes in the blood circulation, while sourcing from the Red Cross or cord blood remains impractical and often provides variations in quality due to donor variations. In addition, reticulocytes obtained from these donors will need to undergo a further labor-intensive enrichment process before they can be used as a reagent, causing a delay in everyday work. More importantly, the stages of the reticulocytes obtained from these sources are too old for the parasite.

As a *vivax* researcher and user of reticulocytes, Dr. Wanlapa Roobsoong sees this challenge as an inspiration and opportunity to develop a product called *Young Blood,* a ready-to-use reticulocyte-like cell generated from immortalized erythroid progenitor. The use of regenerative medicine technology, such as induced pluripotent stem cell (iPS) technology, enables the production of identical, quality reticulocyte-like cells from a single cell source, providing a stable supply of the product. Aside from vivax malaria, Young Blood can also be used for other infectious and hematological diseases.



"Young blood" is a collaboration between the Mahidol Vivax Research Unit (MVRU), Faculty of Tropical Medicine, Mahidol University in Bangkok and MiCAN Technologies, in Japan. Given the product's usefulness and consumer value, Dr. Wanlapa and collaborators see a huge possibility for commercialization. Dr. Wanlapa describes the market space for their product as a "blue ocean", as there are no competitors in the market at present.

The Young Blood Company aims to sell at least 50 units for the first year and 100-150 units in the following year. In addition, the phenotype and quantity of *Young Blood* can be customized according to the customers' demands or research needs. In the near future, Dr. Wanlapa plans for the product to be widely accessible and marketed as a laboratory supply.

Dr. Wanlapa sees a huge potential for the success of this product in the global research marketplace, and hopes that "Young Blood" will help accelerate vaccine and drug development for vivax malaria.

RESEARCH TO IMPACT: INSTITUTE TRANSLATIONAL PARTNERSHIP PROGRAM

Dr. Maneerat Ekkapongpisit

Dr. Maneerat Ekkapongpisit is Translational Partnership Manager at Mahidol Oxford Tropical Medicine Research Unit (MORU) under the Wellcome Trust Institute Translational Partnership Program (iTPA). The program aims to close the gap between research and implementing interventions, and to build capacity and expertise for supporting early research translation that improves the health of people in low- and middle-income countries (LMICs).

Researchers encounter many barriers throughout the journey of research translation and innovation. Dr. Maneerat's mission is to help minimize these barriers, to accelerate the transition of research output to outcome and public-health impact. Outputs could be in the forms of preventive drugs, vaccines, point-of-care diagnostic tools, or operational science that will provide tangible and sustainable impacts on improving public health.

Dr. Maneerat develops the institute Translational Partnership Program (iTPA) platform, which includes a funding mechanism for innovative projects. This platform is different from other funding schemes in which the supports are not focused largely on financial outcomes, but rather on all stages of translational research development, e.g., identification of mentor and expertise needs, project proposal development, project business-model and strategy consultancies, partner identification, finding advisers in the field, and introducing potential collaborators and stakeholders.

In 2018, the iTPA program released funding for 6 projects (est. funding released about GBP 400,000). Several ideas and projects in the innovation portfolio will be further developed and receive additional funding to translate the research to health impact.

Dr. Maneerat is also a registered Thai Patent Agent, keen to see the potential of research as an intellectual-property asset. A patent is a key tool in translational research, as it provides intellectual property (IP) rights for an invention. An IP right attracts stakeholders, industry partners, and manufacturers, who are essential collaborators and another part of the jigsaw moving research to impact.

Dr. Maneerat finds the process of translational research exciting, especially when research outputs finally reach and benefit a community. Being involved in the process of translational research, Dr. Maneerat shares the same fulfillment as the researchers.

The main challenge of the work is mindset. Dr. Maneerat encourages researchers to think outside the box, find more collaborators, consider doing something that is needed and will be accepted by the people in a community, and something new that will improve the health of the people, in order to be successful translational research.

This mindset unlocks potential opportunities. This kind of mindset is the starting point to make the impossible possible.

With the same vision, the Institute Translational Partnership Program goal is achievable!

FACILITIES AND SERVICES

“Alongside the departments, centers, and collaborations, the Faculty has an important set of facilities and services for researchers, students and the general public. The following pages give more information on the work and achievements of –”

The Bangkok School of Tropical Medicine

The Hospital for Tropical Diseases

Central Equipment Unit (CEU)

Laboratory Animal Science Unit

Tropical Medicine Diagnostic Reference Laboratory (TMDR)

BANGKOK SCHOOL OF TROPICAL MEDICINE

2018 HIGHLIGHTS

Graduation rehearsal for FTM Ph.D., M.Sc. and DTM&H graduates for the academic year 2017

The Bangkok School of Tropical Medicine (BSTM) welcomed 50 new students in 2018, comprising 29 international students and 21 Thai students. The Graduate Diploma in Tropical Medicine and Hygiene (DTM&H) had the highest number of enrollees--17 international students from Austria, Bangladesh, Belgium, Cambodia, Italy, Japan, Malaysia, Myanmar, Netherlands, Somalia, and Sudan.

A total of 69 students graduated from the School in 2018; 21 from the PhD (Tropical Medicine) Program, 15 from the DTM&H Program, 14 from the M.Sc. (Tropical Medicine) Program, 12 from the M.C.T.M. Program, 4 from the MSc (Biomedical and Health Informatics; BHI) Program, and 3 from the MSc (School Health) Program.

SCHOLARSHIPS

In 2018, more than 30 international and local students were supported to continue their studies at the School through different grants provided by the Faculty and several international institutions, including the Dr. Sylvia Meek FTM Scholarship for Entomology 2018,

Dr. James Tibenderana, Global Technical Director of Malaria Consortium, awards Mrs. Shobiechah Aldillah Wulandhari the *Dr. Sylvia Meek FTM Scholarship for Entomology 2018*

which was awarded to Mrs. Shobiechah Aldillah Wulandhari from Indonesia, and Mr. Kiattiyos Ruengthamchariya, from Thailand.

This scholarship was granted as an honor to the late Dr. Sylvia Meek, former Malaria Consortium Technical Director, who devoted her life to the field of medical entomology.

Dr. James Tibenderana, Global Technical Director of the Malaria Consortium, awards Mr. Kiattiyos Ruengthamchariya the Dr. Sylvia Meek FTM Scholarship for Entomology 2018

ENVIRONMENTALLY FRIENDLY CAMPUS

The School is moving to BSTM Automation, where all information, including thesis and request forms which are available online- moving to a paperless system by digitizing documents and papers. Automation will also be a support to the Faculty's TM Green campaign, which aims to develop an environmentally friendly campus. In 2018, BSTM won the Gold Save Energy Award from the Energy Conservation and Environment Committee, Faculty of Tropical Medicine, Mahidol University.

INTERNATIONAL COLLABORATION

A Memorandum of Understanding (MOU) between the Faculty of Tropical Medicine, Mahidol University and the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Indonesia, was signed in 2018. The student exchange program, starting in 2019, will allow up to 2 exchange students from each university per academic year to take their elective courses for at least 4 weeks.

Furthermore, the Faculty's student exchange agreement with the Faculty of Medicine Universitas Airlangga, Indonesia will be implemented in 2019.

OUTCOME-BASED EDUCATION

The Outcome-Based Education (OBE) curriculum, approved by Mahidol University Council for the first time, was implemented in 2018. The newly OBE-approved programs are the Graduate Diploma in Tropical Medicine and Hygiene, Master of Clinical Tropical Medicine, M.Sc. in Tropical Medicine, and Ph.D. in Tropical Medicine.

BSTM is committed to transforming all the programs into OBE curricula, while simultaneously meeting the criteria set by ASEAN University Network Quality Assurance (AUNQA), a network that promotes and improves quality assurance in higher-education institutions. The Master of Clinical Tropical Medicine will be the first FTM Program being assessed, in early 2019.

ACTIVITIES

The Wai Khru & Bai Sri Su Kwan ceremonies for the academic year 2018 were held on 6 September 2018. During the ceremony, a number of awards and recognitions were presented, including the Tranakchit Harinasuta Award and the 2017-2018 Student Activities Award.

Students pay respects to their teachers to express their gratitude during the Bai Sri Su Kwan Ceremony and Wai Khru Ceremony

THE HOSPITAL FOR TROPICAL DISEASES

2018 HIGHLIGHTS

The Hospital for Tropical Diseases has operated since 1961 under the administration of the Faculty of Tropical Medicine, Mahidol University. The facility specializes in Tropical Medicine and Travel Medicine and has a human resource complement of 31 medical doctors, 83 nurses and 81 nurse assistants. It has a 106-bed capacity and is a well-equipped, modern facility. Each year, the hospital provides medical services to over 30,000 outpatient visits and on average more than 2,000 inpatients. The HTD is a specialized Tropical Medicine hospital that provides comprehensive care including the diagnosis, laboratory testing, and treatment of diseases endemic to the Asian region, in particular. All of its treatment staff are highly specialized in tropical medicine and certified in various other medical specialties. Apart from tropical medicine, they provide diagnosis and treatment for various general medical problems, such as diabetes mellitus, hypertension, hyperlipidemia, kidney disease, liver disease, etc. The Hospital for Tropical Diseases maintains its reputations as one of Thailand's high-quality healthcare providers, particularly well-known for its high quality of care, safety, and data management. The Hospital has continued to develop its services and improve its quality of care to become a national center of expertise in tropical diseases, such as dengue, malaria, parasitic infections, and other infectious diseases. As a result of its stellar reputation and improved visibility, patients from around the country are consistently being referred to specialists at the hospital, with patient numbers increasing steadily each year. The HTD has distinguished itself from other hospitals in Bangkok through the development of niche areas and by providing timely treatment services. Short patient waiting times are a special feature of the hospital. The average wait time is thirty minutes compared with an average wait time of two hours for comparable medical services provided at most other hospitals in the surrounding area. The Hospital for Tropical Diseases also often provides outside support for other hospitals with specialist services, such as diagnostic tests and analysis. In addition, the Hospital has always prided itself on working closely with affiliated researchers and other external partnerships that help to advance clinical drug trials and other studies of significance to the field of tropical medicine. Such collaborations, with some the world's leading Tropical Medicine researchers working in the Faculty's departments, will undoubtedly result in important public-health benefits and innovations.

HTD STATISTICS

Currently, the HTD treats mostly non-communicable diseases - cardiovascular diseases (such as hypertension), cancer, chronic respiratory diseases (such as chronic obstructed pulmonary disease), and diabetes mellitus. In total, the Hospital provided treatment for over 35,000 cases in 2018, with the vast majority being outpatients. Hypertension was the most treated condition, at almost 10,000 individual cases, followed by hyperlipidemia and dermatitis being the top three ailments managed on an outpatient basis. Due in large part to the Hospital's reputation for dengue fever treatment, dengue was the most treated inpatient condition, with almost 1,000 cases. Diarrhea and pneumonia followed dengue as the most treated inpatient cases.

THE THAI TRAVEL CLINIC

In addition to tropical diseases, the Hospital has positioned itself as a main center for travel medicine in Bangkok with the Hospital's Travel Clinic acting as a hub for travel medicine in Bangkok. Local and international visitors visit the Thai Travel Clinic for a range of services, including vaccinations, health certificates, and pre- and post-travel health advice. Many national and international travelers

visit the hospital for consultation of travel-related diseases, especially for preventive and diagnostic matters. Because it links closely with the Hospital for Tropical Diseases, the facility can also provide comprehensive medical care on both inpatient and outpatient basis. Since the Travel Clinic falls under the Faculty of Tropical Medicine, it also plays major roles in education and research, as staff are consistently invited to lecture in various TropMed academic and training courses while also collaborating with many academic institutes globally. Its research activities fall under the administration of the Travel Medicine Research Unit, which is responsible for three major areas of travel medicine - services, education, and research. Over 25 different vaccines are available at the clinic, including full certification in yellow fever vaccine administration, which has very limited authorization in Thailand. Every year, due to online promotion and general word of mouth, the Travel Clinic has been increasing in popularity. Also contributing to its excellent reputation is its online appointment system, which makes the scheduling process very convenient for arriving customers; it can be found at the domain www.thaitravelclinic.com which makes the service easy to remember and readily accessible to the public. Last year saw a major expansion of the Travel Clinic facility to accommodate increased public demand for comprehensive services provided to a growing customer base.

HM King Maha Vajiralongkorn Bodindradebayavarangkun comfering the Dusdi Mala Award Upon Prof. Polrat Wilairatana

AWARDS

As testament to the very capable leadership of the Hospital for Tropical Diseases, Prof. Polrat Wilairatana received the "Dushdi Mala Medal for Great Eminence in Medicine, 2018". The award is in recognition of his outstanding work in malaria research, which has contributed significantly to substantial reductions in the morbidity and mortality of malaria patients in Thailand. The Dushdi Mala Medal is a civil decoration in the honours system of Thailand, and the highest-ranked medal among those granted for services to the state. Historically, recipients of the Dushdi Mala Medal have had widespread positive impacts on vast numbers of people or have introduced beneficial innovations to the country. The medal was presented to Prof. Polrat by HM King Maha Vajiralongkorn Bodindradebayavarangkun this year in a private royal ceremony.

Thai Travel Clinic online appointment system

CENTRAL EQUIPMENT UNIT (CEU)

A student uses equipment in the Unit

The Unit moved to a digital-based system where all activities such as registration, reservation, request, and other documentation are now being done online. This paperless system will accelerate the process interface between the Unit and users. Unit machines and equipment were relocated to the Bangkok Hospital for Tropical Diseases in the Rajanagarindra Building.

It is hoped that an advanced flow cytometry apparatus will be acquired for the Unit in the following years. The machine is very efficient for emerging- and re-emerging-disease research, especially immunological research.

The Unit is preparing for the opening of the BSL3 laboratory. A BSL3 laboratory typically includes work on microbes that are either indigenous or exotic, and can cause serious or potentially lethal disease through inhalation. This facility is capable of tackling the most virulent, complex, and difficult viruses and pathogens that can cause serious threats to global health, increasing the scope and impact of tropical-medicine research in the Faculty.

The Unit is preparing training for students and staff on how to use the equipment proficiently and responsibly. The goal of the training is to introduce a standardized protocol and instill an idea that 'users are owners' and should provide the outmost care for the equipment. The training is planned to be held annually.

LABORATORY ANIMAL SCIENCE UNIT (FTM-LAU)

The Unit served 14 research projects for the departments and units of the Faculty and other faculties of Mahidol University, including the Faculty of Public Health, Faculty of Dentistry, and Faculty of Science.

A total of 573 animals, comprising mice, rats, and guinea pigs, were used in 2018. About 12-15 projects are conducted in FTM-LAU annually. Various kinds of research projects have been performed, including those related to parasitology, immunology, non-infectious diseases, nutrition, dental research, and many others.

Walailak University visited and observed the Laboratory Animal Science Unit and animal facilities on 16 July 2018.

Ms. Thanyaluk Krasae, staff of the Unit, shows the animal facilities to visitors from Walailak University.

FTM-LAU will continue to improve the quality of its animal facilities and services, and develop standard operating procedures (SOPs) for effective services, to promote the welfare of laboratory animals, and support Faculty research.

TROPICAL MEDICINE DIAGNOSTIC REFERENCE LABORATORY (TMDR)

TMDR joined the "Enhancement of Safety Practice of Research Laboratory in Thailand: ESPReL" project in 2018. The ESPReL program aims to enhance the procedure of laboratory safety in research settings in Thailand. TMDR was one of the successful laboratories to complete the program and was recognized nationally as a model laboratory for meeting all the program's extensive checklist as a safe research facility.

TMDR received numerous awards and recognition from Mahidol University and the National Research Council of Thailand (NRCT).

TMDR was chosen as the representative laboratory from the Faculty of Tropical Medicine to join the ESPReL program. Consequently, with the impressive performance of TMDR, it was chosen to be the representative laboratory from Mahidol University and won awards from NRCT nationwide forums.

The award received from NRCT

SPECIAL FOCUS

OFFICE OF RESEARCH INTEGRITY AND COMPLIANCE

2018 HIGHLIGHTS

The Office of Research Integrity and Compliance (ORIC) is part of the Office of Research Services (ORS), headed by Mrs. Pornpimon Adams. The role of ORIC is to oversee and direct the research integrity activities of the Faculty of Tropical Medicine, Mahidol University. Its main focus is to foster the responsible conduct of research, to ensure that research performed in the FTM system is conducted safely, ethically, and legally.

ORIC was established to perform the following functions; provide clear policies on the manner in which FTM research should be conducted, facilitate high standards of research practice through regular training, compliance checks, and the promotion of a culture of research integrity, and compliance with all applicable regulations, laws, and Mahidol University policies.

TRAINING, MEETINGS, AND WORKSHOPS

ORIC organized "Biosafety Training for FTM Graduate Students: Principle and Practice" 31 January 2018. While the Training Course on Biosafety: "Train the Trainer" was held at FTM by Mahidol University-Institutional Biosafety Committee (IBC), 22-23 March 2018.

ORIC is actively participating in national and international meetings and workshops on research integrity and relevant practices.

ORIC participated in the Advanced Research Ethics Training Course at Amari Watergate Hotel, presented an oral presentation at the event "Research Capacity Building for TropMed Researchers" in the topic "Research Integrity: Practices" at Khao Yai, Nakhon Ratchasima Province, 23-24 July and 17-19 September 2018, respectively.

On 28 November 2018, ORIC staff attended the forum "Academic Alliance in Research Integrity", organized by the National Science and Technology Development Agency (NSTDA), at the Century Park Hotel, in Bangkok.

On 26-28 February 2018, ORIC presented an oral presentation at the Asia Pacific Research Integrity Network Meeting 2018 in Taipei, Taiwan. ORIC participated in APEC Guiding Principles for Research Integrity, Consensus Workshop in Tokyo, Japan, 20-21 November 2018.

ACTIVITIES AND SERVICES

Chemical waste collection is one of the services of ORIC. In January and July 2018, they collected 991.8 kg and 490.9 kg chemical waste, respectively.

On 23 May 2018, ORIC distributed biological spill kits to 19 FTM departments and centers.

In compliance with the "Pathogens and Animal Toxins Act", ORIC facilitated FTM researchers for their pathogens registrations, which is being renewed annually.

CHALLENGES

Although the subject "research integrity" is regarded as fundamental, fostering its awareness may have received understated attention. ORIC was created to facilitate awareness of this issue. Moreover, in these days of disruptive technology, ORIC must keep FTM staff up to date on research compliance issues.

JOINT INTERNATIONAL TROPICAL MEDICINE MEETING 2018 (JITMM2018)

Prof. Ric Price delivers his keynote speech entitled, "The safe and effective radical cure of malaria" during the JITMM2018 Opening Ceremony

The annual Joint International Tropical Medicine Meeting (JITMM), organized by the Faculty of Tropical Medicine, Mahidol University and the Parasitology and Tropical Medicine Association of Thailand (PTAT) was held 12-14 December 2018 at the Amari Watergate Hotel, in Bangkok, Thailand.

Under the theme "Innovation, Translation, and Impact in Tropical Medicine", JITMM2018 featured a number of symposia and presentations on the recent advancements and developments in tropical medicine research. The Meeting attracted over 700 participants from more than 30 countries all around the world, including international authorities in the field of tropical medicine.

Among the Keynote Speakers were Prof. Ric Price of the Menzies School of Health Research and Oxford University, who has just completed the largest ever multi-continent trial of the radical cure of *P. vivax*, and Prof. Donald McManus of QIMR Berghofer Medical Research Institute, who was awarded the 2018 Sornchai Looaresuwan Medal for his distinguished and sustained contributions to the field of eliminating parasitic helminth diseases.

JITMM2018, with support from the Wellcome Trust, has enabled 28 early-career researchers from LMICs to attend the conference and present their research on a global stage.

JITMM2018 continued to achieve its aims, including providing a platform for researchers, both local and international, to introduce their work and build relationships with people who share the same research interests.

Assoc. Prof. Pratap Singhasivanon, Chair of the Organizing Committee, announced during his Closing Remarks that JITMM will be postponed in 2019. This is to allow preparation for the 20th International Congress for Tropical Medicine and Malaria (ICTMM2020), which will be held in Bangkok, Thailand 20-24 September 2020. He also shared the news that the following JITMM will be concurrently held with ICTMM2020 and enthusiastically invited everyone to attend such an oustanding event.

JITMM2018 in numbers					
Participants	717	Nationalities	43	Chairpersons and speakers	111
Posters	120	Sessions	39	Travel Awards	28

20th INTERNATIONAL CONGRESS FOR TROPICAL MEDICINE AND MALARIA (ICTMM2020)

The 20th International Congress for Tropical Medicine and Malaria (ICTMM) will be held 20-24 September 2020 at the Bangkok International Trade and Exhibition Centre (BITEC), Thailand. ICTMM is one of the largest tropical medicine conferences in the world, bringing together thousands of researchers, experts, policy-makers, stakeholders, and international authorities in the field of tropical medicine and malaria.

ICTMM2020 Highlights

- The Congress will cover topics and updates on tropical medicine, including malaria, infectious diseases, non-communicable diseases, neglected diseases, drug resistance, parasitology, zoonoses, travel medicine, and other public-health issues.
- More than 3000 participants from across the globe will attend
- The program will include international session speakers, oral presentations, exhibitions, and social events.

Why you should join us

- Get involved in the latest developments and discussions on tropical medicine and malaria
- Present your research on a global stage
- Meet world-renowned experts, researchers, and luminaries in tropical medicine and other related disciplines
- Make new friends, find a mentor
- Strengthen and widen your professional network
- Find potential collaborators
- Experience Thailand's exquisite cuisine and warm hospitality
- Travel to Bangkok, one of the world's top tourist destinations

Who should attend

Students, doctors, scientists, experts, researchers, educators, academicians, physicians, science communicators, healthcare practitioners, product and brand promoters, and all interested in tropical medicine and public-health are welcome to attend

The Organizers

The Faculty of Tropical Medicine, Mahidol University is the major tropical medicine research hub in Southeast Asia. The Parasitology and Tropical Medicine Association of Thailand (PTAT) is the lead supporter and promoter of study and research in parasitology and tropical medicine in Thailand. Both have organized and co-organized several national and international conferences over the years, including the annual Joint International Tropical Medicine Meeting (JITMM).

The ICTMM2020 Bangkok Organizing Committee promoted ICTMM2020 at the 14th International Congress of Parasitology (ICOPA), 19-24 August 2018, Daegu, Korea

AWARDS

DATE	AWARDEE	AWARDS	FROM
05 January 2018	Mallika Imwong	Outstanding Alumni Award 2017	Graduate School Alumni Association Mahidol University
02 February 2018	Mallika Imwong	National Research Council Award 2017	The National Research Council of Thailand (NCRT)
02 March 2018	Saranath Lawpoolsri Niyom	Role Model Teacher Award 2017	Mahidol University Faculty Senate
09 March 2018	Supachai Topanurak	Science and Technology Award in the field of Agriculture and Biology	Thailand Toray Science Foundation
17 March 2018	Dumrongkiet Arthan	Outstanding Student Activity Advisor 2017	College Alumni Association, Mahidol University
19 March 2018	Pratap Singhasivanon	National Outstanding Preventive Medicine Award in the field of Epidemiology 2017	The Association of Preventive Medicine of Thailand
19 March 2018	Songsak Petmitr	Honorable Plaque	Faculty of Medicine, Thammasat University
22 May 2018	Saengduen Moonsom	Honorary certificate for being a main contributor to the campaign: "Build community participation in prevention and control of rabies outbreaks"	Department of Disease Control, Ministry of Public Health
09 August 2018	Kraichat Tantrakarnapa	Outstanding Contribution Award for Environmental Health of Asia	Korean Society of Environmental Health
14 August 2018	Sasithon Pukrittayakamee	Appointed Fellow of Royal Society of Thailand, Academy of Science, Medicine and Dentistry Branch, Tropical Medicine field	Royal Society of Thailand

DATE	AWARDEE	AWARDS	FROM
13 - 15 Sept 2018	Narisara Chantratita	Gold Medal Award and Outstanding Award for the invention of Rapid Immunochromatography test for melioidosis	10th International Exhibition of Inventions and 3rd World Invention & Innovation Forum
01 October 2018	Sasithon Pukrittayakamee	Distinguished Professor in Tropical Medicine	Faculty of Tropical Medicine, Mahidol University
02 November 2018	Saengduen Moonsom	Named "Educational Developer"	US Agency for International Development (USAID) and Thailand International Cooperation Agency (TICA)
23 November 2018	Athit Phetrak	Outstanding Oral Presentation Award	3rd Environmental and Natural Resources International Conference Global Development with Environmental Sustainability (Chonburi, Thailand)
06 December 2018	Dorn Watthanakulpanich	Role Model Teacher Award 2018	Mahidol University Faculty Senate
21 December 2018	Narisara Chantratita	Honorary certificate for Thai researchers who presented their inventions internationally.	National Research Council of Thailand (NRCT)

ACTIVITY




ข่าวสังคม
หนังสือพิมพ์แนวหน้า
25 กรกฎาคม 2539


outlook
Under the microscope


สยามโพสต์
กรงสนพระทัยด้านเวชศาสตร์เขตร้อน