5TH ASIA DENGUE SUMMIT 2022

ROLL BACK DENGUE

13 – 15 JUNE 2022 • SINGAPORE

PROGRAMME BOOK

Co-convenors:

ADVA Asia Dengue Voice & Action Group

Fondation Mérieux

gdac Global Dengue+Aedes-Transmitted Diseases Consortium

Tropical Medicine and Public Health Network TROPMED SEAMEO

The International Society for Neglected Tropical Diseases

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www.asiadenguesummit.org

Cell-mediated Response and Dengue

14 June 2022, Tuesday

12:00 hours – 13:00 hours, GMT +8

Faculty

Dr. Gonzalo Perez
Senior Medical Director,
Global Medical Lead,
Takeda Vaccines

Dr. Laura Rivino
Senior Lecturer, University of Bristol, UK
Adjunct Asst. Professor,
Duke-NUS Medical School, Singapore

Dr. Vianney Tricou
Medical Director,
Takeda Vaccines

Agenda

12:00 hours
Welcome and Introduction
Dr. Gonzalo Perez

12:05 hours
Understanding the Human T-cell Response to Dengue Virus
Dr. Laura Rivino

12:25 hours
Immunocharacterization of TAK-003
Dr. Vianney Tricou

12:45 hours
Q&A
All

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WELCOME MESSAGE

Dear Colleagues,

On behalf of the Asia Dengue Summit Organising Committee, we are pleased to invite you to the 5th Asia Dengue Summit to be held from 13th-15th June 2022 in Singapore.

Riding on the overwhelming success of the past four Asia Dengue Summits, the organising committee is geared for the 5th Asia Dengue Summit, this time themed as “Roll Back Dengue”. The summit will once again provide a unique opportunity for everyone in the dengue community (clinicians, researchers, government public health leaders and policymakers) to come together to exchange ideas, updates and achievements on dengue management strategies for the region.

The 5th Asia Dengue Summit is co-convened by Asia Dengue Voice and Action (ADVA), Global Dengue and Aedes transmitted Diseases Consortium (GDAC), Southeast Asian Ministers of Education Tropical Medicine and Public Health Network (SEAMEO TROPMED), and the Fondation Mérieux (FMx).

Along with dengue experts from academies and research institutions, representatives from the Ministries of Health, the regional and global World Health Organization (WHO), ADVA, SEAMEO TROPMED, GDAC, the International Vaccine Institute (IVI), the FMx and others will participate to provide a broad overview of the current status of dengue and its management across Asia.

Dengue is not only an endemic disease in the region – rising population densities and climate change are also interlocking to make Asia epicenters for the world’s largest dengue fever outbreaks. In the face of these regional threats, being ever-vigilant with ready responses to dengue outbreaks are every Asian country’s key to lowering fatality rates. Additionally, even as curative action coupled with vector control remain the backbone of dengue control strategies, dengue vaccination should be integrated into dengue control programs in Asia in the longer term. As an independent organization in Asia, it is hoped that ADVA can guide the introduction and use of dengue vaccines to the region.

Singapore, the host country for the 5th Asian Dengue Summit, has like its neighbours been battling a sharp rising trend in domestic dengue infections over the last two years. Therefore, this summit will be an opportunity for the city-state to showcase its dengue-fighting efforts, as well as share the results of any novel dengue-control strategies to date.

To this end, the 5th ADS features a scientific programme that has been updated to reflect the region’s rising awareness of and sharpened focus on dengue. Participants can look forward to engaging speakers and invigorating discussions on key topics such as the latest dengue epidemiology research from Asia, updates on dengue case classifications, diagnosis, infection treatment and vaccine trials; the current state of vector control and other interventions; proposed modifications to vaccination guidelines, overcoming vaccine hesitancy, and more.

To sum it all up, the 5th Asia Dengue Summit will serve as a platform for dengue experts from across the region (and worldwide) to discuss the issues that surround dengue disease management and propose strategies that can enhance dengue control. Such a wide representation of key stakeholders will help throw light on the burden of dengue, its management, new vector control strategies and successful vaccine introduction across the region.

The local organizing committee is working relentlessly to make this summit a fruitful platform of learning and collaboration. I urge you to come and join us in Singapore and take home with you valuable insights on dengue management and the many wonderful sights, sounds and experiences from this scenic country!

Warmest Regards,

Prof Ooi Eng Eong
Organizing Chairperson
5th Asia Dengue Summit

Prof Zulkifli Ismail
Co-Chairperson
Asia Dengue Voice and Action Group (ADVA) Chairperson

Assoc Prof Daniel YT Goh
Co-Chairperson

ABOUT US

The Asia Dengue Voice & Action Group (ADVA) was officially set up in 2013 with a mission to identify opportunities to make practical recommendations in dengue-related areas such as improving surveillance and laboratory capacity for dengue disease confirmation with other relevant dengue initiatives, including V2V (vaccine to vaccination) and the Dengue Vaccine Initiative.
ADVA advocates for a collaborative approach to sharing surveillance data and relevant information to ensure the success of dengue prevention through vaccination across regions. ADVA also reinforces the importance of a united front against dengue, and presents a collaborative model for joint effort in the region to prevent the disease through the introduction and implementation of dengue vaccination.
The group has formulated recommendations with an ultimate aim of translating the science of dengue vaccination into messages for policy makers, general public and health care workers.

The Global Dengue & Aedes-Transmitted Diseases Consortium (GDAC) is a consortium composed of the Partnership for Dengue Control (PDC), the International Vaccine Institute (IVI), the International Vaccine Access Center (IVAC) at the Johns Hopkins Bloomberg School of Public Health and the Sabin Vaccine Institute. The World Health Organization advises and collaborates with GDAC.

The Southeast Asian Ministers of Education Organization (SEAMEO) is a regional intergovernmental organization established in 1965 among governments of Southeast Asian countries to promote regional cooperation in education, science and culture in the region.

Fondation Mérieux's mission is to fight the infectious diseases that affect vulnerable populations in developing countries, especially mothers and children, by building local capacities. They work in over 20 countries worldwide, in regions prone to infectious outbreaks, and mount their own projects, working closely with local and international partners.

The ISNTD is an independent organisation providing a multidisciplinary global platform to an international network of individuals working in the fields of Neglected Tropical Diseases, diseases of poverty and global development. The aim of the ISNTD is to focus on and highlight the research and programmes of colleagues and organisations worldwide, to ultimately have an impact on the health and prosperity of the world's poorest and most vulnerable, while sharing the goal of reaching sustainable healthcare provision & poverty reduction in the developing world.
The ISNTD believes that this goal cannot be achieved without strengthening the ties between all the parties already involved in NTD alleviation and addressing the socio-ecological and socio-political context of NTDs, in order to achieve not only the cure but also the prevention of NTDs with true and sustainable local leadership.

COMMITTEE

ORGANISING CO-CHAIRS:

Prof Ooi Eng Eong
Prof Zulkifli Ismail
Assoc.Prof Daniel Y.T Goh

ADVA STEERING COMMITTEE:

Prof Usa Thisyakorn
Prof Sutee Yoksan
Dr Maria Rosario Capeding
Prof Sri Rezeki Hadinegoro
Prof Terapong Tantawichien

ADVA INTERNATIONAL ADVISORS:

Prof Duane Gubler
Prof Tikki Pang
Prof Lulu Bravo

Johnson & Johnson

Advancing breakthrough science in the global fight against dengue

The Global Public Health team at Johnson & Johnson is advancing breakthrough science against dengue, building on our longstanding commitment to accelerate solutions for neglected tropical diseases with innovation and collaboration.

Johnson & Johnson is committed to accelerating solutions to combat the significant growing global health threat of dengue, especially as the climate continues to change and more communities are put at risk.

Our work against dengue is just one part of our larger, decades-long commitment to address the burden of neglected tropical diseases (NTDs). Beyond our work on dengue, we are also investing in R&D for other NTDs, including leprosy, and are continuing to donate our medicine for intestinal worms around the world.

JOIN US THIS WEEK

On Wednesday, June 15th, attend the Johnson & Johnson lunch symposium, *The Role of Antivirals in Dengue Prevention.*

OUR EFFORTS

2007

The Janssen dengue compound discovery program started in 2007 to address the unmet medical need for treatment and prevention options for dengue.

2013

Janssen entered into an agreement with Wellcome Trust, the KU Leuven Rega Institute and the Centre for Drug Design and Discovery (CD3) to identify a compound series capable of inhibiting the dengue virus in lab-grown cells and animals.

2021

In 2021, Janssen announced the completion of a Phase 1, first-in-human clinical study, and are now evaluating the compound in Phase 2a clinical studies.

Learn more at jnj.com/NTDs

AGENDA

Date: **Monday 13th – Wednesday 15th June 2022**
Venue: **Orchard Hotel Ballroom, Level 3, Singapore**

DAY 1 - MONDAY 13th JUNE 2022

TIME	PROGRAMME	SPEAKERS
0800 – 0830	Log in to Zoom Webinar Onsite Registration	
0830 – 0845	Welcome & Opening Remarks	Ooi Eng Eong
	Moderator: Ooi Eng Eong	
0845 – 0915	**Keynote Address** The Worlds Mosquito Program's Wolbachia Method and prospects for dengue elimination	Cameron Simmons
0915 – 1000	**Symposium 1** Dengue – Clinical Insights	Bridget Wills Tineke Cantaert
1000 – 1030	Tea Break and Posters	
	Moderator: Cameron Simmons	
1030 – 1215	**Symposium 2** Dengue Pathogenesis – Inflammation	Paul Young Sylvie Alonso Subhash Vasudevan Luo Dahai
	Moderator: Neelika Malavige	
1215 – 1330	**Lunch Symposium** by Fujifilm	
	Evaluation of FUJIFILM SILVAMP as the New Rapid Diagnostics Test for Onsite Detection of Dengue NS1 Antigen in Patients with Acute Febrile illness	Sutee Yoksan
	FUJIFILM SILVAMP Dengue NS1 Antigen RDT Innovation for Diagnostics and Pathway to Improve Patient Management	Naoto Kimura
	Moderator: Panisadee Avirutnan	
1330 – 1500	**Symposium 3** Dengue Pathogenesis – Virus-Host Interactions	Ooi Yaw Shin Setoh Yin Xiang Milly Choy Kitty Chan Allyson Choi
1500 – 1530	Tea Break and Posters	
	Moderator: Neelika Malavige	
1530 – 1700	**Symposium 4** Dengue Virology and Immunology	Sheemei Lok Sansanee Noisakran Chin Wei Xin Andrew Teo
	Moderator: Kamran Rafiq	
1730 – 1900	**ISNTD Webinar** - Digital Diagnostics for Dengue	Nick Moser
Close of Day 1		

AGENDA

DAY 2 - TUESDAY 14th JUNE 2022

TIME	PROGRAMME	SPEAKERS
0800 – 0820	Log in to Zoom Webinar Onsite Registration	
0820 – 0830	Welcome Back	Ooi Eng Eong
	Moderator: Tikki Pang	
0830 – 1030	**Symposium 5** Dengue Vaccines	Vianney Tricou Louis Macareo Stephen Thomas
	Panel Discussion on Rolling out Dengue Vaccines in Asia	Tikki Pang Louis Macareo Vianney Tricou Stephen Thomas Rosario Capeding Lulu Bravo Olivia Chua
1030 – 1045	Tea Break	
	Moderator: Sansanee Noisakran	
1045 – 1215	**Symposium 6** New Tools for Studying Dengue Vaccines and Immunity	Chan Kuan Rong Adam Waickman Vanessa Goh An Qi Ngoh Satoru Watanabe
1215 – 1330	**Lunch Symposium** by Takeda Cell Mediated Response and Dengue	
	Welcome and Introductions	Gonzalo Perez
	Understanding the Human T-cell Response to Dengue Virus	Laura Rivino
	Immunocharacterization of TAK-003	Vianney Tricou
	Q&A	
	Moderator: Stephen Thomas	
1330 – 1500	**Symposium 7** Dengue Antivirals	Tine De Marez Isabela Ribeiro Alvin Tan Colin Cheng Thomas Loy
1500 – 1520	Tea Break	
	Moderator: Paul Young	
1520 – 1700	**Symposium 8** Developments in Therapeutics and Vaccines	Panisadee Avirutnan Ashley St John Neelika Malavige Amanda Bifani
	Moderator: Kamran Rafiq	
1800 – 1930	**ISNTD Webinar** - Dengue and Climate Change	Rachel Lowe Sophie Lee Raquel Lana Kim van Daleen
Close of Day 2		

AGENDA

DAY 3 - WEDNESDAY 15th JUNE 2022

TIME	PROGRAMME	SPEAKERS
0800 – 0820	Log in to Zoom Webinar Onsite Registration	
0820 – 0830	Welcome Back & Introduction to WDD	Daniel Goh
	Moderator: Daniel Goh	
0830 – 0850	**Keynote Address**	Minister Grace Fu
0850 – 0920	**A New Chapter in 6 Decades of Mosquito Control in Singapore**	Ng Lee Ching
0920 – 0940	Tea Break	
	Moderator: Bridget Wills	
0940 – 1040	**Symposium 9** Dengue Epidemiology	Hasitha Tissera Tedjo Sasmono Moi Meng Ling
	Moderator: Gabriela Paz-Bailey	
1040 – 1215	**Symposium 10** Dengue Epidemiology and New Challenges	Shirin Kalimuddin Somia Iqtadar Crisostomo Maria Vinna Leo Yee Sin
1215 – 1330	**Lunch Symposium** by Johnson & Johnson Role of Antivirals in Dengue Prevention	Maria Rose Capeding Cameron Simmons Martin Hibberd Ooi Eng Eong Marnix Van Loock
	Moderator: Jody Hobson-Peters	
1330 – 1500	**Symposium 11** Vector Control and Surveillance	Martin Hibberd Dafydd Green Tanamas Siriphanitchakorn Ng Youming
1500 – 1520	Tea Break	
	Moderator: Ng Lee Ching	
1520 – 1620	**Symposium 12** Vector Biology and Ecology	Eggi Arguni Jody Hobson-Peters Gabriela Paz-Bailey
	Moderator: Kamran Rafiq	
1620 – 1645	**In Conversation: Integrating the Sciences for Dengue Prevention**	Duane Gubler
1645 – 1700	Closing Address	Ooi Eng Eong Daniel Goh
Close of 5th Asia Dengue Summit 2022		

There is much to be done in healthcare, and when it comes to COVID-19, we are leveraging our resources and expertise in ways that can make a real difference. For example, we're equipping front-line workers with our state-of-the-art, mobile X-ray and point-of-care ultrasound systems to facilitate diagnoses and help prevent spread of infection. In our further contribution to ending the pandemic, we're accelerating clinical trials of our antiviral drug. We are also expanding our contract bioprocessing facilities and strategically making partnerships to help ensure, through our manufacturing capabilities, a steady supply of vital medications and vaccines are available for people around the world. As long as there are healthcare needs to be met, we will NEVER STOP.

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ORGANISING CO-CHAIRS

PROF OOI ENG EONG

BMBS, PhD, FRCPath

Professor and Deputy Director,
Programme in Emerging Infectious Diseases, Duke-NUS Medical School
Singapore

Prof. Ooi trained in medicine at the University of Nottingham and conducted his doctoral studies on molecular epidemiology at the National University of Singapore. He has been working in the field of dengue for 20 years and his research interest spans dengue epidemiology to molecular pathogenesis of arboviral diseases. His laboratory interfaces clinical studies with virology and immunology to address research questions. He has published in journals such as The Lancet, Science and Nature Medicine. He is a three-time recipient of the Clinician-Scientist (Senior Investigator) Award by the National Medical Research Council of Singapore.

PROF ZULKIFLI ISMAIL

Clinical Professor,
KPJ Healthcare University College,
Malaysia

Prof. Zulkifli Ismail is a consultant paediatrician and paediatric cardiologist at a private hospital and Clinical Professor at the KPJ Healthcare University College. He was formerly a professor of paediatrics and paediatric cardiology in the Universiti Kebangsaan Malaysia (UKM). Dr. Ismail has served as the head of the paediatric department and the director of Hospital Universiti Kebangsaan Malaysia (HUKM) as well as the medical director of its private wing, UKM Specialist Centre.

Prof. Zulkifli also served as a past president of the Malaysian Paediatric Association (MPA) and is currently the editor of Berita MPA, a quarterly newsletter publication distributed to fellow members of the Association. He chairs the Positive Parenting Management Committee (www.mypositiveparenting.org) and serves as the chief editor of the Positive Parenting Guide, a quarterly publication aimed to equip Malaysian parents with reliable and practical local information on maternal, child and family care since 2002. He is the Technical Chairman of Immunise4Life (www.ifl.my), a vaccination advocacy programme of the Ministry of Health Malaysia.

Prof. Zulkifli is currently the president of the Asia Pacific Paediatric Association (APPA) and current chairman of the Asian Strategic Alliance for Pneumococcal disease prevention (ASAP). He also serves as a board member of the National Population and Family Development Board (LPPKN), a member of the Ministry of Health Unrelated Transplant Approval Committee (UTAC) and in the editorial board of the Malaysian Journal of Paediatrics & Child Health (MJPCH). He has also served as a reviewer for the Medical Journal of Malaysia and the Philippines Paediatric Infectious Disease Journal.

Prof. Zulkifli has more than 35 publications in peer-reviewed international and local journals in addition to numerous abstracts and articles for the lay-public on various issues involving child health, paediatrics and vaccinology. He has authored or co-authored two books for parents, one for medical students and one for nurses. In 2008, he was conferred the Darjah Panglima Mahkota Wilayah by the Malaysian King that carries the honorific title of ‘Datuk’.

ORGANISING CO-CHAIRS

ASSOC PROF DANIEL YT GOH

M.B; B.S, M.Med (Paediatrics), FRCPCH(UK), FCCP(USA), FAMS (Singapore)
Senior Consultant Paediatrician, Paediatric Pulmonary and Sleep Service,
National University Hospital, Singapore and Associate Professor, Department of Paediatrics,
Yong Loo Lin School of Medicine, National University of Singapore

Dr Daniel Goh is an Executive Committee member of the **Asian Strategic Alliance for the Prevention of Pneumococcal Diseases *(ASAP)***, Executive committee member of the **Asian Dengue Voice and Action *(ADVA)*** and member of the organizing committee of the 5th Asia Dengue Summit. He is also a Standing Committee Member of the **Asia Pacific Pediatric Association *(APPA)***.

Dr Goh is Past-President of the **Singapore Paediatric Society** and Past-President of the **Asean Paediatric Federation**.

His main clinical interests are in Childhood Respiratory diseases, including chronic lung diseases in children and allergic airway diseases, Sleep and sleep-related breathing disorders as well as Bronchology and childhood fiberoptic bronchoscopy.

He has a keen interest in vaccinology and vaccine advocacy.

Dr Goh was the recipient of the **Young Investigator Award 1994** at the 28th Singapore-Malaysia Congress of Medicine, Singapore Academy of Medicine for his research on Local Airspora Allergens. He was recipient of the **NUHS-Mochtar Riady Pinnacle Awards for Excellence** in 2015 and recipient of the Singapore **National Day Award 2018** - Public Administration Medal (Bronze), Ministry of Education. He was awarded the **Outstanding Asian Paediatrician Award 2018**, presented by the Asia Pacific Paediatric Association.

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SPEAKERS' BIOGRAPHIES

PROF CAMERON SIMMONS

Regional Director Oceania
World Mosquito Program

Cameron Simmons is the Director of the Institute of Vector-Borne Disease and Director of the Oceania Hub of the World Mosquito Program, both at Monash University, Australia. He is also an NHMRC Leadership Fellow and a Fellow of the Australian Academy of Health Medical Sciences. He lead an international team deploying Wolbachia to stop dengue transmission in endemic countries.

His international experience includes 13 years working in Vietnam at the Hospital for Tropical Diseases in Ho Chi Minh City. It is here, seeing severe pediatric dengue patients on a daily basis, that has motivated my career. He was co-Principal Investigator of the AWED trial - a cluster randomised trial in Indonesia that recently reported a 77% reduction in virologically-confirmed dengue cases following Wolbachia deployments.

PROF BRIDGET WILLS

Professor of Tropical Medicine &
Honorary Consultant in Paediatrics
at the Centre for Tropical Medicine
and Global Health,
University of Oxford

Bridget Wills is Professor of Tropical Medicine and Honorary Consultant in Paediatrics at the Centre for Tropical Medicine and Global Health, University of Oxford. She trained in paediatrics and infectious diseases in the UK and worked at the Oxford University Clinical Research Unit in Ho Chi Minh City, Viet Nam, for more than 20 years before returning to Oxford in late 2018. Her clinical research has been primarily on dengue, and incorporates studies directed towards improving diagnosis and risk prediction for severe dengue, randomised trials of therapeutic interventions designed to improve dengue management, and research to investigate the pathophysiological mechanisms responsible for the systemic vascular leak syndrome and coagulopathy that are the major complications of dengue. Latterly, she has focused on exploring the potential for establishing dengue human challenge studies in endemic settings like Viet Nam.

SPEAKERS' BIOGRAPHIES

DR TINEKE CANTAERT

Head of Unit
HHMI-Wellcome International Research Scholar
Immunology Unit
Institut Pasteur du Cambodge

Dr. Tineke Cantaert obtained a PhD in Clinical Immunology in 2008, from the University of Amsterdam, the Netherlands. In 2009, she received the Young Investigator Award from the European League against Rheumatism. In 2010, she moved to Yale University undertaking a second postdoctoral study. Here, she studied the mechanisms that establish both central and peripheral B cell tolerance in humans. As her interest was to understand the response of the human immune system to infectious diseases, she moved to Cambodia in 2015, where she is currently head of the Immunology Unit at Institut Pasteur Cambodia.

Her research is focused to understand the immunopathology of arboviral infections, where her studies have identified protective B and T cell responses in individuals that can control dengue virus infection without excessive immune activation leading to vascular damage. Moreover, she has shown that the absence of specific sugar moieties on anti-dengue antibodies can lead to severe dengue disease.

In 2017, Dr Cantaert was awarded the Early Career Research Price in Vaccinology R&D from the International Union of Immunological Societies. Since 2017, she has been a HHMI/Wellcome Trust International Research Scholar.

PROF PAUL R YOUNG

BSc, PhD (London)
Head of School, Professor of Virology

School of Chemistry & Molecular Biosciences (SCMB)
Australian Infectious Diseases Research Centre (AID)
The University of Queensland

Paul Young is Professor of Virology and Head of the School of Chemistry & Molecular Biosciences at The University of Queensland, Brisbane, Australia. He gained his PhD from the London School of Hygiene & Tropical Medicine and joined the University of Queensland in 1991. His research aims to understand the molecular basis of virus induced disease, develop new and improved diagnostics as well as vaccine and therapeutic control strategies for a number of viral pathogens of both human and animal origin. Prof Young is Chair of the Virology Division of the International Union of Microbiological Societies and has been the President of the Australian Society for Microbiology (2012-2014), the Australasian Virology Society (2001-2011) and the Asia-Pacific Society for Medical Virology (2012-2015).

SPEAKERS' BIOGRAPHIES

ASSOC PROF SYLVIE ALONSO

Infectious Diseases Translational Research Programme (ID TRP)
Department of Microbiology & Immunology;
Yong Loo Lin School of Medicine;
National University of Singapore, Singapore

Dr Alonso obtained her PhD degree in Microbiology and Molecular Biology from the University Claude Bernard Lyon I (France). She then continued her post-doctoral training at Pasteur Institute of Lille (France) where she developed bacterial vaccine delivery systems, followed by another 2 years at Cornell University (NY, USA) where she worked on Tuberculosis. In 2004, she was awarded the Lee Kuan Yew post-doctoral Fellowship and joined the Department of Microbiology at NUS, Singapore. She was recruited as an Assistant Professor in 2007 and promoted to Associate Professor with tenure in 2013. For the past 15 years, Dr Alonso's research at NUS has focused on studying the pathogenesis of Enterovirus 71 (HFMD) and Dengue virus, and apply this knowledge to develop novel treatment options against these viral diseases.

PROF SUBHASH VASUDEVAN

Program in Emerging Infectious Diseases, DUKE-NUS Medical School

Subhash Vasudevan is a Professor and Principal Investigator in the Signature Program for Emerging Infectious Diseases at Duke-NUS Medical School and the lead PI of the Johnson & Johnson Satellite Centre for Global Health Discovery in Flaviviruses@Duke-NUS. He obtained his PhD at The Australian National University (ANU) and post-doctoral training at the Max-Planck Institute for Biophysics (Germany) and Research School of Chemistry@ANU. His major research interest is in the area of structure and function of flaviviral non-structural proteins and antiviral drug discovery against dengue and related flaviviruses. He is an Editor for Antiviral Research (Elsevier), member of the Editorial Board of Journal of Virology (ASM) and Board member of the International Society for Antiviral Research.

SPEAKERS' BIOGRAPHIES

ASSOC PROF LUO DAHAI

Associate Professor in Infection and Immunity,
Provost's Chair in Medicine,
Lee Kong Chian School of Medicine

Dahai is an Associate Professor in Infection and Immunity, Provost's Chair in Medicine, Lee Kong Chian School of Medicine. He received his BS.c in 2006 and Ph.D. in 2010 from SBS-NTU, Singapore. He studied at Yale University as a postdoctoral research associate between 2010-2013. Dahai then joined the newly established Lee Kong Chian School of Medicine in Sept 2013 as a Nanyang Assistant Professor and received his tenure in 2019. His laboratory studies the molecular mechanisms of how infectious viruses, such as dengue, Zika, and Chikungunya viruses, infect humans and how our body's defense system fights back.

PROF NEELIKA MALAVIGE

Professor and Head of the Department of Immunology and Molecular Medicine,
University of Sri Jayewardenepura, Sri Lanka

Neelika Malavige is a Professor and Head of the Department of Immunology and Molecular Medicine, University of Sri Jayewardenepura, Sri Lanka and also an academic visitor at the MRC Weatherall Institute of Molecular Medicine, University of Oxford. She is a member of the Executive Committee of the International Society of Infectious Diseases since 2020 and a member of the technical advisory group to the WHO-COVID-19 technology access pool. She is Fellow of the Royal College of Physicians in London the Royal College of Pathologists. She serves as an expert member on several government COVID-19 related technical advisory groups on public health response, control strategies, vaccine evaluation, regulation and vaccine deployment strategies.

She leads a large research group working on dengue, and COVID-19, focusing on immunopathogenesis of and vascular leak in dengue and translating these findings into clinical trials. Since the onset of the COVID-19 pandemic, her laboratory has been carrying out genomic sequencing, while also investigating immune responses to COVID-19 vaccines and the kinetics of T cell and antibody responses in patients with COVID-19. She has strong research collaborations with University of Oxford and her laboratory is a part of the A2CARES, which is one of the Centers for Research in Emerging Infectious Diseases, NIH, USA.

SPEAKERS' BIOGRAPHIES

EMERITUS PROF SUTEE YOKSAN

M.D., Ph.D. (Pathobiology)

Director,
Centre for Vaccine Development,
Mahidol University
Thailand

Prof. Sutee Yoksan graduated from Mahidol University with a M.D. in 1979 and a Ph.D. in 1987. After obtaining his MD he trained in clinical pathology at the Department of Pathology, Ramathibodi Hospital Faculty of Medicine, Mahidol University. To increase his research capability he continued laboratory work at the Department of Tropical Medicine and Medical Microbiology, U. Hawaii, USA, Sir William Dunn School of Pathology, U. of Oxford, UK. and Queensland Institute of Medical Research, Brisbane, Australia.

From 1984-2014, he served as Director of the Center for Vaccine Development, Mahidol University. Prof. Sutee is a world leader in research on dengue and other arthropod-borne viral infections. He has published over 180 scientific papers and book chapters on many areas of vaccine research and development, namely dengue, Japanese encephalitis, Chikungunya and Zika vaccines.

At present he serves as a consultant of the Center for Vaccine Development, Institute of Molecular Biosciences, Mahidol University, Thailand.

MR NAOTO KIMURA

Product Application Specialist
In Vitro Diagnostics Div., Medical Systems Business Div.
FUJIFILM Corporation.
Tokyo, Japan

Naoto Kimura is currently in charge of product application for several IVD medical devices at FUJIFILM Corporation based in Tokyo, Japan.

His work experience has mainly been focusing on infectious diseases throughout his career, including R&D expericence at a different IVD medical devices manufacturer prior to joing FUJIFILM.

SPEAKERS' BIOGRAPHIES

DR PANISADEE AVIRUTNAN

M.D., Ph.D.

Head, Division of Dengue Hemorrhagic Fever Research &
Siriraj Center of Research Excellence in Dengue and
Emerging Pathogens,
Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok 10700, THAILAND
Email: panisadee.avi@mahidol.edu

Panisadee Avirutnan joined the MD/PhD scholar program of Mahidol University and China Medical Board in 1988. She received Ph.D. (Microbiology) degree in 1998 and Doctor of Medicine (M.D.) degree in 2001 from Mahidol University. She later became a postdoctoral fellow at Washington University in St. Louis, USA between 2006-2011, working on Flavivirus and complement biology. After that she worked for Faculty of Medicine Siriraj Hospital, Mahidol University and was promoted to an Associate Professor in 2013. In 2010, she was appointed Head of Dengue Hemorrhagic Fever Research Division and became a Director of Siriraj Center of Research Excellence in Dengue & Emerging Pathogens in 2019. She oversee clinical cohorts of patients with dengue in three major city hospitals in Thailand. Her research interests are to find specific dengue therapeutics using drug repositioning strategies, to understand molecular mechanisms responsible for protective and pathogenic functions of dengue virus nonstructural protein NS1, to interrogate the mechanism by which the virus evades and exploits the complement system to spread the infection and to search for biomarkers for predicting the development of DHF, the serious clinical syndrome that can be life-threatening.

ASST PROF OOI YAW SHIN

Emerging Infectious Diseases,
Duke-NUS Medical School

Yaw Shin received his B.Sc. (Hons.) in Genetics and Molecular Biology and M.Sc. in Microbiology degrees from the University of Malaya, Malaysia. He earned his M.S. and Ph.D. degrees from Albert Einstein College of Medicine in New York under the tutelage of Margaret Kielian, discovering novel host factors that impact alphavirus (e.g., Chikungunya virus, Semliki Forest virus) entry and exit. After that, he pursued his postdoctoral research in the laboratory of Jan Carette at Stanford University School of Medicine, California, focusing on the discovery of host factors critical for several biomedically important RNA viruses, such as flaviviruses (e.g., Dengue virus, Zika virus) and enteroviruses (e.g., Enterovirus D68, Rhinovirus C). In late 2019, he joined the Emerging Infectious Diseases (EID) Program of Duke-NUS Medical School in Singapore as a tenure-track assistant professor.

Yaw Shin has a long-established interest in the discovery and mechanistic studies of host genetic determinants essential for RNA virus infections using functional genomic approaches. Through collaborative research efforts, he has contributed to the discoveries of several key host factors, such as TSPAN9, which facilitates alphavirus membrane fusion, SETD3, which governs enterovirus replication and pathogenesis, and a catalog of the endoplasmic reticulum-associated proteins, e.g., Vigilin and RRBP1, that are essential for Dengue virus infection. His laboratory at Duke-NUS has focused on discovering key host factors for bat- and mosquito-borne viruses of medical importance to bridge knowledge gaps on the cell biology of virus infection and innovate antiviral strategies.

SPEAKERS' BIOGRAPHIES

DR SETOH YIN XIANG

Senior Scientist
Virology Branch
Environmental Health Institute (EHI)
National Environment Agency

Setoh is a Senior Scientist leading the Virology Branch within the Environmental Health Institute (EHI) of NEA. The theme of Setoh's research is focused strongly on molecular virology, grounded on a versatile reverse genetics platform for the generation of recombinant viruses and virus libraries from several different families of RNA viruses. His past work has translated into several important technical advancements for the field, including the establishment of in vivo screens to identify antiviral host genes against flaviviruses, a deep mutational scanning platform for flaviviruses, and a recombinant flavivirus vaccine platform based on insect-specific flaviviruses.

In EHI, the Virology Branch investigates the molecular and immunological determinants of dengue infections in Singapore. We utilise reverse genetics approaches to probe the molecular underpinnings of virulence and outbreak potential of dengue viruses, in particular those isolated in Singapore. In addition, we complement national dengue surveillance by conducting unbiased population-based dengue seroprevalence studies to estimate the true burden of dengue on our population.

PROF SHEEMEI LOK

Emerging Infectious Diseases,
Duke-NUS Medical School

Dr Shee-Mei Lok is a Professor in the Emerging Infectious program in Duke-NUS, Singapore. She was also a National Research Foundation (NRF) fellow (2009-2014) and is now a NRF Investigator. She is a structural virologist specializing in x-ray crystallography and cryo-electron microscopy. Her research interest focus on the structural changes of flavivirus particles during its infection cycle and the effect of anti-viral therapeutics on them. She obtained her Msc and PhD in NUS and did her post-doctoral training in Purdue University under the supervision of the late Hanley Prof Michael Rossmann. Her laboratory made significant discoveries in the understanding of the structures of the Zika and dengue viruses, the morphological variants of dengue viruses, also how potent human antibodies neutralize flaviviruses and the structural changes of flavivirus during maturation.

SPEAKERS' BIOGRAPHIES

DR SANSANEE NOISAKRAN

Principal Researcher
National Center for Genetic Engineering and Biotechnology (BIOTEC)
National Science and Technology Development Agency (NSTDA), Thailand

Dr. Sansanee Noisakran received B.Sc. (Medical Technology, First-Class Honors) from Mahidol University, Thailand and M.Sc. and Ph.D. (Virology/ Immunolgy) from Louisiana State University Health Sciences Center (LSUHSC), New Orleans, USA. She has been working at the National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency, Thailand since 2000. She had postdoctoral research training at the Department of Microbiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand in 2000 and at the Department of Immunoregulation, Research Institute for Microbial Diseases (BIKEN), Osaka University, Osaka, Japan in 2005. She also worked as a research associate at the Department of Pathology and Laboratory Medicine and Emory Vaccine Center, Emory University, Atlanta, GA, USA during 2008–2010 under a memorandum of understanding between the research partners. Currently, she is a principal researcher at the Molecular Biology of Dengue and Flaviviruses Research Team, Medical Molecular Biotechnology Research Group, BIOTEC. Her research expertise includes molecular/ cellular virology, virus-host interaction, mammalian cell-based recombinant protein expression systems and in vivo virus infection. Her research interest aims at investigating mechanisms of dengue virus infection, dengue pathogenesis/ disease protection, and predictive markers for severe dengue. Dr. Noisakran's research studies have focused on (i) dengue virus and human host cell interactions, (ii) functional contributions of the nonstructural protein 1 of dengue virus, its specific antibodies and related human proteins to dengue virus infection and dengue pathogenesis, (iii) potential development of target-based anti-dengue drugs/inhibitors to control dengue virus infection, and (iv) applications of replication-defective adenovirus system expressing dengue viral proteins for use in dengue vaccine development. She is a recipient of the Royal Thai Government Scholarship (1995-2000), Chancellor's award, LSUHSC (2000), Robert E. Shope International Fellowship in Infectious Diseases from the American Society of Tropical Medicine and Hygiene (2009), and L'Oréal (Thailand) For Woman in Science Fellowship (2012). She has 64 peer-reviewed international publications and is a member of L'Oréal-UNESCO For Women in Science Community.

DR CHIN WEI-XIN

Researcher
Department of Microbiology and Immunology and Infectious Diseases Translational
Research Programme in the National University of Singapore

Chin Wei-Xin is a research fellow under from the Department of Microbiology and Immunology and Infectious Diseases Translational Research Programme in the National University of Singapore. Wei-Xin is currently working under A/Prof. Justin Chu in the MARVAS lab, where he has interests in developing reverse genetics systems and technologies for RNA viruses. These reverse genetics systems are used to facilitate high-throughput screening studies or to characterise host-viral interactions. Wei-Xin is also hopes to leverage these technologies for the development of next-generation vaccines for RNA viruses.

SPEAKERS' BIOGRAPHIES

MR KAMRAN RAFIQ

Co-Founder and Communications Director
International Society for Neglected Tropical Diseases

Kamran is the Co-Founder and Communications Director at the International Society for Neglected Tropical Diseases. After graduating from The School of Pharmacy, University of London in Pharmacology and Toxicology Kamran went on to complete his Masters in Neuroscience at the Institute of Psychiatry and The Maudsley, Kings College London. He has worked as a research scientist at Schering-Plough Research Center at the San Raffaele Hospital in Milan, Italy working on neuropeptides and novel mechanisms of pain transmission and Parkinson's Disease modelling. Upon returning to the UK he worked for Reuters Business Insights setting up their drug discovery intelligence unit and then as Sales Director for Datamonitor being an integral part of the acquisition and subsequent integration of the company Life Science Analytics and then as Managing Director at Global Data overseeing both Pharma/Biotech and Medical Device Diagnostics market teams. As well as co-founding the ISNTD he sits on the editorial board of Break Dengue and also has co-founded the behavioural research company Actingforhealth.org

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PROF TIKKI PANGESTU

Visiting Professor,
Lee Kuan Yew School of Public Policy,
National University of Singapore,
Singapore

Prof. Pang joined the Lee Kuan Yew (LKY) School of Public Policy after 13 years at the World Health Organisation (WHO) in Geneva, Switzerland as Director of its Research Policy & Cooperation department. In this capacity he worked with countries to strengthen their national health research systems, developed mechanisms and initiatives to improve the efficiency and transparency of global health research, and helped formulate an Organisation-wide research policy.

Prior to his WHO career, Prof. Pang was the Professor of Biomedical Sciences at the Institute of Postgraduate Studies & Research, and Associate Professor/Lecturer at the Faculty of Medicine, the University of Malaya, Kuala Lumpur. He was previously Co-Director of the WHO Collaborating Centre for Dengue & Dengue Haemorrhagic Fever at the University of Malaya, Kuala Lumpur, Malaysia (1982-1995), and a member of the WHO Technical Advisory Group which developed the guideline Dengue Haemorrhagic Fever: Diagnosis, Treatment and Control (1986).

Prof. Pang's main research and academic interests lie in the area of infectious diseases, the impact of genomics on public health, global health governance, national health research systems, knowledge translation, research transparency and accountability, and the use of evidence in health policy development. In these areas, he has published more than 200 scientific articles and 12 books, edited volumes and reports, which includes several major WHO reports, including Genomics and World Health (2002), the World Report on Knowledge for Better Health (2004) and a History of Research in WHO (2010). Prof. Pang's involvement with the LKY School of Public Policy began in 2009 through the ST Lee Project on Global Health Governance.

Prof. Pang is a Fellow of the Royal College of Pathologists (UK), American Academy of Microbiology (USA), Institute of Biology (UK) and the Academy of Medicine of Malaysia. He was the Founding Editor of Health Research Policy & Systems and the Asia-Pacific Journal of Molecular Biology and Biotechnology.

SPEAKERS' BIOGRAPHIES

DR VIANNEY TRICOU

Medical Director,
Takeda Vaccines

Dr. Vianney Tricou is a Clinical Development professional, trained as PharmD with a PhD, and specialized in Infectious Diseases. My current role is Medical Director at Takeda's Vaccine Business Unit, working toward the development of TAK-003, a novel dengue tetravalent vaccine candidate. He is based in Zurich, Switzerland.

DR LOUIS MACAREO

MD, JD, MPH
Executive Director, New Products Vaccines Lead

Louis Macareo is currently the EDMA for new products in Global Medical & Scientific Affairs. Louis is an internal medicine physician, attorney and clinical pharmacologist originally from Wilkes-Barre, Pennsylvania. Louis completed his undergraduate degrees in psychology and Arab and Islamic studies at Villanova University. He attended law school at the Catholic University of America and completed his medical degree and a Master of Public Health at Tulane University in New Orleans.

Louis served in the U.S. Army since 1985, first in the artillery and subsequently, for 21 years on active duty as a physician. Louis has been assigned to several locations in the continental United States as well as Egypt, Italy, Kenya, Iraq, and Thailand and has conducted advanced phase drug and vaccine clinical trials and disease surveillance throughout Asia and Africa. His most recent position prior to coming to Merck was as the Chief of the Department of Virology at the Armed Forces Research Institute of Medical Science (AFRIMS), in Bangkok, Thailand where he supervised the conduct of two phase III dengue vaccine clinical trials and conducted arboviral and respiratory disease surveillance studies in a dozen Asian countries as well as the validation of several arboviral and respiratory diagnostic devices.

SPEAKERS' BIOGRAPHIES

PROF STEPHEN J. THOMAS, MD

Chair (interim), Department of Microbiology & Immunology
Director, Institute for Global Health and Translational Science
SUNY Upstate Medical University
Syracuse, NY

Dr. Thomas is a Professor of Medicine, Professor of Microbiology & Immunology, and Infectious Diseases physician-scientist from SUNY Upstate Medical University. He is the Director, Institute for Global Health and Translational Science (IGHTS) and the interim Chair, Microbiology and Immunology. Prior to joining Upstate Dr. Thomas spent twenty years in the U.S. Army serving at the Walter Reed Army Institute of Research and completing his career as the institute's Deputy Commander for Operations. Dr. Thomas specializes in the study of viruses and vaccine development and spent more than 5 years of his early career living and working in Thailand. He played key leadership roles in the U.S. government response to the West Africa Ebola outbreak (2014-2016) and MERS-CoV and Zika epidemics and was instrumental in the development and advancement of vaccines for each. Currently, he is the global coordinating principal investigator for Pfizer's phase 1/2/3 COVID vaccine trial. Dr. Thomas earned his Bachelor of Arts with Honors in Biomedical Ethics from Brown University, his Medical Degree from Albany Medical College, and completed his Internal Medicine residency and Infectious Diseases fellowship at Walter Reed Army Medical Center.

DR. MARIA ROSARIO Z. CAPEDING

Head, Department of Microbiology and the Dengue Study Group
Research Institute for Tropical Medicine, Philippines

Dr. Capeding is a pediatrician, an infectious disease specialist, and a clinical microbiologist of the Research Institute for Tropical Medicine, Philippines. She is the Head of the Department of Microbiology, Consultant of the Medical Department, and Head of the Dengue Study Group of the said institute. She is the Section Head of Infectious Diseases of the Department of Pediatrics, Asian Hospital and Medical Center, Philippines.

She has engaged in significant researches on the safety, immunogenicity and efficacy of childhood vaccines: Haemophilus influenzae type b, Pneumococcal and Meningococcal Conjugate; Influenza; Hepatitis A; Hepatitis B; DtaP-Hib-IPV-HepB combination vaccine; Typhoid Conjugate; Cholera; Japanese Encephalitis, and Dengue.

She is an accomplished medical researcher though her contributions: 54 original articles and reviews in peer reviewed international and local journals; presented scientific papers in 77 international medical conferences; acted as an expert or member of advisory board to 31 international consultative meetings; and 47 completed and current researches and clinical trials. She is an active member of national and international professional medical societies and global, regional scientific fora. She is also a frequent lecturer to numerous conventions of medical societies, postgraduate courses and local chapter meetings.

Dr. Capeding is an awardee of the 23rd Dr. Jose P. Rizal Memorial Award for Research by the Philippine Medical Association (PMA). She was given the distinction as one of the world's Top Women in Biotech Industry 2014. The paper, Clinical Efficacy and Safety of a Novel Tetravalent Vaccine in Healthy Children in Asia: Phase 3, Randomized, Observer-Masked, Placebo-Controlled Trial, Maria Rosario Capeding, Ngoc Huu Tran, Sri Rezeki, et. al. (The Lancet, 2014. 384:1358-1365 was adjudged Paper of the Year 2014 by the International Society for Vaccines (ISV). She is a recipient of the 2015 Outstanding Professional of the Year Award in the Field of Medicine and Eric Nubla Excellence Award given by the Philippine Professional Regulation Commission.

SPEAKERS' BIOGRAPHIES

PROF EMERITUS LULU C. BRAVO, MD

Professor Emeritus College of Medicine,
University of the Philippines Manila

Lulu Bravo is a Professor Emeritus at the College of Medicine, University of the Philippines Manila. She is the former Vice Chancellor for Research and Executive Director of the National Institutes of Health, University of the Philippines Manila (2005 – 2011) and current head of the Vaccine Study Group of the NIH – UPM.
She is the President of the Immunization Partners in Asia Pacific (IPAP), current Executive Director and past President of the International Society of Tropical Pediatrics (ISTP) 2008 – 2011, past Chair and Founder of the Asian Strategic Alliance for Pneumococcal Disease Prevention (ASAP) 2007 – 2011, and Executive Director, Sec-General (1998 – 2006) & past President of the Asian Society for Pediatric Infectious Disease (ASPID) 2006 – 2008. She has served in various capacities in many other Asian medical and professional societies and as WHO Technical Advisor. She has served as well in national medical organizations such as PMA, PPS, PIDPS, PSMID and the Philippine Foundation for Vaccination (PFV) of which she is the founding President and current Executive Director. In the international scene, she is a member of the Rota Council, Pneumococcal Awareness Council of Experts (PACE) and member of the Dengue Vaccine Initiative (DVI). Her work has earned for her various national and international honors and awards in the professional, academic and research fields, including the Outstanding Physician (2009) and the prestigious Dr. Jose P. Rizal Memorial Award for Academe (2011) given by Philippine Medical Association, the 2012 Asian Outstanding Pediatrician Award given by the Asia Pacific Pediatric Association and 2018 Outstanding Professional in Medicine given by the Professional Regulation Commission of the Philippines. As vaccine advocate, she was named Pneumonia Fighter in 2018 by the JustActions Organization, a US-based movement and corporation associated with People Empowerment.
Dr. Lulu Bravo completed her MD, pediatric residency and subspecialty training in infectious disease at Philippine General Hospital-College of Medicine of the University of the Philippines Manila. She supplemented her fellowship in pediatric infectious disease at the University of Texas Southwestern Health Science Center in Dallas, USA in 1986.

DR CHAN KUAN RONG

Principal Research Scientist
Emerging Infectious Diseases
Duke-NUS Medical School

Kuan Rong Chan is a Principal Research Scientist in the Programme in Emerging Infectious Diseases at Duke-NUS Medical School. He received his undergraduate from the National University of Singapore (NUS) and obtained his PhD from the NUS Graduate School for Integrative Sciences and Engineering. He then did his postdoctoral training in Duke-NUS Medical School and is a Principal Research Scientist since 2018.

Dr. Chan's lab specializes in applying systems biology approaches to the field of virology, to study how viruses cause disease in humans. He is also interested in understanding how human heterogeneity influence vaccine and virus infection outcome. His lab focuses on using and developing computational tools and interactive apps, so as to facilitate the understanding of host responses to viruses and vaccines.

For more details, please visit the Kuan Rong Chan Lab homepage at: https://kuanrongchan.com

SPEAKERS' BIOGRAPHIES

ASST PROF ADAM WAICKMAN

Department of Microbiology and Immunology
Upstate Medical University

Dr. Adam Waickman, PhD is an Assistant Professor in the Department of Microbiology and Immunology and Laboratory Director at the Institute for Global Health and Translational Sciences at SUNY Upstate Medical University in Syracuse, NY. He received his PhD from the Johns Hopkins University School of Medicine in Baltimore, MD, and performed his postdoctoral training at the National Institutes of Health (NIH) and the Walter Reed Army Institute of Research (WRAIR). His group at SUNY Upstate is dedicated to understanding how the interactions between infectious organisms and the human immune system result in pathogenesis and/or durable immunity. His work is primarily focused on viral pathogens – such as dengue, Zika, and SARS-CoV-2 - and leverages "next generation" technologies such as single cell RNA sequencing, multi-parametric flow cytometry, and computational modeling.

DR GONZALO PEREZ

Senior Medical Director, Global Medical Lead,
Takeda Vaccines

Dr. Gonzalo Perez is an established professional with strong academic, research and clinical background founded on extensive experience as a Vaccine expert, Clinician (Cancer surgeon) and as a former Primary Investigator for various Vaccine Clinical Trials.
Dr. Perez has a proven track record working for Fortune 500 Pharmaceutical Leader in Global Medical Affairs – vaccines, and Enterprise Leadership (Merck). He is also a world-renowned HPV expert with over 60 publications in peer review journals.
Since November 2020 he joined Takeda as the US Medical Director; since November 2021 he was appointed as the Global Medical Lead- Dengue. Dr. Perez is currently working with a very talented and enthusiastic team on a Dengue vaccine clinical program.

SPEAKERS' BIOGRAPHIES

DR LAURA RIVINO

Senior Lecturer, University of Bristol, UK
Adjunct Asst Professor, Duke-NUS Medical School, Singapore

Dr. Laura Rivino is a Senior Lecturer at the University of Bristol, UK and Adjunct Assistant Professor at Duke-NUS Medical School in Singapore. Dr. Rivino graduated with a MSc at the University of Milan, Italy and completed a PhD training in Immunology in Prof. A. Lanzavecchia's laboratory at the Institute for Research in Biomedicine in Bellinzona, Switzerland.
Her PhD work focused on the study of human memory T cell generation and maintenance during health and disease. During her post-doctoral training at the National University of Singapore (NUS) in the laboratories of A/Prof. P. MacAry and Prof. M. Kemeny (2008-2013), Dr. Rivino developed a keen interest in understanding the human T cell response to viral infection, particularly during dengue.
Dr. Rivino moved to Duke-NUS Medical School in 2014 where she was Co-Head of the Flow cytometry Core Facility and Senior Research Fellow in Prof. A. Bertoletti's laboratory (2014-2015). During this time Dr. Rivino was awarded a New Investigator CBRG and Open Fund Individual Research Grant (IRG) by NMRC and in 2016 was appointed Assistant Professor. In 2019 she joined the University of Bristol, UK to lead the anti-viral immunity laboratory which focuses on understanding the immune correlates of protection/immunopathology during dengue infection and SARS-CoV-2. The team's work is supported by funding from the UK Academy of Medical Sciences, Royal Society, Elizabeth Blackwell Institute/Wellcome Trust and MRC.

DR TINE DE MAREZ

Senior Director,
Compound Development Team Leader - Dengue
Johnson & Johnson

SPEAKERS' BIOGRAPHIES

DR ISABELA RIBEIRO

Viral Diseases Cluster Director, DNDi

Dr Isabela Ribeiro joined DNDi as a Senior Project Manager in March 2007, after working as a consultant on DNDi projects since 2005. Previously Head of DNDi's Chagas Clinical Programme and Head of Dynamic Portfolio Unit, Dr Ribeiro is now Viral Diseases Cluster Director.

Dr Ribeiro has over fourteen years of drug development experience with a focus on neglected diseases, most recently serving as a consultant to the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR).

With WHO-TDR, Dr Ribeiro contributed to several projects involving the management of large community-based clinical studies in endemic countries.

A member of the Scientific Advisory Committee of the PDTIS, Oswaldo Cruz Foundation, since 2005, Dr Ribeiro completed a post-doctoral fellowship in infectious diseases and an internal medicine residency at Ohio State University and worked as clinical research fellow based at the Communicable Disease Unit of St. George's Hospital, London, after earning her MD from the Federal University of Rio de Janeiro in Brazil.

ASSOC PROF ASHLEY ST JOHN

Emerging Infectious Diseases
Duke-NUS Medical School

Ashley St. John is an immunologist and Associate Professor in the Programme in Emerging Infectious Diseases at Duke-NUS Medical School. She also holds appointments in the Department of Microbiology and Immunology, National University of Singapore, the Department of Pathology, Duke University and the SingHealth Duke-NUS Global Health Institute. Her research program focuses on understanding host immune responses to virulent pathogens and their vaccines, particularly relating to Flaviviruses, such as dengue, Zika, Japanese encephalitis viruses and others, as well as viral respiratory pathogens including RSV and SARS-CoV-2. Through those studies, she has advanced the field's understanding of the mechanisms of cross-protection or immune-enhanced pathology that can occur in the context of cross-reactive immune responses to viruses. Her research also defined the role of mast cells in antiviral immunity and immune pathology. Beyond mechanistic studies of how immunity is generated and recalled during infection, she has an interest in translating her basic science findings into applications with clinical relevance. Towards this aim, she has led and contributed to numerous studies aiming develop novel vaccination strategies, diagnostics, and therapeutics for infectious diseases.

SPEAKERS' BIOGRAPHIES

ASSOC PROF NG LEE CHING

Group Director, Environmental Health Institute at National Environment Agency

Associate Professor Ng Lee Ching is Group Director of National Environment Agency's Environmental Health Institute in Singapore and a WHO Collaborating Centre. She spent 20 years contributing to building laboratory capability for Singapore's public health and developing tools and strategies for mitigation of risks. Dr Ng is also associated with the Nanyang Technological University; serves as Advisor to WHO for dengue and chikungunya surveillance and control and is Director of the WHO Collaborating Centre for Reference and Research of Arbovirus and their Associated Vectors.

DR HASITHA TISSERA

Consultant Epidemiologist,
National Coordinator for Dengue Prevention and Control,
Ministry of Health,
Sri Lanka

Dr. Hasitha Tissera is a Medical Epidemiologist leading the National Dengue Control Programme of the Ministry of Health, Sri Lanka. He joined the Central Epidemiology Unit in 2002 after serving as a Regional Epidemiologist in the then war-torn Eastern Province of Sri Lanka. His responsibilities at the Epidemiology Unit encompass national surveillance of dengue, coordination of dengue case management based on National Guidelines and training of alllevels of clinical and public health staff. Heading the National Dengue Control Programme since 2013 he is involved in planning, implementation and evaluation of all dengue control activities at national and sub-national levels. Dr. Tissera is responsible for the technical evaluation of dengue vaccines registration in Sri Lanka. He is also the Principal Investigator of a number of International Research Projects on Dengue including vaccine studies and has authored a number of original publications in peer-reviewed journals. He serves as an expert on dengue prevention and control internationally. He received his Post-doctoral training in public health both at the Health Protection Agency – Centre for Infections (former Public Health Laboratory Services) and the Department of Health, London during 2006/08. Dr. Tissera has also been a researcher at the London School of Hygiene and Tropical Medicine, University of London.

SPEAKERS' BIOGRAPHIES

DR R. TEDJO SASMONO

Head & Senior Research Fellow
Dengue Research Unit
Eijkman Institute for Molecular Biology,
Ministry of Research, Technology, and Higher Education, Jakarta,
Indonesia.

Dr. R. Tedjo Sasmono is a Senior Research Fellow at the Eijkman Institute. He started his scientific career at the Institute back in 1994, and soon after graduated from Gadjah Mada University, Indonesia as a research assistant. He then pursued a postgraduate diploma study in molecular biology in 1997 at the University of Queensland, Australia. In 2000, he continued his education in molecular biology and obtained his Ph.D. degree from the Institute for Molecular Bioscience, University of Queensland in 2003. Afterward, he performed a short postdoctoral fellowship at the same institute and in 2004 he continued his postdoctoral training in the Department of Biochemistry and Molecular Biology at Monash University, Australia. He then moved back to Indonesia and set up the Dengue Research Unit at the Eijkman Institute. Dr. Sasmono received several scholarships/awards such as the Australian IPRS and UQ-IRPS scholarships (2000), the University of Queensland Indonesian Alumni Award (2011), Australia Awards Fellowship (2016), ASTMH Travel Award (2016), and World Intellectual Property Organization (WIPO)-Bioventures for Global Health (BVGH) Sabbatical Fellowship (2018). Currently, Dr. Sasmono is the group leader for Dengue Research Unit. His other activities include serving as a member of the National Ethics Commision for Health Research and Development, Indonesia and member of the Medical Research Ethics Committee of the National Institute for Health Research and Development (NIHRD), Ministry of Health of the Republic of Indonesia.

PROF MOI MENG LING

School of International Health,
Graduate School of Medicine,
the University of Tokyo,
Japan

Prof. Moi Meng Ling is Professor at the School of International Health, the University of Tokyo. She received her MSc and PhD in Medicine from Tsukuba University, Japan, after graduating from University Putra Malaysia with first class honors.

She is a virologist that is working on prevention measures against tropical and emerging virus diseases. She has been working on research fields from viral pathogenesis and transmission, diagnostics and vaccine development, surveillance of viral emergence, and population immunity to tracking viral spread, epidemiology, and field research. Her projects have led to the successful development of in vitro and in vivo models for flaviruses and COVID-19 vaccine evaluation studies. The novel models have also led to a better understanding of the immune responses induced after dengue and zika virus infection. She was previously the Deputy Head of WHOCC for Reference and Research of Tropical and Emerging Virus Diseases (JPN-67) and is working closely with WHO GLAD-HP and GOARN, local and international community to reduce the international spread of high treat pathogens disease and to improve rapid diagnostics to these outbreaks, including Zika and SARS-CoV-2.

She became the first foreigner to receive the prestigious Japan's AMED President Prize for her work in dengue and arboviruses in 2020, and is one of the few leading arbovirologists specializing in dengue in the country.

SPEAKERS' BIOGRAPHIES

DR GABRIELA PAZ-BAILEY

MD, PhD, MSc, DTM&H
Chief of the Dengue Branch, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID)

Gabriela Paz-Bailey, MD, PhD, MSc, DTM&H is the Chief of the Dengue Branch (DB), Division of Vector-Borne Diseases (DVBD), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) in San Juan, Puerto Rico. Dr. Paz-Bailey completed a degree in Medicine and Surgery at the University of San Carlos of Guatemala. She continued her graduate studies at the London School of Hygiene and Tropical Medicine in London, England, where she pursued a Master of Science in Tropical Medicine and International Health, and a PhD in Clinical Epidemiology. She joined the Centers for Disease Control and Prevention (CDC) in 2000 as an Epidemic Intelligence Service Officer.
Dr. Paz-Bailey has over two decades of experience in public health and epidemiology in the United States, Central America, Africa, and Asia. She has studied the natural history of several infectious diseases, focusing on their acquisition and response to therapies. These include tuberculosis, Chagas disease, HIV infection, hepatitis B and C viruses, herpes viruses, and arboviral diseases such as dengue and Zika. She has focused her efforts on strengthening treatment programs, surveillance systems and comprehensive disease prevention programs, and has authored over 170 publications. Her most recent work includes the implementation of dengue research cohorts and enhanced surveillance and obtaining Advisory Committee on Immunization Practices recommendations for the first dengue vaccine approved for use in the United States. Dr. Paz-Bailey is passionate about working on disease control and prevention and the use of science-based tools to improve public health.

DR SHIRIN KALIMUDDIN

MBBS, MRCP(UK), MPH

Senior Consultant,
Department of Infectious Diseases,
Singapore General Hospital

Assistant Professor,
Duke-NUS Medical School

Dr. Shirin Kalimuddin is a senior consultant with the Department of Infectious Diseases at the Singapore General Hospital, and is a faculty member of the Program in Emerging Infectious Diseases at Duke-NUS Medical School. Her research focuses on infectious disease outbreaks and emerging viral infections. Her goal is to combine clinical epidemiology with deep molecular investigations to define the etiology and identify potential therapeutic strategies to control outbreaks. In 2019, she was awarded the National Medical Research Council Transition Award to develop new antiviral strategies for pandemic response. Since the onset of the COVID-19 pandemic, she has led clinical trials for novel anti-SARS-CoV-2 therapeutics, and has also played a key role in a multi-institutional research collaboration to study the immunopathogenesis of SARS-CoV-2. These investigations have led to insights on how host response to viral infection shapes disease outcome, which has led her to now explore novel therapeutic strategies that modulate host response to infections. Dr Kalimuddin currently serves on the executive committee of the Singapore Infectious Disease Clinical Research Network (SCRN), which aims to foster collaborative cross-institutional clinical research within Singapore and the region.

SPEAKERS' BIOGRAPHIES

ASSOC PROF SOMIA IQTADAR

King Edward Medical University
Lahore, Pakistan

A Fellow in Medicine and Associate Professor of Medicine at King Edward Medical University, Prof. Somia graduated from Kinnaird College in 1998. She received her bachelor's degree in sciences in 2001 and completed her bachelor's in medicine & surgery in 2004 from her country's top medical institution, King Edward Medical University. Prof. Somia completed her post graduation in internal medicine in 2010 and is one of the youngest medical fellows in her faculty at King Edward Medical University.

She is the focal person for infectious diseases and epidemic control and has prepared guidelines and teaching modules for medical students and doctors. She is also trained at Asian Institute of Technology Thailand, Sri Lanka and WHO Singapore in Dengue fever and is currently working as a Master Trainer of Dengue Fever for the government of Punjab, and for WHO for the Asia Pacific. She is the Associate Secretary of Dengue Expert Advisory Group (DEAG), which provides national guidelines on clinical management of Dengue infection and imparts training to doctors and paramedical staff nationally.

Prof. Somia has also been very actively involved in research, infectious diseases being her prime focus. She has numerous publications to her name in indexed journals. She has also contributed three chapters on Dengue, Ebola and Chickungunya in Kumar and the latest edition of Clark Textbook of Medicines. She has authored an information booklet on Dengue for public awareness, and represented Pakistan in numerous international infectious disease conferences, presenting her research and experiences.

PROF LEO YEE SIN

Executive Director
National Centre for Infectious Diseases
Singapore

Professor LEO Yee Sin is the Executive Director of the National Centre for Infectious Diseases, Singapore.

As an adult Infectious Disease specialist, Prof Leo has led her team through multiple outbreaks in Singapore. These include Nipah in 1999, SARS in 2003, the pandemic influenza in 2009, Zika in 2016 and multiple surges of Dengue. She successfully managed Singapore's first imported case of the Monkeypox in May 2019. Her current priority is now in the fight against COVID-19.

Prof Leo has published close to 400 peer-reviewed scientific papers. Her experience and expertise in outbreak management is frequently called upon as advisor and conference speaker at the national, regional and international level. Apart from her clinical and administrative duties, she is also heavily involved in research and teaching. Topics of her research interest include dengue, influenza, emerging infections, HIV and COVID-19.

She has won many awards among which are three National Day Awards including the most prestigious Public Service Star in recognition for her outstanding battle against SARS in 2003 and two Public Administration Medals in 2012 and 2020. Other awards include the Excellence Service Star Award 2005, Red Ribbon Award 2014, Lee Foundation-NHG Lifetime Achievement Award 2021 and the NUS Distinguished Alumni Service Award 2021.

Prof Leo is also named in BBC's 100 women list in 2020 and was inducted into the Singapore Women's Hall of Fame in 2022.

In April 2022, Prof Leo was conferred the title of Knight of the French Order of the Legion of Honour, by France's Ambassador to Singapore Marc Abensour on behalf of the President of the French Republic.

SPEAKERS' BIOGRAPHIES

DR MARNIX VAN LOOCK, PH.D.

R&D Lead Emerging Pathogens
Johnson & Johnson Global Public Health R&D

Marnix Van Loock is the R&D Lead for Emerging Pathogens in Johnson & Johnson Global Public Health, located in Beerse, Belgium. In his current role, he leads dengue compound development and coronavirus therapeutic drug discovery. Additionally, Marnix is a member of the Research and Development Committee, as well as the Development Management Committee which together steers the direction of discovery and development for Global Public Health.
In his work with Dengue, Marnix leads the clinical development of a first-in-class antiviral small molecule for the prevention and treatment of dengue, tackling a major unmet medical need. As part of his role with Coronavirus, Marnix coordinates the antiviral discovery efforts on COVID-19 and related coronaviruses; in collaboration with Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health & Human Services. In addition, he is the project lead of the Innovative Medicines Initiative (IMI) Coronavirus Accelerated R&D in Europe (CARE) consortium.
Marnix has held roles with increasing responsibility throughout his career. In 2004, he joined Tibotec as a Scientist in the HIV Entry Discovery team. After Tibotec was acquired by Johnson & Johnson, he became a member of the HIV Integrase team, coordinating the cell-based assay development. In the 2009-2012 timeframe, Marnix was the biology project lead for the cytomegalovirus latency project. He began leading the dengue compound development starting in 2012 and coronavirus drug discovery in January 2020. Marnix has co-authored more than 25 scientific peer-reviewed publications. He is also the winner of the International Society for Antiviral Research 2019 William Prusoff Young Investigator Award.

DR JODY HOBSON-PETERS

Advance QLD Senior Research Fellow
School of Chemistry and Molecular Biosciences
The University of Queensland
Australia

Dr Jody Hobson-Peters is a virologist based at The University of Queensland and specializes in mosquito-borne virus discovery and the development of novel vaccine and diagnostic platforms. Following almost a decade working in industry, Jody undertook a PhD with the Australian Biosecurity Co-operative Research Centre for Emerging Infectious Disease, with a primary research focus on the diagnosis of West Nile virus infection. From these studies, Dr Hobson-Peters developed expertise in the development of monoclonal antibodies (mAbs), leading to the production of extensive suites of antibodies to significant arboviruses such as dengue, yellow fever, West Nile, Zika and chikungunya viruses. More recently, she has developed monoclonal antibodies to a range of insect-specific viruses – the only mAbs available worldwide. Many of these antibodies have become crucial research tools internationally and a subset have been commercialized.
Dr Hobson-Peters' most recent research interests have focused on strategies to detect emerging viruses and benign mosquito symbionts. This research has culminated in a greater understanding of the mosquito virome, and the isolation and in-depth characterization of numerous novel insect-specific viruses. The use of these viruses as a platform to generate effective vaccine candidate antigens against numerous flaviviral diseases has been demonstrated in mice studies and patented. Her breakthrough discovery was that of Binjari virus – an insect-specific flavivirus with remarkable tolerance for exchange of its structural genes with those of other flaviviruses, including dengue, Zika and Japanese encephalitis viruses. The Binjari chimeric virus platform has provided a unique pipeline for generating effective and scalable vaccines, rapidly generating diagnostic antigens, facilitating the structural study of pathogenic viruses safely and as a tool to develop new antiviral immunotherapies.

SPEAKERS' BIOGRAPHIES

PROF MARTIN HIBBERD

EMERGING INFECTIOUS DISEASE
Department of Pathogen Molecular Biology
London School Of Hygiene & Tropical Medicine

Dr Martin Hibberd BSc(Hons) PhD; is Professor of Emerging Infectious Diseases since 2012 and Head of the Department of Infection Biology (since 2022) at the London School of Hygiene and Tropical Medicine (LSHTM).
He has adjunct positions at University of the Philippines, Manila, in Human Genetics (at NIH) and the Genome Institute of Singapore (where he was previously associate director from 2003 to 2016). He also has a visiting position at the Philippine Genome Centre.
He graduated from Brunel University in 1985 in Applied Biology and received his Doctorate from King's College, London in 1994. He has worked at UK public health agencies, Imperial College London and the Genome Institute of Singapore, before his current job at LSHTM.
He has a broad scientific background spanning both microbial and human determinants of infectious and inflammatory diseases. His current research interests utilize genomic applications to cover both pathogen and host aspects of infectious disease; together with integrating modelling and genomic approaches to understand transmission and outbreaks.
He has over 220 publications, in journals with an impact factor averaging 9, with more than 22,000 citations in total, and an h-index of 76.

MR DAFYDD GREEN

Business Development Director

Dafydd holds a degree in Chinese Studies from Oxford University, where he focused on health policy and researched province-level rural healthcare financing initiatives He previously worked on the healthcare desk of the UK Embassy in China, focusing on lung health policy and industry partnerships.
Now based in Singapore, Dafydd works on various digital health initiatives, including: Health informatics , PROM gathering , Registry development, eLearning . In his work, Dafydd has partnered closely with tertiary and primary care groups, patient societies, pharmaceutical and insurance companies, government bodies, as well as academic institutions. He is passionate about centralising, structuring and analysing various health datasets, and using this to communicate healthcare matters in a more visual and engaging manner.
Dafydd was also a member of a team that set up The Global Health Network, an initiative led by Oxford University and the Gates Foundation to enable easier, faster, and better research across a range of disciplines in the world's most challenging settings

SPEAKERS' BIOGRAPHIES

DR EGGI ARGUNI

MD., MSc., PhD.
Pediatric Infection Disease Consultant

Dr Eggi Arguni is a clinician, lecturer and researcher at the Department of Child Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Indonesia. She obtained a Master degree in Pediatric Clinical Sciences and Pediatric degree in the same institution. She completed her PhD on molecular biology and immunology at Graduate School of Medicine, Chiba University Japan. Her current clinical work is as Pediatrician at Dr. Sardjito General Hospital, Yogyakarta at the Division of Infectious and Tropical Disease. Her research interests are in the fields of immunology, infectious and tropical disease, especially in dengue and HIV in children.
One of her present research collaborations is World Mosquito Program in Yogyakarta (WMP Yogyakarta) as a part of WMP Global, which implementation research to develop more effective tool to prevent and control outbreak of dengue by new novel method using a non-pathogen bacterium, Wolbachia.

PROF DUANE J GUBLER

Professor and Founding Director
Signature Research Programme in
Emerging Infectious Disease
Duke-NUS Graduate Medical School,
Singapore

Prof. Duane J Gubler, ScD, FAAAS, FIDSA, FASTMH, is Emeritus Professor and founding director of the Signature Research Program in Emerging Infectious Diseases at the Duke-NUS Medical School, Singapore. He is Adjunct Professor in his alma mater, Johns Hopkins Bloomberg School of Public Health, the Duke University School of Medicine and Duke Global Health Institute. He has spent his entire career working on tropical infectious diseases with an emphasis on dengue and other Aedes-transmitted diseases. He has extensive field experience in Asia, the Pacific, tropical America and Africa, and has published extensively on all aspects of dengue and other vector-borne infectious diseases, with over 350 publications and 2 books to his credit. Prof. Gubler was founding Chief of the Dengue Branch, United States Centers for Disease Control and Prevention (CDC) in Puerto Rico for 9 years, Director of the Division of Vector-Borne Infectious Diseases, CDC in Fort Collins, Colorado for 15 years and Chair, Department of Tropical Medicine, Medical Microbiology and Pharmacology, University of Hawaii School of Medicine, in Honolulu for 5 years. He has and continues to serve on numerous WHO, national and international committees and study groups, and on the Scientific Advisory Boards of a number of companies and institutions. Prof. Gubler was founding Chair, Board of Councillors, Pediatric Dengue Vaccine Initiative in Seoul, Korea, founding Chair, Partnership for Dengue Control in Lyon, France, and the Global Dengue and Aedes-transmitted Diseases Consortium in Seoul, Korea, for which he currently serves as Chairman. Prof. Gubler is a Fellow, Infectious Disease Society of America, Fellow, American Association for the Advancement of Science, and Fellow and Past President of the American Society of Tropical Medicine and Hygiene.

Antibody Fucosylation Predicts Disease Severity in Secondary Dengue Infection

S Bournazos[1], HTM Vo[2], V Duong[3], H Auerswald[3], S Ly[4], A Sakuntabhai[5], P Dussart[3], JV. Ravetch[1,#], Tineke Cantaert [2,#, $]

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[#] co-last author, [$] presenting author

Background:

Severe dengue patients are characterized by increased abundance of afucosylated IgG1 glycoforms. Whether afucosylated anti-DENV IgG is the result of secondary DENV infection, or their increased abundance truly represents a prognostic factor for susceptibility to severe dengue disease remains unknown.

Methods:

We examined Fab and Fc structures from a Cambodian pediatric cohort pre- and post-infection (n=18) and from individuals who were inapparent infected (n= 23) or hospitalized (n=48) and classified according to WHO1997 criteria. Fucosylated IgG was determined by LC-MS/MS at time of dengue diagnosis (2-6 days of fever (DOF), at 6-10 DOF and at convalescence (23-100 DOF)

Results:

Neither antibody titers nor neutralizing activity correlated with disease severity in DENV-infected populations. Afucosylation is associated with dengue disease susceptibility as secondary inapparent infected individuals had lower levels of DENV-specific and total afucosylated IgG1 compared to hospitalized cases. Moreover, IgG1 afucosylation is associated with dengue disease severity and correlates with biological features of severe disease. Analyzing plasma samples from individuals before and after infection revealed that afucosylation increases after secondary dengue infection and during convalescence. Moreover, IgG1 afucosylation was specifically modulated by DENV infection, as we did not observe any changes after West Nile or Zika virus infection.

Conclusion:

The IgG1 fucosylation status represents a robust prognostic tool for dengue disease and highlights the key role of the Fc glycan structure in dengue pathogenesis.

A Single Nucleotide U59C Substitution in the Dengue Virus 5' Untranslated Region Destabilized an Attenuating Mutation in Mosquitoes.

Amanda Makha Bifani, Hwee Cheng Tan, Dorothy Ng, Kitti Chan, Subhash Vasudevan, Milly Choy, Eng Eong Ooi

Duke-NUS, Programme in Emerging Infectious Diseases, Singpaore

Abstract:

The majority of dengue vaccine development has used a live attenuated vaccine (LAV) method. However, LAVs run the risk of reverting to their wild-type ancestors. Understanding genome stability of LAVs is therefore critical to promote vaccine safety. Here, we hypothesize that the stability of attenuating mutations could be impacted by the genetics of the LAV backbone. We employed a dengue 2 wild-type strain 16681, and its LAV derivative strains, PDK53 to investigate the stability of attenuating mutations in the context of different genetic backbones. A glycine to aspartic acid change at position 53 (G53D) of the non-structural protein 1 is primarily responsible for PDK53's attenuated phenotype and is stable in the genomic context of PDK53. This, G53D mutation was introduced into the dengue 2 16681 backbone and genomes stability was determined. We found a U to C single nucleotide variant (SNV) at position 59 of the 5'untranslated region (5'UTR) of our dengue 2 16681 population that was present in approximates 12% of the 16681 population. This 5'UTR U59C mutation was found to increase in the number of SNVs present throughout the 16681 backbone and facilitated the reversion of G53D in C6/36 insect cells and in live mosquitoes by engendered a SNV at the attenuating G53D site, destabilizing the attenuating mutation and allowing it to revert to the wildtype residue. Our findings imply that the sequence of the 5'UTR can influence the stability of attenuating mutations, at least in part. This has implications on the stability of dengue virus genomes.

DELEGATES' ABSTRACTS

Baseline Human Immune Variations that Influence Yellow Fever Live-Attenuated Vaccine Immunogenicity

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4 School of Cellular and Molecular Medicine, University of Bristol, UK

5 Saw Swee Hock School of Public Health, National University of Singapore, Singapore

Background:

Vaccines are important public health tools for the control of infectious disease. However, even the best vaccine does not have 100% efficacy against disease prevention. We posit that host factors at the point of vaccination influence vaccine immunogenicity and hence level of protection against disease pathogenesis.

Methods:

Here, we analysed in 34 seronegative individuals, the baseline transcriptome and immune parameters that are associated with activation of CD4+ and CD8+ T-cells as well as neutralizing antibody titres after live-attenuated yellow fever (YF17D) vaccination.

Results:

We found baseline gene expression signatures associated with cellular and humoral responses. Increased abundance of baseline B- and T-cell transcripts, as well as lower expression on monocyte-related transcripts at baseline, were significantly correlated with neutralizing antibody titres. In contrast, higher baseline frequencies of activated CD4+ and CD8+ T-cells with increased expression of cell-cell junction assembly proteins were correlated with stronger CD8+ responses after YF17D vaccination. Based on these findings, we curated a set of baseline gene signatures, which we have named CD8Sig and AbSig, that respectively predict CD8+ T-cell and neutralizing antibody responses to YF vaccination. Critically, we show that AbSig predicted antibody responses to YF17D in an independent cohort. However, AbSig was not predictive of the antibody response to inactivated influenza vaccination, suggesting that different baseline states govern response to different forms of vaccines.

Conclusion:

Our findings indicate there exist baseline immune correlates of YF17D immunogenicity and raise the prospect using such correlates to personalise vaccination.

DELEGATES' ABSTRACTS

Associations of Neutrophils Granular Proteins with Dengue-Associated Cardiac Impairment in Adults

Andrew Teo[1], Chia Po Ying[2], Yeo Tsin Wen[1]

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2 National Centre for Infectious Diseases, Singapore

Background:

Cardiac dysfunction in dengue contributes to pathogenesis of severe dengue. Extracellular histones released by neutrophils have been shown to mediate cardiac dysfunction in sepsis, and in a murine mode of dengue, oxidative stress was associated with dengue-associated pathology. However, their roles in mediating cardiac complications in clinical dengue have not been examined.

Methods:

Adult dengue patients and controls were prospective enrolled. Cardiac parameters, stroke index, stroke volume and Granov-Goor Index, were documented with a bioimpedance device. Blood plasma levels of citrullinated histones H3 (citH3), myeloperoxidase (MPO) and Troponin-T were determined by ELISA. Dengue samples were taken at febrile, critical and recovery phases.

Results:

One hundred and thirty-seven patients were recruited: 44 dengue fever, 51 dengue with warning signs, 12 severe dengue and 30 controls. In critical phase, all cardiac parameters were significantly decreased in severe dengue, suggesting dengue-associated cardiac dysfunction. CitH3 levels was elevated in severe dengue but did not correlate with cardiac parameters. In contrast, MPO levels were elevated, and levels negatively correlated with cardiac parameters and positively correlated with Troponin-T.

Conclusion:

In critical phase, cardiac function was significantly decreased, and both MPO and citH3 levels were significantly increased in severe dengue compared to dengue fever and controls. MPO but not citH3 may contribute to dengue-associated cardiac dysfunction.

DELEGATES' ABSTRACTS

Targeting Glycolysis Reduces Infection and Dampens Inflammation in a Host-Directed Therapy for Dengue

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Abstract:

Monocytes are key mediators of inflammatory responses in dengue patients and are also the only blood cell type that supports productive virus replication both in vitro and in vivo. In this study we assessed how dengue infection alters the glycolytic response of monocytes and affects ensuing inflammatory mechanisms. We show that primary human monocytes infected by dengue virus (DENV) in vitro and monocytes isolated from thrombocytopenic dengue patients, during critical stage of the disease, have increased glycolysis. Single cell transcriptomics revealed an enhanced expression of interferon-related genes and glycolytic genes in classical and intermediate monocytes of dengue patients with more pronounced thrombocytopenia. Targeting glycolysis by 2-deoxy-glucose (2DG) reduce dengue infection and dampened pro-inflammatory cytokines in monocytes, both in vitro and in mouse models. Collectively, these results suggest that glycolysis could be a possible target to regulate pathogenic host responses in dengue.

Potential Serological Cross-Reactivity Between Dengue Antibody and Severe Acute Respiratory Syndrome Coronavirus 2

K Tayong, T Hunsawong, D Buddhari, K Rungrojcharoenkit, R Suthangkornkul, J Lohachanakul, K Sirikajornpan, P Rodpradit, C Klungthong, T S. Cotrone, S Fernandez, A R. Jones

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Abstract:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreaks continue to increase and affect worldwide including the endemic areas of dengue virus (DENV) infection. Serological cross-reactivity between DENV and SARS-CoV-2 is being aware as it can lead to misdiagnosis for both diseases. Here, we demonstrated the potential cross-reactivity of DENV antibodies with SARS-CoV-2 using well-characterized acute and convalescent samples collected before SARS-CoV-2 outbreak including normal human serum (n=6), Febrile illness (n=23), primary DENV (n=20) and secondary DENV (n=20). The majority of anti-SARS-CoV-2 antibodies positive samples was fall under primary DENV infection (16.9% of positive rate) and we found the moderate correlation between DENV IgM antibody and EUROIMMUN SARS-CoV-2 spike 1 ELISA. Among ELISAs positive samples, only four samples had detectable neutralizing antibody against SARS-CoV-2 luciferase reporter virus particles Wuhan strain. These data indicate a potential of serological cross-reactivity between these two viruses and provide an awareness on antibody testing especially in the endemic areas of DENV infections.

A single histidine to arginine substitution on the pre-membrane (prM) protein attenuated a type-2 dengue virus that caused the South Pacific Island Outbreaks in the 1970s

ANX Choi, MM Choy, T Siriphanitchakorn, M Manuel, LZ Lin, X. Yap, EE Ooi, and DJ Gubler
Duke-NUS Medical School, Singapore.

Background:
Dengue is an acute mosquito-borne viral disease that is caused by four antigenically distinct dengue viruses (DENVs). Transmitted by Aedes mosquitoes, DENVs are hyperendemic throughout the tropics and subtropics, with frequent cyclical and explosive epidemics. Despite the worsening trends, the molecular basis of DENV fitness in its natural epidemiological settings remain poorly understood. We examined the American genotype DENV-2 which caused outbreaks in the South Pacific Islands in the 1970s, where the disease that was initially severe became attenuated when the virus, which first emerged in Tahiti, reached the Kingdom of Tonga.

Methods:
Phylogenetic analysis found three main amino acid changes within the pre-membrane (prM) and non-structural genes NS2A and NS4A that defined the Tongan viruses. We constructed infectious clones of these DENVs using published viral genome sequences for characterization in vitro and in vivo.

Results:
We identified a single Histidine to Arginine substitution at position 86 of the prM protein (H86R) as the main driver of DENV-2 attenuation seen in Tonga. This single substitution reduced the in vitro and in vivo viral replication rate of DENV-2 in mammalian systems; however viral replication remained unimpaired in Aedes aegypti mosquitoes. Reversing arginine back to histidine on a Tongan DENV backbone restored virus replication to levels comparable to the New Caledonia DENVs, where a large outbreak of severe disease occurred. The prM H86R switch did not compromise DENV maturation.

Conclusions:
Our findings suggest that prM may have functional roles in influencing DENV egress from infected cells and may have other functions besides a chaperone for the envelope protein. These functions may be critical for the epidemiological fitness of DENVs.

Case Report: Dengue hemorrhagic fever with hepatitis B and C virus patient in Thailand.

Kongkaew Younboonhlim[1]
Hospital for Tropical Diseases, Mahidol University

Abstract:
A case report of dengue hepatitis B and C was reported. In Thailand, there are still few reports. In most cases, only one type of hepatitis B or C is reported.

From the review of medical history data from medical records, it was found that a 38-year-old male patient had a history of alcohol dependence, high blood pressure, hepatitis B and C infected. The patient came to have wisdom teeth surgery. The blood pressure was measured 3 times and the value was in the range; 180-190/110-125 mmHg. The dentist did not perform the wisdom tooth removal. Then the patient had a severe tremor, headache, and was send to the Hospital for Tropical Diseases. Found that there was scurvy. Blood pressure was 210/121 mmHg.

Laboratory showed positive for dengue NS1Ag, anti-dengue IgG and IgM. Hepatitis B virus test found the virus does not multiply or multiply in small quantities. He had acidosis, bleeding in the urine, low platelet count, abnormal liver function.

The patient was taken to the intensive care unit with fluids and blood transfusion. The patient was hospitalized for five days until recovered.

Evaluation of alternative methods for determining dengue serotype-specific immunity in serum samples

VSL Goh[1], CCW Ang [1], PX Lee[1], LC Ng[1,2], YX Setoh[1,3,4], JCC Wong[1]

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2 School of Biological Sciences, Nanyang Technological University, Singapore

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4 Infectious Diseases Translational Research Programme (ID TRP), Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Background:

The quantification of serotype-specific dengue neutralising antibodies from serum samples is performed using the gold-standard plaque reduction neutralisation test (PRNT). PRNTs are known to be labour-intensive, time-consuming, requiring manual plaque counting and not adaptable for high-throughput screening. In this study, we report the evaluation of three candidate alternative methods 1) xCELLigence Real-Time Cell Analyzer (RTCA), 2) MTT cell-viability assay, and 3) Immuno Plaque Assay (IPA), and their performance against standard PRNT.

Methods:

All the three methods, as well as the standard PRNT, were performed using 22 serum samples (11 dengue serotype 2 positive, 8 dengue IgG positive, and 3 dengue IgG negative) against a dengue serotype 2 virus.

Results:

We found the PRNT50 titres from IPA and RTCA methods to correlate best with standard PRNT method with R2 values of 0.74 and 0.68 respectively (R2=1 being a perfect fit). The MTT method correlated poorly, with a R2 value of 0.47. At a more stringent PRNT70 titre, MTT method was not suitable, recording a R2 value of 0.06; while the IPA and RTCA methods produced R2 ¬values of 0.67 and 0.93 respectively.

Conclusion:

Overall, the IPA method was the most consistent across PRNT50 and PRNT70 titres, while offering the highest throughput format with the most rapid time to experiment completion and at the lowest cost.

DELEGATES' ABSTRACTS

A national dengue virus surveillance programme for early warning and timely risk assessment

G Yeo[1,*], VSL Goh[1,*], S Tan[1], C Koo[1], YL Lai[1], YX Setoh[1,3,4], HC Hapuarachchi[1], JCC Wong[1], LC Ng[1,2]

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4 Infectious Diseases Translational Research Programme (ID TRP), Yong Loo Lin School of Medicine, National University of Singapore, Singapore

* These authors contributed equally to this work

Abstract:

The National Environment Agency (NEA) adopts an integrated approach in arbovirus surveillance and control, where circulating dengue viruses (DENV), vector populations, case notifications and population immunity are regularly monitored in Singapore. Circulating DENV lineages are monitored through a joint national arbovirus surveillance programme by NEA and the Ministry of Health (MOH) to provide situational assessment and alerts of outbreaks based on DENV serotype/genotype switches and the emergence of new viral strains with potentially high epidemic potential. Residual dengue-positive patient samples collected from an extensive network across all public hospital laboratories, large private laboratories and the Diagnostic Laboratory at the Environmental Health Institute (EHI), are tested at NEA and MOH for serotype and genotype characterisation. Additionally, EHI maintains a virus bank of DENV isolates for in vitro and in vivo virus characterisation studies; for this, we have developed a high-throughput cell-based enzyme-linked immunosorbent assay for the rapid recovery and detection of successful dengue virus isolations from patient serum, a pipeline we named DIPS. Viral RNA purified from isolated virus stocks is used for full genome sequencing, to further advance the genetic resolution of DENV surveillance efforts. Since 2005, NEA's progressive surveillance efforts have guided vector control operations through risk identification and stratification. The surveillance had also detected new/emerging arboviruses, such as chikungunya in 2008/2013, and Zika in 2016. Besides contributing to outbreak predictive tools, the virus bank also provides an invaluable source of information allowing deeper understanding of evolutionary and transmission dynamics of virus populations and on host-immune responses.

Retrospective Analysis of Envelope Gene of Dengue Virus in Thailand, 2003-2013

P. Rodpradit[1], P. Chinnawirotpisan[1], S. Kalayanarooj[2], W. P. Vandepitt[2], W. Manasatienkij[1], K. Joonlasak[1], T. Phonpakobsin[1], K. Hussem[1], Y. Poolpanichupatam[1], A. R. Jones[1], S. Fernandez[1], C. Klungthong[1]

1 Department of Virology, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand

2 Department of Pediatrics, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Background:

Dengue virus (DENV) has been circulated in Thailand since 1950. AFRIMS Thailand has started sampling DENV in Thailand since 1974 to study circulation and epidemiology of all four serotypes.

Method:

In this study, 316 envelope (E) gene sequences of DENV collected in Thailand from 2003 to 2013 included 114, 81, 78, and 43, of DENV-1 to 4, respectively, were sequenced and genetically analyzed.

Results:

Maximum-likelihood phylogenetic trees of DENV E gene sequences revealed that all DENV-1 from 2003 to 2013 were clustered in genotype I (114/114), all DENV-2 from 2003 to 2013 were clustered in Asian I genotype (81/81), DENV-3 from 2003 to 2013 were clustered in genotype I (1/78), II (59/78), and III (18/78), and all DENV-4 from 2003 to 2012 were clustered in genotype I (43/43). DENV genotypes/clades in each serotype of these old viruses were found to evolve and circulate in recent years. Increasing of E gene sequences from these old viruses in phylogenetic analysis defined emerging of new clades in DENV-1, DENV-3, and DENV-4. Unique amino acid substitutions of genotypes/clades in each serotype were also identified in this study.

Conclusion:

Information of DENV E gene sequences in Thailand from the past 11 years, 2003 to 2013, was revealed and increased background sequences resulting in more accurate DENV evolution analysis.

Secondary dengue antibody elicits neutralizing antibody against zika virus infection, in vitro

P. Ong-ajchaowlerd, T. Hunsawong, R. Suthangkornkul, S. Apichirapokey, T.S. Cotrone, S. Fernandez, A.R. Jones

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Abstract:

Dengue (DENV) and zika (ZIKV) viruses are members of the flavivirus family that circulate in overlapping areas in Thailand. Serological cross-reactivity is routinely observed due to amino acid sequence homology between the two. This study aims to evaluate the functional activity of cross-reactivity by determining the levels of neutralizing antibody production against four DENV serotypes and ZIKV in the sera of primary DENV (n=59), secondary DENV (n=58) and ZIKV (n=60) infected patients in Thailand. Using a 90% neutralizing antibody titer (NT90) at a greater than 15 as cut-off, the assay performance was up to 77.5% (95%CI, 62.50-87.68) sensitive and 90.6% (95%CI, 83.95-94.67) specific. None of primary DENV sera had detectable positive NT90 titers whereas 18.9% (n=11) of secondary DENV sera were positive with mean titers of 100.6 (95%CI, 0-224.6). On the other hand, the ZIKV sera showed NT90 titers against all four DENV serotypes with levels comparative to secondary DENV infected samples (p=0.203). Although exposure history data were unavailable, it is likely that those patients from which the Zika sera were collected have been exposed to DENV. This is due to the fact that DENV is endemic to Thailand coupled with the average age of the subjects at 46 (± 17.8) years old. These data indicate a potential for serological cross-protection between these two viruses and provide NT90 cut-off titers to distinguish ZIKV from DENV infections especially in an endemic region.

DELEGATES' ABSTRACTS

A Pre-Membrane Protein PrM D29V Substitution Attenuates a Clinically Tested Live Dengue Vaccine

Milly M. Choy[1], Dorothy H. Ng[2], Hwee Cheng Tan[1], Summer L. Zhang[1], Nanthini Ramanathan[1], Justin Ooi[1], Kuan Rong Chan[1], Eng Eong Ooi[1,3,4]

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2 Department of Infectious Diseases, Singapore General Hospital, Singapore
3 Viral Research and Experimental Medicine Centre, SingHealth Duke-NUS Academic Medical Centre, Singapore
4 Saw Swee Hock School of Public Health, National University of Singapore, Singapore

Background:

A tetravalent dengue vaccine development has been challenging due to insufficient knowledge on dengue virus (DENV) pathogenesis. Understanding the genetic and molecular basis of attenuation will allow us to develop a targeted mutagenesis approach to derive all 4 attenuated DENVs that is sufficiently safe but immunogenic. This knowledge will also be useful in the identification of host dependency factors that can be targeted for the development of antiviral therapeutics.

Methods:

We have been studying the molecular properties of a live-attenuated DENV2 strain, PDK53, derived through 53 serial passages of wild-type 16681 strain, in primary dog kidney cells. PDK53 has successfully completed a phase-3 clinical trial, and differs from its parental 16681 strain by five amino acid substitutions and one consensus mutation in the 5' untranslated region of the genome. To identify attenuating mutations, we use site-directed mutagenesis on a 16681 infectious clone.

Results:

We identified the aspartate-to-valine substitution in the pre-membrane protein that attenuated 16681 in mammalian cells but not mosquitoes. Using genomics coupled with proteomics approaches, we found that prM D29V resulted in the loss of binding of wild-type prM to HMGB1, a cytokine mediator of inflammation. Binding of prM could influence the nuclear localization of HMGB1 to reduce antiviral activity that might otherwise attenuate infection.

Conclusions:

We propose that the loss of binding to HMGB1 is responsible for restricted virus dissemination in mammalian cells observed in our mutant. More mechanistic studies to study the interaction with HMGB1 will further define the role of prM as an inhibitor of host antiviral response.

DELEGATES' ABSTRACTS

Comparative Effects of Ivermectin and Moxidectin on Anti-Dengue Activities and Cellular Responses in Hepatocytes

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Background:

The number of dengue cases reported to WHO increased steadily over the last 20 years. Currently, there is no specific treatment for dengue; therefore the use of repurposed drugs could be one of the best strategies. While ivermectin, a FDA-approved anti-parasitic medication, has been studied for its DENV inhibitory effect, the role of its structurally related drug with longer half-life in humans, moxidectin, has not yet been shown in dengue. Herein, we investigated the anti-DENV effects of moxidectin in comparison with ivermectin in human hepatocytes.

Methods:

The CC50 and EC50 values of both drugs were determined. The viral replication steps affected by these drugs were determined by time-of-drug addition and time course assays. Expression levels of major cytokine genes in hepatocytes upon drug treatment were measured by qRT-PCR.

Results:

Moxidectin had lower cytotoxicity but similar anti-DENV efficiency, as compared to ivermectin. Significant reduction in viral production was observed when the drugs were added to the cells 2-8 hours post-infection. Both drugs exhibited antiviral properties against all four DENV serotypes (both laboratory and clinical strains) with the lowest efficacy on DENV-4. Interestingly, both ivermectin and moxidectin could reduce pro-inflammatory cytokine gene expressions, but only ivermectin could up-regulate antiviral gene responses.

Conclusion:

In conclusion, our study demonstrates, for the first time, the potential use of moxidectin as a safe dengue medication. Both ivermectin and moxidectin disrupt DENV replication/production at the early stages in the virus life cycle and possess anti-inflammatory properties, but only ivermectin has additional effects on antiviral immune responses.

DELEGATES' ABSTRACTS

Role of T-cell immunity in skin and blood in Dengue virus infection

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Background:

DENV is transmitted via the Aedes mosquito bite on the human skin. Circulating dengue-specific T-cells express the Cutaneous Lymphocyte-Associated Antigen (CLA) marker to home to the skin, where they potentially become tissue-resident memory T (TRM) cells. In other viral infections, TREM cells are necessary for immune protection but their role in dengue remains unknown.

Methods:

Flow cytometry was used to investigate the phenotype and relationship of T-cells derived from peripheral blood and skin-suction blisters of acute dengue patients in Singapore. We studied the total CD4+ and CD8+ T-cells, as well as virus-specific T-cells using dengue peptide-HLA tetramers.

Results:

Preliminary results from t-Distributed Stochastic Neighbor Embedding (tSNE) and clustering algorithm PhenoGraph show that skin and blood T-cell populations are largely distinct from one another. CD4+ and CD8+ T-cells in the skin are more activated and proliferating compared to the blood. They highly express markers of tissue residency CD69 +/- CD103, which suggest their roles as TRM cells. Significantly higher proportions of responding Ki67+CD4+ T-cells in the skin express Granzyme B compared to those in the blood, suggesting that the skin CD4+ T-cells may be different from their blood counterparts. Furthermore, dengue-tetramer+ cells are largely activated, with an effector memory phenotype. Ongoing analyses of T-cell populations aim to show the correlations of their features in the skin and blood with clinical data.

Conclusions:

This study of the features of cell populations in blood versus skin in acute infections may give us insights into the role of dengue-specific T-cells and TREM cells for immune protection and/or immunopathology.

DELEGATES' ABSTRACTS

Acute dengue virus infections among blood donors in Thailand

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Background:

Most people with dengue virus (DENV) infection remain asymptomatic, increasing the risk of DENV transfusion transmission (TT-DENV) in endemic areas. This study aimed to determine the evidence of DENV infection in blood donors from different geographic regions of Thailand.

Methods:

We performed a cross-sectional study on blood donor samples collected from the Thai red cross-national blood center and four regional blood centers, including Chiang Mai, Khon Kaen, Chon Buri, and Phuket province between March to September 2020. The residual blood of 1,053 donors was screened for the presence of DENV nonstructural protein 1 (NS1), anti-DENV immunoglobulin G (IgG) antibodies, and IgM using enzyme-linked immunosorbent assay (ELISA) kits.

Results:

Anti-DENV IgG seroprevalence was 89%, and the prevalence increased with age, with the lowest in the 18–20 years age group (80.6%) and the highest in the 41-50 years age group (96.0%). In addition, 0.4% and 2.1% of Thai blood donors were NS1 and IgM positive, respectively, reflecting the acute stage of dengue infection during their donation time.

Conclusions:

There was a high rate of asymptomatic dengue virus infection among healthy blood donors in Thailand. It can hypothetically result in TT-DENV. Particular attention should be devoted to the donor selection criteria, and additional screening tests might be required.

Isolation and characterization of an insect-specific flavivirus (Quang Binh virus) from *Culex spp* mosquitoes in Singapore

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Abstract:

Insect-specific flaviviruses (ISFs) have increasingly been isolated from mosquito species from different parts of the world. Compared to medically important flaviviruses like dengue, Zika, and West Nile viruses that replicate efficiently in both mosquitoes and mammalian hosts, ISFs replicate efficiently in mosquitoes but appear to be defective in their replicative ability in vertebrate hosts. As such, ISFs are not a human health concern. However, they may provide insights into transmission mechanisms and also have potential applications in the development of vaccines and diagnostic antigens. Using the established MAVRIC assay (monoclonal antibody against viral RNA intermediates in cells), we report here the isolation of an ISF from Culex gelidus pools collected in the northern coastal region of Singapore, that showed a partial NS5 sequence homology of 95% to Quang Binh virus (QBV). QBV was first reported in Vietnam, and later shown to also be present in China. Similar to other ISFs, the QBV isolated in this study grows efficiently in C6/36 mosquito cells but failed to replicate in a Vero vertebrate cell line. We also demonstrated that QBV was able to inhibit the replication of dengue virus in co-infected C6/36 cells via the mechanism of superinfection inhibition. To determine the spatiotemporal distribution and prevalence of QBV in Singapore, a qRT-PCR specific to the NS5 region obtained will be used to screen mosquito samples collected from various geographical sites across the country. This report represents the first virus isolation of an ISF in Singapore and paves the way for more comprehensive investigations to understand the mosquito virome of urban and rural mosquitoes in Singapore.

DELEGATES' ABSTRACTS

Burden, risk factors and clinical characteristics associated with dengue among Filipino children presenting with an acute febrile illness: An interim analysis of a community-based cohort study

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Background:

Symptomatic dengue infection generally presents as an acute febrile illness that is difficult to differentiate from other causes of fever. We aimed to assess the risk factors and clinical characteristics associated with dengue fever versus non-dengue illness in older children in Cebu, Philippines.

Methods:

This is a prospective community-based cohort study in Cebu that enrolled 2,996 healthy children 9 to 14 years of age in May 2017. Baseline sera were collected and batch tested by indirect IgG ELISA and focus reduction neutralization test (FRNT). From June to August 2017, 1,810/2,996 (60.4%) children received a single dose of CYD-TDV. Active surveillance for an acute febrile illness in the cohort started in November 2017 and is on-going. Those who develop an acute febrile illness are identified, epidemiological and clinical data are collected, and blood drawn for confirmation of dengue by RT-PCR. We compared baseline dengue serostatus, epidemiological and clinical characteristics among those with virologically-confirmed dengue (VCD) and a non-dengue illness.

Results:

From November 2017 to November 2020, 652 children had an acute febrile episode, of which 141 (21.6%) were VCD. The estimated incidence is 15.7 symptomatic VCD cases/1000 persons/year. Of the 141, 67 (47.5%) were classified as dengue fever, and 74 (52.5%) dengue fever with warning signs and none with severe dengue. VCD cases were more likely to be dengue seronegative at baseline ($p<0.001$) and have a lower baseline geometric mean IgG ELISA titer ($p<0.001$) than non-dengue cases. VCD cases were more likely to be admitted to hospital ($p<0.001$), have not received a dose of dengue vaccine ($p=0.001$) and have a neighbor diagnosed with dengue within the past 7 days ($p=0.001$). Clinical manifestations predictive of dengue included nausea/vomiting ($p<0.001$), rash ($p<0.001$), retroorbital pain ($p=0.038$), anorexia ($p=0.040$), and flushed skin ($p=0.016$).

Conclusion:

Symptomatic dengue causes a considerable burden in this age group and setting, with nearly a quarter of cases requiring hospital admission and evidence of community clustering. Baseline serostatus is a strong predictor of VCD versus non-dengue illness.

Perception of Dengue and acceptability of Dengue vaccines in University students: a worldwide survey

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Background:

Dengue is the most prevalent arbovirus at present. Almost half of the global population are at risk of dengue virus infection along with 50-60 million people each year with clinical manifestations. Currently, there is only one licensed dengue vaccine. Several other vaccine candidates are at different stages of clinical development. Acceptability studies of dengue vaccines in university students are scarce. The objective of this study was to understand the level of awareness about dengue disease and dengue vaccines in university students of science, commerce, and humanities worldwide.

Method:

An online survey containing questions regarding demography, dengue disease history, acceptance for a future vaccine and rationale for vaccine hesitancy, was launched and circulated in different social media platforms: WhatsApp, Facebook, LinkedIn, Twitter, and Instagram. It was open for 6 weeks to the targeted population- University students.

Result:

225 students from 50 countries took the survey. Due to the number of responses from each country, they were grouped into 8 clusters (Africa, Western Europe, Eastern Europe, South Asia, Asia Pacific, Latin America, North America, and Bangladesh). 1/3rd of the respondents had personal exposure to dengue. Overall, 80% (n=147) of the sample were willing to take any dengue vaccine, however, the key reason behind the reluctance of 20% of the respondents was inadequate information about dengue vaccine.

Conclusion:

Results of the survey provides an overview of the perception on dengue and dengue vaccines in university students around the world, grouped by regions of different endemicity levels. This study can inform future education needs and help design future studies and surveys in this population.

DELEGATES' ABSTRACTS

T Cell Responses to Dengue 2 NS1 Linear Peptides in a Sri Lankan Cohort

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Background:

Dengue virus (DENV) NS1 causes vascular leak and induce cytokines in blood mononuclear cells. As T cell responses to NS1 has not been extensively studied, we investigated the T cell responses in individuals with varying severity of past dengue infection.

Materials and Methods:

NS1-specific IFNγ ELISpot responses were assessed for 47 overlapping peptides (five pools) spanning DENV2 NS1 protein in 36 healthy adults with past non-severe (NSD=23) and severe dengue (SD=13). Responses to peptides with the highest frequency of T cell responses were further evaluated. The probable HLA restriction was further evaluated using the SYFPEITHI (http://www.syfpeithi.de/) epitope prediction program.

Results:

15/36 responded to pool 2 overlapping pool of peptides and 18/36, to pool 3. During further dissection of T cell responses, pep22 of pool 3 elicited a response in 9/20 individuals, while other peptides in pool 2 and 3 elicited responses in <5 individuals.No difference was seen in the frequency of ELISpot responses to pool 2 (p=0.511), pool 3 (p=0.99) or peptide 22 in those with SD and NSD. HLA predictions gave the highest binding score to peptide 22 and was predicted to be restricted through HLA-A*68.01 (Score30), HLA-A*24.02 (score28) and HLA-DRB1*11.01 (score24).

Conclusions:

Peptides representing the wing domain of dengue NS1 elicited the highest T-cell responses. Peptide22 was the most immunodominant peptide irrespective of past dengue severity. The clinical significance of these findings should be further evaluated.

Secreted dengue virus NS1 is predominantly dimeric and in complex with high-density lipoprotein

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Abstract:

Severe dengue infections are characterized by endothelial dysfunction shown to be associated with the secreted nonstructural protein 1 (sNS1), making it an attractive vaccine antigen and biotherapeutic target. To uncover the biologically relevant structure of sNS1, we purified the native form of sNS1 from cells infected with either the DENV WT or T164S mutant identified from a severe dengue outbreak in Cuba. We determined the cryoEM structures of sNS1 and its complex with a monoclonal antibody/Fab and found that the major species of sNS1 is a 1:1 complex of the NS1 dimer embedded in a High Density Lipoprotein particle. Cross-linking MS studies confirm NS1:ApoA1 dimer formation with most ApoA1 interaction sites mapped to the NS1 wing and hydrophobic domains. Our results shed fresh light on the molecular pathogenesis of dengue and may have broad implications for managing dengue infection.

The impact of NS5 localisation on dengue pathogenesis

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Background:

Dengue virus (DENV) non-structural protein 5 (NS5) is critical for viral RNA synthesis within endoplasmic reticulum (ER)-derived replication complexes in the cytoplasm, however a proportion of NS5 is known to be localised to the nucleus of infected cells. The importance of nuclear DENV NS5 on viral replication and pathogenesis is still unclear.

Methods:

We generated wildtype and mutant DENV infectious clones to identify NS5 P884 as a major determinant of NS5 nuclear localisation. We utilised various cell line and animal models of infection to study the impact of NS5 relocalisation on viral replication and pathogenesis.

Results:

We show that a single NS5 P884T amino acid substitution is sufficient to relocalise a significant proportion of DENV2 NS5 from the nucleus to the cytoplasm of infected cells. This P884T mutant replicates similarly to the parental wild-type infectious clone-derived virus while inducing a greater type I interferon and inflammatory cytokine response. In both AG129 mouse and *Aedes aegypti* mosquito infection models, the P884T virus exhibits lower levels of viral replication only at early timepoints. Intriguingly, there appears to be selection pressure to revert to the wild-type proline in P884T-infected *Aedes aegypti*, in agreement with the high conservation of this residue in DENV2, 3 and 4.

Conclusion:

Our results suggest that the predominantly nuclear localisation of DENV NS5, while not required for viral RNA replication, plays a role in pathogenesis and modulation of the host immune response, and contributes to viral fitness in the mosquito host.

Experimental Evidence for Maternal-Fetal Transmission of Dengue Virus in Pregnant Mice

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Background:

Congenital disorders associated with prenatal vertical transmission of Zika virus (ZIKV) is well established since the 2016 outbreak in the Americas. However, despite clinical reports of similar mode of transmission for other flaviviruses such as dengue virus (DENV), the phenomenon has not been experimentally explored.

Methods:

Pregnant AG129 mice were infected with DENV1 in the presence or absence of enhancing antibodies at different gestational time points. ZIKV was used for comparison. We quantified viral load in fetus and placentas and performed comprehensive gene expression profiling in the maternal (decidua) and fetal portion of placenta separately.

Results:

We demonstrate for the first time in a laboratory experimental setting that DENV can be transmitted vertically in a gestation stage-dependent manner similar to ZIKV, and this incidence drastically increases in the presence of enhancing antibodies. Interestingly, a high rate of DENV fetal infection occurs even though the placental viral load is significantly lower than that found in ZIKV-infected dams. Comprehensive gene expression profiling revealed DENV infection modulates a variety of inflammation-associated genes comparable to ZIKV in decidua and fetal placenta in early pregnancy.

Conclusion:

Our findings suggest that the virus-induced modulation of host gene expression may facilitate DENV to cross the placental barrier in spite of lower viral burden compared to ZIKV. This new mouse model may serve to identify the host determinants required for the vertical transmission of flaviviruses and develop appropriate countermeasures.

DELEGATES' ABSTRACTS

Comparative proteomic analysis of dengue virus-human interactions during virus infection reveals host targets for antiviral therapeutics

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Background:

Dengue virus causes a wide variety of dengue diseases that endanger over half of the world's population. At present, there is no antiviral therapeutics against dengue infection. Virus infection and its associated pathologies are the result of a myriad of interactions between the virus and its host. Protein-protein interactions (PPIs) make up a significant proportion of these interactions as the virus-encoded proteins modulate the host environment for its own benefit by interacting with host proteins individually or together with its fellow virus proteins. Thus studies of these virus-host PPIs are most informative when performed in the context of an infection.

Methods:

We co-expressed tagged DENV proteins in the context of virus infection, and then performed comparative affinity purification-mass spectrometry (AP-MS) to generate a comprehensive DENV-human protein interactome during virus infection.

Results:

The top enriched terms of these interacting proteins were related to RNA metabolism, asparagine N-linked glycosylation and the molecular chaperone CCT complex. We expanded on our understanding of previously identified host protein targets of DENV such as the oligosaccharyltransferase (OST) complex, CCT/TRiC chapherone and U5 snRNP spliceosome, and identified novel members of the human mRNA processing machinery as interactors of DENV proteins. Finally, targeting these pathways through RNA interference or small molecule inhibitors led to the impairment of virus replication.

Conclusion:

In summary, we present a comprehensive virus-host protein-protein interactome in the context of virus replication, which uncovered multiple host pathways and protein complexes that are viable targets for antiviral therapeutics.

Understanding Disease Pathogenesis Of Two Different Denv2 Strains From The Cosmopolitan Genotype

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Background:

Dengue viruses (DENV) cause severe and sudden human epidemics around the world, with DENV2 being a common serotype causing outbreaks in Singapore. From the dengue surveillance perspective, it is important to understand the disease pathogenesis of endemic strains for better disease control.

Methods:

We compared the disease/infection phenotype of two DENV2 cosmopolitan genotypes: Clade1A DENV2-3295 (EDEN2) and Indian sub-continent lineage DENV2 (D2Y10) using an in vitro human peripheral blood mononuclear cells (PBMCs) assay and DENV viremic AG129 mouse model. The infectivity and transmission potential of these two viruses were also assessed in an Aedes aegypti mosquito infection model.

Results:

The Indian sub-continent lineage strain D2Y10 resulted in prominent virus infection enhancement of PBMCs in the presence of sub-neutralizing anti-E protein antibodies compared to Clade1A DENV2 (EDEN2; EU081177) despite a slower replication rate than the latter. This higher enhancement of infection by D2Y10 appears to correlate with better binding of the virus-antibody complex to the cells leading to greater internalization. AG129 mice infected with D2Y10 displayed a delayed mortality accompanied with higher peak viremia compared to the infection with non-lethal EDEN2 infection. A higher infection rate and infectivity in the salivary glands of the mosquitoes infected with D2Y10 was observed. Collectively our results demonstrated a potentially more virulent phenotype and greater transmissibility of D2Y10. On-going efforts in identifying critical viral determinants contributing to the observed pathogenicity of D2Y10 through NextGen Sequencing are underway.

Conclusion:

This study has implicated the potential importance of identifying the viral determinants of severity as predictive markers for public health management of future severe dengue outbreaks.

DELEGATES' ABSTRACTS

Co-circulation of dengue virus serotypes in Cebu, Philippines

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Background:

Repeat dengue infections may occur and there is an increased risk of severe dengue during secondary infection. We aimed to determine whether there is concomitant circulation of all four DENV serotypes by time and place in Cebu, Philippines.

Methods:

Blood samples from children participating in an ongoing observational study at four study sites in Cebu were collected and tested by dengue RT-PCR. We analysed the dengue virus (DENV) serotypes detected between 2018 to 2020 by date of illness (defined as the day of fever onset for an acute febrile illness) and by place of residence of the case (city or municipality in Cebu) empirically grouped into three geographic clusters (Western, Eastern and Northern clusters).

Results:

There were 507 virologically confirmed dengue cases detected out of the 712 children who presented with febrile illness in our study from 1 February 2018 to 15 February 2020. Of the 507 virologically-confirmed cases, 276 (54.4%) were DENV-3, 170 (33.5%) DENV-2, 39 (7.7%) DENV-1, and 22 (4.3%) DENV- 4. All four DENV serotypes were identified in each time period during the surveillance and across the geographic clusters, with consistent predominance of DENV-3 and DENV-2.

Of the 507 dengue cases, 162 (31.9%) had a final clinical diagnosis of dengue fever, 340 (67%) dengue fever with warning sign(s) and five (0.9%) severe dengue.

Conclusion:

In summary, our study provides strong evidence on the concomitant presence of the four DENV serotypes in Cebu, Philippines. Co-circulation of all four serotypes place the members of the community at risk of repeat dengue infections and highlights the need for effective strategies against dengue.

DELEGATES' ABSTRACTS

Sulfonyl anthranilic acid (SAA) derivatives as a potent inhibitor against Dengue virus infection

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Background:

The lack of effective antivirals and lower protective efficacy of the licensed vaccine against DENV prompted the need to search for better therapeutic interventions. A new Sulfonyl anthranilic acid (SAA) series was designed based on scaffold hopping strategy of the dioxide series to improve the compounds' membrane permeability and reduced cytotoxicity.

Methods:

Dose-response inhibition experiment of SAA against DENV was performed to determine the EC50 and CC50 values. Time-of-drug-addition assay (TODA) was carried out to investigate the mechanism of action of the most potent compound - FlaR18, followed by quantification of viral RNA level and viral protein production. The efficacy of FlaR18 is also evaluated in different cell lines. Thermal proteome profiling (TPP) was performed to investigate the binding target of FlaR18.

Results:

FlaR18 exhibited good efficacy against all four DENV serotypes in HuH7 cells with low sub-micromolar range of EC50 value. TODA study revealed that FlaR18 is a post-entry stage inhibitor acting on viral replication. Quantification of viral RNA by qRT-PCR showed a decrease in both extracellular and intracellular RNA, coupled with a reduction in infectious virus production. Differences in FlaR18 efficacy was observed in different cell lines, indicating that host factors may be implicated in its mode of action during viral infection. Preliminary results of TPP showed that membrane trafficking proteins could be the potential target of FlaR18.

Conclusion:

FlaR18 is active across all four dengue serotypes with low-submicromolar of EC50 value. FlaR18 is potentially targeting host factors during viral infection.

First-in-class, potent, pan-serotype dengue antiviral inhibitor JNJ-1802 targets the nonstructural protein 3-4B interaction

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Background:

Dengue is reported as the most rapidly spreading mosquito-borne viral disease worldwide. Each of the four globally distributed dengue virus (DENV1-4) serotypes can induce the full spectrum of clinical symptoms. Currently, no antiviral drugs are available for the treatment or prophylaxis of dengue. We previously reported the identification of a potent, pan-serotype dengue antiviral inhibitor JNJ-1802. Here, we aimed to identify the molecular target of JNJ-1802 that has further progressed in clinical development.

Methods:

For target identification, in vitro selection experiments were performed in the presence of increasing JNJ-1802 concentrations. Using site-directed mutagenesis, we inserted the identified mutations into a subgenomic DENV-2/16681 reporter and assessed the replication fitness and inhibitor resistance caused by these mutations. Finally, the effect of JNJ-1802 on the nonstructural protein 3 (NS3)–NS4B interaction was studied using immunoprecipitation experiments.

Results:

Persistent resistance mutations only emerged in vitro following a lengthy period of selection indicating that the compound has a high genetic barrier to resistance. These mutations reduced the activity of JNJ-1802 and were mapped to NS4B, pointing towards NS4B as the possible target of JNJ-1802. We then studied the possible effect of JNJ-1802 on NS4B and found that JNN-1802 blocks the interaction between NS3 and NS4B but does not disrupt existing NS3-NS4B complexes.

Conclusion:

JNJ-1802 is a first-in-class, antiviral agent with pan-serotype activity and a high barrier to resistance that can potentially be used for the prevention and/or the treatment of dengue.

Metabolic processes are differentially regulated during wild-type and attenuated dengue virus infection in *Aedes aegypti*

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Background:

Dengue virus (DENV) must successfully complete its life cycle in its mosquito vectors in order to be sustained in a human-mosquito-human transmission cycle. However, the virus-mosquito interactions that underpin this critical event have been remained poorly defined. Here, we explored the transcriptomic changes of Aedes aegypti mosquito, the principal DENV vector, in response to infection with the wild-type DENV2 16681 strain and its attenuated derivative, PDK53, which has been shown to be refractory in infecting Aedes aegypti.

Methods:

We intrathoracically infected Aedes aegypti with 16681 and PDK53. We then measured virus replication using RT-qPCR and probed for differences in host transcriptomics responses using high-throughput RNA sequencing.

Results:

As expected, the replication rate of attenuated PDK53 was lower than that of wild-type 16681. At an early time-point where there are no differences in 16681 and PDK53 RNA levels, we identified 1,629 differentially expressed genes (DEGs) during 16681 infection, compared with only 22 DEGs identified during PDK53 infection, indicating that 16681 infection triggers more transcriptomic changes compared to PDK53 infection. Functional classification of the DEGs unique to 16681 infection further revealed that most of these genes are related to metabolism, suggesting the involvement of metabolic alterations for efficient DENV replication.

Conclusion:

The findings reveal differential regulation of metabolic transcripts during wild-type DENV infection, and suggest involvement of metabolic processes for efficient DENV replication in mosquito vectors.

Efficacy and Safety of Takeda's Tetravalent Dengue Vaccine Candidate (TAK-003) After 4.5 Years of Follow-Up

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Background:

An ongoing long-term efficacy trial in eight dengue-endemic countries is evaluating a recombinant tetravalent dengue vaccine based on a DENV-2 backbone (TAK-003). Here we present an additional 18 months of follow-up data for a total of 4.5 years of follow-up.

Materials and methods:

From September 2016 to March 2017, healthy 4–16-years-old children (n=20,099) were randomized 2:1 to receive two doses of TAK-003 or placebo three months apart and were under active febrile illness surveillance to detect symptomatic dengue (both outpatient and hospitalized) using a serotype-specific RT-PCR. Serious adverse events (SAEs) were collected throughout the trial.

Results:

20,071 children received ≥1 dose of TAK-003 or placebo; 27.6% (5547/20,063) were seronegative at baseline. 18,260 (91.0%) completed up to 4.5 years post vaccination follow-up and 27,684 febrile illnesses were reported. These led to detection of 1007 RT-PCR confirmed dengue cases, 188 of which required hospitalization. The cumulative vaccine efficacy from first dose until 4.5 years after the second dose was 61.2% (95% confidence interval, 56.0–65.8) against virologically-confirmed dengue (VCD) and 84.1% (77.8–88.6) against hospitalized VCD. Efficacy continued beyond 3 years of vaccination regardless of baseline serostatus with sustained robust protection against hospitalized VCD. SAE rates were similar between the vaccine and placebo groups. No important safety risks were identified.

Conclusion:

Two doses of TAK-003 three months apart were well-tolerated and protected against symptomatic dengue through 4.5 years after vaccination in dengue-naïve and pre-exposed children in dengue-endemic countries. Efficacy was higher and sustained against dengue leading to hospitalization.

Funding:

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Immunogenicity and safety of concomitant and sequential administration of a yellow fever and tetravalent dengue vaccine: a phase 3 randomized, controlled study

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Background:

A dengue vaccine that can be administered regardless of previous exposure remains an unmet need. As dengue and yellow fever (YF) are often endemic in the same regions, this phase 3 randomized controlled study evaluated the immunogenicity and safety of concomitant and sequential administration of a tetravalent dengue vaccine (TAK-003) with YF-17D vaccine in 18–60 year-olds (NCT03342898).

Methods:

900 participants were randomized 1:1:1 to receive on Days 1/90/180: YF-17D+placebo/TAK-003/TAK-003 (Group 1); TAK-003+placebo/TAK-003/YF-17D (Group 2); TAK-003+YF-17D/TAK-003/placebo (Group 3). The primary objective was non-inferiority (upper limit of 95% confidence interval [UL95%] of difference <5%) of YF seroprotection (neutralizing titer ≥10) rate one-month post-YF-17D co-administered with TAK-003 (Group 3) versus alone (Group 1). Secondary objectives included non-inferiority of YF and dengue geometric mean titers (GMTs) [UL95% for GMT ratio <2.0], and safety.

Results:

One month after vaccination, co-administration of YF-17D and TAK-003 provided non-inferior YF seroprotection rate versus YF-17D alone (99.5% vs 99.1%; difference: 0.4% [−1.85 to 2.69%]). GMTs were non-inferior for YF (UL95% for GMT ratio: 1.26) and dengue serotypes DENV-2 (1.75), DENV-3 (1.61), and DENV-4 (1.46) but not DENV-1 (2.22). Adverse event rates following TAK-003 were consistent with previous studies. No important safety risks were identified.

Conclusion:

TAK-003 and YF-17D were immunogenic and well-tolerated when concomitantly or sequentially administered. Concomitant administration demonstrated non-inferiority of immune responses to both, except against DENV-1, with lower titers versus sequential vaccination, but similar to titers observed in other TAK-003 trials.

Funding:

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Co-administration of a tetravalent dengue vaccine (TAK-003) with hepatitis A vaccine

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Background:

Vaccination against hepatitis A virus (HAV) is recommended for many travellers worldwide, including travel to dengue-endemic regions. This phase 3, randomized controlled study evaluated co-administration of HAV vaccine with 2-dose tetravalent dengue vaccine (TAK-003) in adults aged 18–60 years (NCT03525119).

Methods:

900 participants were randomized 1:1:1 to receive HAV+placebo (Group 1), TAK-003+placebo (Group 2), or TAK-003+HAV (Group 3). The primary objective was non-inferiority (upper bound of 95% confidence interval [CI] of difference <10%) of HAV seroprotection (anti-HAV >12.5 mIU/mL) in Group 3 versus Group 1 one-month post-first vaccination in HAV- and dengue-naïve participants. Sensitivity analyses were performed on combinations of baseline HAV and dengue serostatus. Secondary objectives included evaluation of the immune response to HAV and TAK-003, and safety.

Results:

One-month post-first vaccination, the immune response to HAV following co-administration with TAK-003 was non-inferior (Group 3: seroprotection 98.7%) to HAV alone (Group 1: 97.1%; difference: -1.68%, 95% CI: -8.91 to 4.28). Sensitivity analyses supported this finding. HAV geometric mean concentrations one-month post-first vaccination were 82.1 (95% CI: 62.9 to 107.1) mIU/mL in Group 1 and 93.0 (76.1 to 113.6) mIU/mL in Group 3. By Day 120, 90.9–96.8% of TAK-003 recipients were seropositive to all four dengue serotypes. Both vaccines were well tolerated, and no important safety risks were identified.

Conclusion:

The results support the co-administration of HAV vaccine and TAK-003, with no impact on immunogenicity or safety observed for either vaccine.

Funding:

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Binding IgG Response to a Tetravalent Dengue Vaccine Candidate Includes Affinity-Matured and Functional Antibodies

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Background:

Affinity-matured antiviral binding IgG antibodies with neutralizing and complement-fixing effector functions, play an important role in protection from disease caused by dengue virus (DENV). Takeda's attenuated tetravalent dengue vaccine, TAK-003, has been shown to elicit tetravalent neutralizing antibody (nAb) responses in phase II and III trials. The relationship between virus-binding IgG concentration, avidity and antibody effector function following TAK-003 vaccination is not fully understood.

Methods:

The magnitude and avidity of virus-binding IgG as well as complement-fixing and nAb responses were assessed in samples from TAK-003 recipients from a phase II clinical trial (DEN-203 - NCT01511250) collected at various time points (days 1, 28, 90, 120, 180 and 360). Data across the four readouts were analyzed to assess correlation and agreement between responses.

Results:

Results indicate a high degree of agreement and correlation between virus-binding IgG concentration, avidity, complement-fixation and nAb responses irrespective of virus serotype.

Conclusion:

These data suggest TAK-003 induces affinity maturation of the virus-binding IgG responses that consist of complement-fixing and nAb effector functions. Given the roles for these responses in protection from dengue disease, the vaccine-driven tetravalent, affinity matured, functional effector anti-dengue binding antibody responses are likely to be an important part of the immune response repertoire linked to the efficacy profile of the vaccine.

Funding:

This study was funded by Takeda.

Assessment of anti-dengue binding antibody avidity driven by a tetravalent dengue vaccine candidate and the association of antibody avidity with protection against symptomatic dengue virus infection

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Background:

Dengue is a mosquito-borne disease caused by four dengue virus (DENV) serotypes. Avidity of the antibody responses elicited by natural infection or vaccination is an important parameter of subsequent potential protection. To study the relationship between this parameter and protection, avidity of antibody responses to a tetravalent dengue vaccine candidate (TAK-003) and of plasma samples collected prior to symptomatic or inapparent secondary DENV infection in the Nicaraguan Pediatric Dengue Cohort Study (PDCS) were assessed and compared.

Materials and Methods:

Immunoglobulin G was purified from PDCS and clinical trial (DEN-203, NCT01511250; DEN-204, NCT02302066) samples in dengue-endemic countries using Protein G Sepharose. The avidity assay was conducted by Octet HTX using biotinylated dengue virus-like particles and a high-precision Streptavidin biosensor. Avidity index was calculated as: response/dissociation constant (koff).

Results:

Assessment of samples from the PDCS revealed a correlation between avidity of anti-DENV antibody responses and outcome of secondary DENV infection. Evaluation of post-vaccination serum from TAK-003 phase II clinical trials showed that the affinity-matured antibody response remained high through one-year post-vaccination. Additionally, TAK-003 clinical trial study participants with the highest neutralizing antibody magnitudes also displayed high levels of anti-DENV antibody avidity.

Conclusion:

During natural secondary DENV exposure, the degree of anti-DENV avidity was found to be associated with protection from symptomatic dengue disease. Vaccination with TAK-003 similarly led to an increase in anti-DENV antibody avidity that was sustained over time.

Aknowledgements:

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Specificity and Breadth of the Neutralizing Antibody Response to a Live Attenuated Tetravalent Dengue Vaccine

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Background:

Dengue is a major global health concern with up to 400 million infections annually. There are 4 dengue virus serotypes (DENV-1–4), and multiple genotypes within each serotype. Takeda's tetravalent dengue vaccine candidate (TAK-003) has been shown to trigger neutralizing antibodies (nAbs) against DENV-1–4 in most phase 2 and 3 clinical trial participants, with highest titers against DENV-2. Here, we characterized this nAb response for breadth of coverage against diverse DENV genotypes and frequency of serotype-specificity.

Methods:

To assess breadth of response elicited by TAK-003, a genotypically diverse panel of DENV strains were assayed for neutralization using post-vaccination serum in a microneutralization test. Post immune-depletion of DENV-2 nAbs, remaining DENV-1, -3, and -4 specific nAb levels were assessed using a reporter virus particle neutralization assay.

Results:

The magnitude of post-vaccination nAb response was comparable across genotypes for each DENV serotype. TAK-003 also elicited both type-specific (TS) and cross-reactive (CR) nAbs to DENV-1, -3, and -4, post-depletion of DENV-2 specific and CR nAbs. The frequencies of responses were similar in adult and pediatric populations, and independent of the magnitude of nAb responses.

Conclusion:

Despite the highest nAb responses against DENV-2, TAK-003 elicited TS nAb response to DENV-1, -3 and -4 in adults and children, and comparably neutralized both vaccine-matched and genotypically distant dengue strains. Ongoing work includes testing vaccine-driven neutralization against recently circulating strains.

Funding:

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Seroprevalence of Dengue Infections in Singapore from a Cohort of Healthy Blood Donors in 2021

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Abstract:

Case notification data do not capture all dengue infections and may not reflect the true intensity of disease transmission. To assess the true rate of dengue infection in Singapore, the Environmental Health Institute conducts periodic age-stratified serosurveys among residents. This study reports the most recent serosurvey conducted in 2021, using 7,668 healthy blood donor samples, which showed an age-weighted prevalence of dengue immunoglobulin G among residents (16 to >60 years) to be 42.7% (95% confidence interval, CI: 42.0, 43.8). This highlights a continued decrease in seroprevalence from 48.6% (95% CI: 47.0, 50.0) in 2017, and 49.8% in 2013 (95% CI: 48.4, 51.1). Similar to previous serosurveys, the trend of dengue seroprevalence increased with age, with declining seroprevalence across all age-groups compared to previous years. The seroprevalence for the 46-50 years age group also decreased below 50% for the first time. Year-on-year estimates of the dengue force of infection (FOI) remained below 10 per 1,000 persons since 2013. Notably, geospatial analyses revealed a significantly higher probability of donors being dengue seropositive in the southeastern areas of Singapore, consistent with more reported cases in these regions historically. Despite this survey following the most severe outbreak of dengue in Singapore in 2019/2020, a continued decline in dengue burden on the Singapore resident population was recorded, underscoring the effectiveness of Singapore's dengue control programme. Nevertheless, the low population immunity suggests that Singapore remains at risk of future dengue outbreaks, and may also partially explain the severe outbreak in 2019/2020, and the current outbreak.

DELEGATES' ABSTRACTS

Evolution of Automated Systems for Large-Scale Standardized Rearing of Male *Wolbachia-Aedes* Mosquitoes for Project *Wolbachia* – Singapore

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Background:

Project *Wolbachia* – Singapore focuses on using male *Wolbachia-Aedes* aegypti *(Wolbachia-Aedes)* mosquito in suppressing urban *Aedes aegypti* mosquito, the primary vector of dengue, in residential estates. The project has achieved up to 98% suppression of the urban *Aedes aegypti* population and up to 88% reduction in dengue cases in study sites that receive at least a year of male *Wolbachia-Aedes* releases. To achieve the suppression effects in more areas and benefit larger population, scaling up *Wolbachia Aedes* mosquito mass production is critical.

Methods:

To improve consistency, productivity and scalability of large-scale rearing and field releases of quality male mosquitoes, novel automated modules have been developed and placed previous manual production processes

Results:

Till date, nine modules have been developed and have substantially improved productivity, standardized production quality, and enhanced workers' health and safety by reducing or eliminating reliance on repetitive manual processing. For instance, the automated larvae counter achieves a 40-fold increase in counting efficiency and reduce >50% labour, while the high-density rearing rack achieves a 6-fold increase in large-scale larval rearing productivity.

Conclusion:

Overall, the incorporation of automated modules is expected to effect an 8 to 10-fold increase in productivity and efficiency as compared to past manual processes. This has also allowed *Project Wolbachia* – Singapore to increase the production of stable high-quality mosquitoes for sustainable expansion to more residential neighborhoods and benefit more communities.

DELEGATES' ABSTRACTS

Adult *Aedes* Abundance and Risk of Dengue Transmission

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Background:

Little is known about the impact of adult *Aedes* abundance on the risk of dengue transmission. This study therefore aimed to assess the effect of adult *Aedes* abundance on risk of dengue transmission in Singapore.

Methods:

We analysed nationally representative dengue case and vector surveillance data collected from Singapore, to determine the effect of adult *Aedes* abundance on the risk of dengue transmission. A case was an area with active dengue transmission as indicated by the presence of dengue cluster. A control was an area where no dengue cluster was reported. Using multivariate logistic regression, we analysed 88 cases and 602 controls and estimated the odds of dengue cluster formation at various adult *Aedes* abundance levels, estimated by the mean number of adult female *Aedes* per Gravitrap per week and categorised into Low, Moderate, High and Very High abundance level.

Results:

We found that the risk of dengue cluster formation was positively associated with adult *Ae. aegypti* abundance. We observed a three to four-fold increase in the odds of dengue clusters forming in areas with High (AOR: 3.40, 95% CI: 2.09, 5.52) and Very High (AOR: 3.99, 95% CI: 2.46, 6.46) adult *Aedes aegypti* abundance level compared to those with low *Ae. aegypti a*bundance level.

Conclusion:

Our study strengthens the evidence for the use of adult *Aedes* indices for dengue risk assessment and early warning for dengue outbreaks. Entomological indicators of adult *Ae. aegypti* could be used to anticipate and prioritize areas for dengue control.

Economic Impact of Dengue in Singapore from 2010 to 2020 and the Cost-Effectiveness of *Wolbachia* Interventions

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Background:

The release of *Wolbachia*-infected mosquitoes is a promising disease intervention strategy that aims to control dengue and other arboviral infections. While early field trials and modelling studies suggest promising epidemiological and entomological outcomes, the overall cost-effectiveness of the technology is not well studied in a resource-rich setting nor under the suppression approach that aims to suppress the wild-type mosquito population through the release of *Wolbachia*-infected males.

Methods:

We used economical and epidemiological data from 2010 to 2020 to first ascertain the economic and health costs of dengue in Singapore, a high-income nation where dengue is hyper-endemic. The hypothetical cost-effectiveness of a national *Wolbachia* suppression program was then evaluated historically from 2010 to 2020.

Results:

We estimated that the average economic impact of dengue in Singapore from 2010 to 2020 in constant 2010 US$ ranged from $1.014 to $2.265 billion. Using empirically derived disability weights, we estimated a disease burden of 7,645–21,262 DALYs from 2010–2020. Under an assumed steady-state running cost of a national *Wolbachia* suppression program in Singapore, we conservatively estimate that *Wolbachia* would cost an estimated $50,453–$100,907 per DALYs averted and would lead to an estimated $329.40 Million saved in economic costs over 2010 to 2020 under 40% intervention efficacy.

Conclusion:

Wolbachia releases in Singapore are expected to be highly cost-effective and its rollout should be prioritised to reduce the onward spread of dengue.

DELEGATES' ABSTRACTS

Wolbachia-Mediated Sterility Suppress *Aedes Aegypti* and Dengue in Urban Tropics

The Project *Wolbachia* – Singapore Consortium[1,2,3,4,5,6]

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Background:

Incompatible insect technique (IIT), a promising complementary strategy for the control of arbovirus transmission, involves the releases of male mosquitoes infected with Wolbachia, a maternally inherited endosymbiotic bacterium. Since 2016, phased field trials were conducted in Yishun and Tampines towns to evaluate the effectiveness of the technique on suppressing the population of Aedes aegypti mosquitoes and reducing dengue cases. A rolling carpet approach was adopted where the coverage was progressively expanded to the entire towns. In 2020, a different approach was tested where targeted releases were conducted at high-risk neighbourhoods in Choa Chu Kang and Bukit Batok towns.

Methods:

Male-infected Aedes aegypti mosquitoes were released in designed public locations at high-rise residential estates in the forementioned towns. Releases were conducted twice a week at a ratio of 1-6 male mosquitoes per resident, with the release numbers adaptively guided by data obtained from Gravitraps, which form the national Aedes vector surveillance network within residential estates.

Results:

We demonstrated for the first time that Wolbachia-based IIT dramatically reduces both wildtype Aedes aegypti populations (reductions of up to 98%) and dengue incidence (reductions of up to 88%) in the targeted areas.

Conclusion:

The study highlights the need to ensure adequate vertical distribution of released males in high-rise buildings, address immigration of wildtype females from neighbouring areas, and prevent and mitigate stable establishment of Wolbachia in field mosquito populations. Our results demonstrate the potential of Wolbachia-based IIT (supplemented with irradiation, in Singapore's context) for strengthening dengue control in tropical cities, where dengue burden is the greatest.

Attitude of Leukocytes Activation in Dengue Patients Using Hematology Analyzer Parameters

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Background:

Dengue infections known to cause activation of the patient's leukocytes and various protective responses. Leukocytes have been reported to change their morphology when they encounter pathogens and to change their optical characteristics, thereby changing their position on the scattergram in hematology analyzer. These could be potential prognostic markers for severe dengue. We report our observations of the status of leukocyte activation from the optical information of hematology analyzer in dengue patients.. The optical characteristic was compared between severe and non-severe dengue patients.

Methods:

Blood samples of dengue patients who visited the University Malaya Medical Center were collected daily until recovery and measured by a Sysmex hematology analyzer. Final dengue diagnosis was performed using dengue NS1 antigen, antibodies and one-step RT-PCR serotyping. Severe dengue was classified according to the 2009 World Health Organization Classification.

Results:

In the half of the patients, Lymph-WX and Lymph-WZ, which reflect variations in lymphocyte morphology were increased to 3 times from the 4th to the 7th day (a peak) after fever onset respectively, and then decreased to first state by the 10th day in same timing. Another half of the patients had no peak in both of Lymph-WX and Lymph-WZ. This peak was not related to severity.

Conclusion:

We postulate that lymphocytes were activated to produce antibodies in dengue infection around 7 days post-fever, resulting IgM antibody secretion. Optical parameters of hematology analyzer were very useful to study patient's immunological response. We need to investigate why half of the patients did not have the peak according from patient's serological dengue immune status.

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