IVBDC

INTERNATIONAL VECTOR-BORNE DISEASES CONFERENCE 2023

Programme Booklet

21-23 November

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ABOUT

Vector-borne diseases such as malaria, dengue, schistosomiasis, human African trypanosomiasis, leishmaniasis, Chagas disease, yellow fever, Japanese encephalitis and onchocerciasis, cause more than 700,000 deaths globally. Mosquitoes, sandflies, blackflies, ticks, tsetse flies, mites and lice transmit the pathogens including parasites, viruses and bacteria that cause these diseases. The major vector-borne diseases account for 17% of all infectious diseases. The tropical and subtropical areas, including Singapore, are disproportionately affected. Recent outbreaks of dengue, malaria, chikungunya, yellow fever and Zika afflicted populations, claimed lives and overwhelmed health systems.

To encourage and entice participation of the next generation of young scientists to work in this research area, and to find solutions to reduce the burden of vector-borne diseases, we are organizing an International Conference that will bring local, regional and global scientific leaders and younger researchers together. Participants will present their recent research findings and will exchange cutting-edge strategies in various aspects of vector-borne diseases. The Scientific Sessions include epidemiology, vector control strategies, vaccination, host-pathogen interactions, vector-pathogen interactions, vector-host interactions, pathogenesis, vector barriers, and vector competence.
We look forward to welcoming you all in person!

On behalf of the Organizing Committee,
R. Manjunatha Kini & Sylvie Alonso (Co-chair persons),
NUS

IVBDC
INTERNATIONAL VECTOR-BORNE DISEASES CONFERENCE

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- Prof Lisa Ng (A*STAR, IDLabs)
- Prof Laurent Renia (NTU, LKC)
- A/P Ng Lee Ching (NEA, EHI)
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GUEST OF HONOUR

Senior Parliamentary Secretary

Mr Baey Yam Keng

Yong Loo Ling School of Medicine Vice Dean Research
Vice President, Biomedical Sciences Research,
National University of Singapore

Prof Chng Wee Joo

SCIENTIFIC PROGRAMME
DAY 1, TUESDAY, 21 NOVEMBER 2023
Vector Control Strategies, Vector Dynamics & Disease Transmission

0830
Registration of Participants

0930
Welcome Address by Prof Chng Wee Joo
Yong Loo Ling School of Medicine Vice Dean Research
Vice President, Biomedical Sciences Research,
National University of Singapore

Opening session
Chair: Prof. R. Manjunatha Kini

0945
Keynote speaker: Georges Christophides (Imperial College, UK)
Gene drives for vector population replacement and malaria transmission zero.

1020
Invited speaker: Chong Chee Seng (Environmental Health Institute, Singapore)
Fighting Aedes aegypti with Wolbachia-Aedes aegypti.

1045
Guest of Honor: SPS Baey Yam Keng
(Ministry of Sustainability and the Environment, Singapore)

1100
Coffee/Tea Break

Session 1: Vector Control Strategies
Chair: Prof. R. Manjunatha Kini

1130
Invited speaker: Olaf Horstick (University of Heidelberg, Germany)
Dengue vector control: what works best? Are there answers from evidence synthesis?

1155
Selected Speaker: Piyatida Leelagud (National Chung Hsing University, Taiwan)
Pseudomonas entomophila: a potential alternative for the management of pyrethroid-resistant Aedes aegypti.

1220
Invited Speaker: Johanna Fraser (Monash University, Australia)
Defining the antiviral mechanisms of Wolbachia; the bacterium protecting communities from mosquito-borne viruses.

1245
Lunch

Session 2: Vector Dynamics & Disease Transmission
Chair: Dr Nalini Puniamoorthy

1400
Keynote Address: Jason Rasgon (Penn State Uni, USA)
Pitfalls and breakdown points in the use of Wolbachia to control vector-borne diseases.

1435
Invited speaker: Jamal I-Ching Sam (University of Malaya, Malaysia)
Circulating chikungunya virus variants in Malaysia and potential implications for mosquito vectors and humans.

1500
Selected speaker: Kelvin Ho (Animal and Veterinary Service, National Parks Board, Singapore)
Tick and canine tick-borne disease biosurveillance in free roaming dogs and animal establishments in Singapore: 2019-2023.

1515
Invited speaker: Indra Vythilingam (University of Malaya, Malaysia)
Current status of simian malaria and its vectors in Southeast Asia.

1540
Selected speaker: Zhen Yuan Yeo (Department of Physics, NUS, Singapore)
Inferring the hidden and long-range dengue transmission routes in Singapore.

1555
Invited speaker: Christopher Ang (Environmental Health Institute, Singapore)
Detection and characterisation of the lineage I insect-specific flavivirus, Quang Binh virus, from rural caught mosquitoes in Singapore.

1620
Coffee/Tea Break

Session 3: Vector Dynamics & Disease Transmission
Chair: Dr Nalini Puniamoorthy

1650
Invited Speaker: Sazaly Bin Abu Bakar (University of Malaya, Malaysia)
Dengue Virus, Mosquitoes and Host in Shaping Major Dengue Outbreaks.

1715
Selected speaker: Julie Reveillaud (University of Montpellier, France)
Wolbachia plasmid pWCP is widely distributed and highly conserved in Culex pipiens and Culex quinquefasciatus mosquitoes worldwide.

1730
Invited Speaker: Nalini Puniamoorthy (NUS, Singapore)
Polyandry, population structure and Wolbachia infections in Aedes albopictus across Singapore.

1755
Invited Speaker: Jingwen Wang (Fudan University, China)
The influence of tryptophan metabolism on Plasmodium transmission in mosquitoes.

1820
End of day 1

SCIENTIFIC PROGRAMME
DAY 2, WEDNESDAY, 22 NOVEMBER 2023
Vector Biology

Session 4: Vector-Pathogen Interactions
Chair: Dr Guillaume Carissimo

0900
Keynote Address: Bruce Hay (Caltech, USA)
Engineering the composition and fate of wild populations with gene drive.

0935
Invited speaker: Leen Delang (Rega Institute, Belgium)
Classic and new antiviral strategies to treat infections with mosquito-borne viruses.

1000
Selected speaker: Milly Ming-Ju Choy (Duke-NUS, Singapore)
Species- and tissue-specific micro-evolution of dengue virus in Aedes aegypti and Aedes albopictus mosquitoes.

1015
Invited speaker: Claudia Rückert (University of Nevada, USA)
Defining mechanisms of viral dsRNA sensing in vector mosquitoes.

1040
Coffee/Tea Break

Session 5: Vector Microbiota
Chair: Dr Guillaume Carissimo

1110
Invited Speaker: Cheng Gong (Tsinghua University, China)
Skin Microbiota, Host Volatiles and Viral Transmission by Mosquitoes.

1135
Invited speaker: Emilie Pondeville (Glasgow University, UK)
Microbiota-nutrition-physiology interactions in mosquitoes: treat and trick?

1200
Invited speaker: Wang Si Bao (Shanghai Institutes for Biological Sciences, China)
Mosquito Microbiota and Implications for Disease Control.

1225
Selected speaker: Cassandra Koh (Institut Pasteur, Université Paris Cité, Paris, France)
Exploring the virome of five mosquito genera across diverse geographic regions.

1240
Lunch

Session 6: Vector-Pathogen Interactions
Chair: Dr Cai Yu

1400
Keynote Address: Manjunatha Kini (NUS, Singapore)
Role of Vector Saliva in Vector-Virus-Host Trilateral Interactions.

1435
Invited speaker: Julien Pompon (Institute of Research for Development (IRD); France)
Lipids in mosquito saliva enhance transmission for multiple flaviviruses.

1500
Invited speaker: Guann-Yi Yu (National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Taiwan).
Highly pathogenic DENV-2 strain in mosquitoes and mouse models.

1525
Selected speaker: Hong-Guan Tee (National Health Research Institutes, Taiwan)
Cryptochrome-1 Influences Circadian Clock Resetting and Morning Activity Levels in Aedes aegypti.

1540
Coffee/Tea Break

1600
Poster Session

1800
End of Day 2

1830
Gala Dinner
On invitation only.

SCIENTIFIC PROGRAMME
DAY 3, THURSDAY, 23 NOVEMBER 2023
Pathogen fitness and virulence in its mammalian host and treatment approaches

Session 7: Pathogen fitness and virulence in its mammalian host
Chair: Prof Laurent Renia

0900
Keynote speaker: Sylvie Alonso (Infectious Diseases Translational Research Programme, NUS, Singapore)
Viral determinants of DENV fitness and virulence.

0935
Invited Speaker: Wan Yue (A*STAR Genome Institute of Singapore, Singapore)
RNA structure and interactomes of RNA viruses.

1000
Selected Speaker: Yueh Hsin Ping (National Yang Ming Chiao Tung University, Taipei, Taiwan)
Uncovering novel roles of Dengue virus-induced autophagy during the early infection stage by single-virus tracking.

1015
Invited speaker: Pablo Bifani (Infectious Diseases Translational Research Programme, NUS, Singapore)
Rapid selection of drug resistant mutants for target deconvolution and drug discovery in viruses.

1040
Coffee/Tea Break

Session 8: Pathogen fitness and virulence in its mammalian host
Chair: Prof Laurent Renia

1110
Invited Speaker: Marco VIGNUZZI (A*STAR IDLabs)
Arbovirus population dynamics: the role of defective viral genomes in inhibiting or facilitating virus emergence.

1135
Selected speaker: Ruyue Liu (Pharmacy, NUS, Singapore)
Characterization of naturally occurring Flavivirus host-specific mutations.

1150
Invited Speaker: Amit Sharma (All India Institute of Medical Sciences)
From structural biology to epidemiology.

1215
Selected speaker: Carla Bianca L. Victorio (Cancer & Stem Cell Biology Programme, Duke-NUS, Singapore)
Positron emission tomography (PET) imaging biomarkers of dengue and Zika disease in mouse models.

1230
Lunch

Session 9: Prophylactic and Therapeutic approaches against Vector-Borne pathogens
Chair: A/P Sylvie Alonso

1400
Keynote speaker: Laurent Renia (Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore)
New insights in Plasmodium vivax malaria biology.

1435
Selected speaker: Amanda Leow (Nanyang Technological University, School of Biological Sciences, Singapore)
TNFα promotes sexual conversion of Plasmodium falciparum via a serine/threonine
kinase.

1450
Invited speaker: Jody Peters (University of Queensland, Australia)
Harnessing recombinant mosquito-specific viruses to tackle emerging One Health viral diseases.

1515
Selected speaker: Sébastien Nisole (Institut de Recherche en Infectiologie de Montpellier (IRIM), Montpellier University, CNRS, France)
Identification of Interferon-stimulated genes that interfere with the replication of West Nile and Usutu virus.

1530

Invited speaker: Julien LESCAR (Nanyang Technological University, Lee Kong Chian School of Medicine, Singapore)

Identification and structural validation of purine nucleoside phosphorylase from Plasmodium falciparum as a target of MMV00848.

1555

Coffee/Tea Break

1625

Keynote speaker: Prof Paul Pronyk (Centre for Outbreak Preparedness, Duke-NUS)

The state of genomic pathogen surveillance in Asia and implications for Vector-borne Diseases.

1700

Award Ceremony and Closing Remarks (chairs)

1800

End of the conference

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INTERNATIONAL VECTOR-BORNE DISEASES CONFERENCE

MAIN ORGANISERS

NUS National University of Singapore | Infectious Diseases Translational Research Programme
Yong Loo Lin School of Medicine

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KEYNOTE SPEAKERS

Professor George K. Christophides

Professor Christophides holds the Chair of Infectious Diseases and Immunity at Imperial College London and boasts a rich legacy of spearheading global malaria research endeavours. He is recognized for his ground-breaking research in mosquito genomics, insect innate immunity and vector-pathogen interactions, and for spearheading innovative strategies for combatting malaria transmission. His contributions and impact on the field of vector-borne disease research extends to bridging the divide between laboratory-based investigations and field studies, actively implementing programmes in numerous sub-Saharan African countries to advance our understanding of disease transmission and control.

Gene drives for vector population replacement and malaria transmission zero

Abstract

Gene drives offer promising solutions for malaria control by genetically modifying mosquito populations to reduce transmission. Transmission Zero is a global research programme committed to developing and testing gene drive systems for malaria eradication in Africa. Our innovative first-generation drives separate the transmission-blocking effector mechanism from the gene drive itself, streamlining scientific advancement and field trial readiness. Our lead effector component, involving the expression of exogenous antimicrobial peptides, exhibits exceptional effectiveness in impeding parasite development. When coupled with efficient driver components, it can rapidly disseminate through mosquito populations, rendering them non-vectors. Modelling suggests that this approach could drive malaria elimination in almost all malaria-endemic settings, even in the face of resistance. The next phase of the programme focuses on the evaluation of effector and driver performance and safety in semi-field conditions, paving the way for the initial field trials.

KEYNOTE SPEAKERS

A/Prof Sylvie Alonoso

Dr Alonso obtained her PhD degree in Microbiology and Molecular Biology from the University Claude Bernard Lyon I (France), followed by two post-doctoral trainings at Pasteur Institute of Lille (France) and Cornell University (NY, USA). In 2004, she moved to Singapore and established her lab at the National University of Singapore, Department of Microbiology. Dr Alonso's research has been studying the pathogenesis of Enterovirus-A71 (HFMD) and Dengue virus, and dissecting the molecular interactions between the pathogen and its host, making use of relevant animal models that her lab has developed.

VIRAL DETERMINANTS OF DENGUE VIRUS FITNESS AND VIRULENCE

Abstract

Despite intensified research efforts, our understanding of dengue pathogenesis remains very patchy. Specifically, while the genetic diversity among dengue virus (DENV) strains has long been recognized, the resulting heterogeneity in mechanisms involved in viral fitness and virulence has only started to be acknowledged. It hence appears that a one-size-fits-all treatment approach is not adequate to combat dengue in various parts of the world where different DENV strains circulate.

Our laboratory has been studying the molecular determinants that drive the fitness and virulence of DENV strains that circulate in Singapore and the region. We have been using the D2Y98P strain, a Cosmopolitan DENV2 strain representative of DENV2 isolates that have been circulating in Singapore and Malaysia for the past decade. Using a relevant symptomatic mouse model, I will present recent findings on the role of certain viral determinants that drive the fitness and virulence of D2Y98P virus.

KEYNOTE SPEAKERS

Professor Laurent Renia

Laurent Renia is Professor of infectious diseases and director of the respiratory and Infectious Diseases Program at the Lee Kong Chian School of Medicine, NTU and a senior fellow at the A*STAR ID Labs. He has obtained his Ph.D. in 1991 from University Pierre and Marie Curie (Paris, France) and did his post-doctoral at New York University. He obtained a permanent position as a research scientist at the French National Institute of Health (INSERM) in 1993. He joined the Singapore Immunology Network (A*STAR) in 2007 and became later its Executive Director. His scientific interests cover the immunology of infectious diseases.

NEW INSIGHTS IN PLASMODIUM VIVAX MALARIA BIOLOGY

Abstract

Vivax malaria is deservedly receiving more attention than in the past. However, research into the causative agent of relapsing malaria: P. vivax, lags considerably behind that of P. falciparum. Aside from a general lack of funding, a key reason for the research effort disparity between these two important malaria parasite species is that a robust continuous culture method for P. falciparum has been developed in the late 1970s; whereas the continuous culture of P. vivax erythrocy3c stages s3ll eludes us to this day, principally due to the fact that P. vivax only invades and grows in reticulocytes, the immature erythrocytes. Here, we describe the use of new or improved ex vivo methods and tools to study fresh and thawed isolates from vivax malaria patients that have provided useful data on P. vivax on reticulocyte invasion and immunity.

KEYNOTE SPEAKERS

Professor Paul Pronyk

Professor Pronyk is the Director of the Duke-NUS Center for Outbreak Preparedness (COP) and the Deputy Director of the SingHealth Duke-NUS Global health Institute. As an infectious disease and public health physician, he has over two decades of experience in communicable disease control in low and middle-income countries. Prior to Duke-NUS, he held senior positions in UNICEF, including supporting infectious disease control efforts in Indonesia and Sierra Leone, and was the technical lead for the UN Commission on Life Saving Commodities which provided support to strengthen health systems in 23 countries in Africa and Asia.

THE STATE OF GENOMIC PATHOGEN SURVEILLANCE IN ASIA AND IMPLICATIONS FOR VECTOR-BORNE DISEASES

Abstract

Asia remains particularly vulnerable to new and emerging disease threats. During the COVID-19 pandemic, genomic sequencing emerged as powerful new tool for early detection, with genomic data providing a crucial building block for the development of diagnostics and vaccines. To assess the current status of pathogen genomics in Asia, cross-sectional surveys were conducted between June 2022 and March 2023 among partner institutions across 14 countries in Asia. All countries demonstrated in-country capacity for genomics with priority pathogen groupings identified for human and environmental surveillance. Major barriers limiting adoption and scale included a reliance on external funding, supply chain challenges, laboratory and bioinformatics capacity gaps, and limited quality assurance mechanisms. Coordinated regional efforts are required to support national planning and system design, respond to supply chain challenges, address capacity gaps, enhance quality assurance and facilitate timely data sharing.

KEYNOTE ADDRESS

Dr Jason Rasgon

Dr. Rasgon received a BS degree in Zoology in 1998 from San Jose State University and a PhD in Entomology in 2003 from UC Davis. After a brief postdoc stint at North Carolina State University, he joined the Johns Hopkins Bloomberg School of Public Health in 2004 as an Assistant, then Associate Professor. In 2011 he joined the Department of Entomology and Center for Infectious Disease Dynamics at the Pennsylvania State University where he is currently the Dorothy Foehr Huck and J. Lloyd Huck Endowed Chair in Disease Epidemiology and Biotechnology.

PITFALLS AND BREAKDOWN POINTS IN THE USE OF WOLBACHIA TO CONTROL VECTOR-BORNE DISEASES.

Abstract

Multiple Wolbachia strains can block pathogen infection, replication, and/or transmission in mosquitoes under both laboratory and field conditions. However, Wolbachia effects on pathogens can be highly variable across systems and the factors governing this variability are not well understood. Multiple studies have demonstrated that Wolbachia pathogen blocking phenotypes are dependent not just on the Wolbachia strain used for control, but also on the pathogen, the arthropod species, the genetics of the host, the host microbiome, and the environment, and these factors may interact in unpredictable ways to modulate pathogen suppression phenotypes. In this talk I will attempt to synthesize what is known about Wolbachia pathogen blocking, the parameters that influence this phenotype, and underlying mechanisms, with important considerations for measuring pathogen blocking in laboratory experiments as well as potential issues for the application of Wolbachia for disease control in the field.

KEYNOTE ADDRESS

Dr Bruce Hay

Bruce Hay is a professor of Biology and Biological Engineering at Caltech. The Hay lab has multiple interests, which revolve around altering the composition or fate of populations. At the cellular level we are interested in mutant mitochondrial genomes, which accumulate with aging, and devising ways of selectively eliminating these, but not co-resident wildtype genomes, thereby reversing an important component of aging. At the level of individuals, we are interested in single shot, gene-therapy based contraception. At the level of populations of individuals, we are interested in gene drive for population modification or suppression of pests and vectors of disease.

ENGINEERING THE COMPOSITION AND FATE OF WILD POPULATIONS WITH GENE DRIVE

Abstract

Gene drive provides a way of spreading genes into wild populations of disease vectors. It can bring about population modification, which leaves the population intact but unable to transmit disease. Alternatively, it can bring about population suppression/elimination. Here, we discuss some strategies being used to bring about gene drive, and address important points of control: reversal, how to limit spread in space, and ability to carry out cycles of modification. While most effort has focused on homing-based drives, I will introduce a Toxin/Antidote based approach to gene drive, Cleave and Rescue (ClvR), with applications to self-sustaining and self-limiting population modification. While ClvR spreads more slowly than a high frequency homing drive, it does not require homologous recombination and can carry very large cargos since it sits at a fixed chromosomal position. These features may be particularly useful in contexts in which homing based drive rates are low.

KEYNOTE ADDRESS

Professor Manjunatha Kini

Dr. Manjunatha Kini, a distinguished professor at the Department of Biological Sciences, National University of Singapore (NUS), holds joint positions in the Department of Pharmacology at Yong Loo Lin School of Medicine, NUS, and the Singapore Eye Research Institute. With affiliations at Virginia Commonwealth University, USA, and a rich academic history, Dr. Kini is a global authority in snake venoms and blood-feeding animal saliva. His "From Toxins to Therapeutics" research paradigm focuses on identifying bioactive proteins, understanding their modes of action, and designing potential drug leads. As a prolific author, he has published over 300 research papers, edited monographs, and filed numerous patents. Dr. Kini co-founded ProScience Inc., Richmond, USA, and is the Founder and Chief Scientific Officer of ProTherapeutics Private Limited, Singapore. His impactful leadership extends to serving as President of the International Society on Toxinology and contributing significantly to the International Society on Thrombosis and Haemostasis. A sought-after speaker, he has delivered over 140 plenary/keynote talks globally, shaping the landscape of toxin research and hemostasis.

ROLE OF VECTOR SALIVA IN VECTOR-VIRUS-HOST TRILATERAL INTERACTIONS

Abstract

Blood-feeding arthropods transmit various pathogens and cause various vector-borne diseases, including malaria and dengue, that affect ~400 million people globally every year. Interestingly, the transmission efficiency of purified pathogens remains low, while their transmission efficiency increases 1000- to 5,000- times when mixed with relevant vector saliva. We evaluated the central role of mosquito saliva in vector-virus-host trilateral interactions in Dengue, Zika and Chikungunya transmissions. Here, I will present our new exciting findings.

INVITED SPEAKERS

Dr Chee-Seng Chong

Dr. Chong Chee Seng leads the Applied Entomology Department in the Environmental Health Institute of the National Environment Agency, Singapore. His research interests include understanding the bionomics of mosquito vectors, development of surveillance methodologies, and leading risk assessment and multi-disciplinary research projects. With close to 20 years of experience in entomology, he is committed to developing safe, sustainable, and effective solutions for mosquito control and management in Singapore's green tropical urban environment.

FIGHTING AEDES AEGYPTI WITH WOLBACHIA-AEDES AEGYPTI

Abstract

Incompatible insect technique (IIT), a promising complementary strategy for the control of arbovirus transmission, involves the release of male mosquitoes infected with Wolbachia, a maternally inherited endosymbiotic bacterium. Due to cytoplasmic incompatibility, mating between Wolbachia-infected males and wildtype non-infected females yield non-viable eggs. Results has shown promising suppression of the wildtype Aedes aegypti mosquito population and reduction of dengue cases in study sites. This demonstrates the potential of IIT (supplemented with irradiation) for strengthening dengue control in tropical cities, where dengue burden is the greatest.

INVITED SPEAKERS

Professor Olaf Horstick

Professor and Consultant in Public Health Medicine, as a Medical Doctor, main interest in public health in low- and middle-income countries. More than 30 years' work experience in global public health at local, national and international level, including work as staff member for United Nations organisations (WHO), bilateral organisations (GIZ), governmental agencies (MoH), non-governmental agencies and Academia. Specific interest in Neglected Tropical Diseases, with focus on Aedes control and arbovirus. Currently Director of Teaching at the Heidelberg Institute of Global Health/Heidelberg University, Germany. Founder and coordinator of its Research to Practice Group. Member of the Scientific and Technical Advisory subgroup on monitoring and evaluation of NTDs for WHO, Founding member of HEGTA/Anti-corruption in Health, Chair and founding member of the Eurasian Academic Alliance for Global Health, Associate Editor for PLOS NTD.

DENGUE VECTOR CONTROL: WHAT WORKS BEST? ARE THERE ANSWERS FROM EVIDENCE SYNTHESIS?

Abstract

Mosquito control is of great importance to curb the spread of diseases, particularly for Aedes mosquitoes related to dengue, Zika and chikungunya transmission. Given the climatic conditions and their global changes, particularly focusing on urbanisation, targeted and locally adapted control strategies are required.

We discuss the key methods for dengue vector control, using recently emerging summary evidence, meta–analyses and systematic reviews to conclude on practical public health recommendations for Aedes control.
Furthermore, we focus on enabling factors for programmes such as early warning systems embedded in surveillance systems, and Integrated Vector Management and collaborative efforts, and community engagement and mobilization

INVITED SPEAKERS

Dr Johanna Fraser

Dr. Fraser leads an independent research team co-located alongside the World Mosquito Program (Monash University, Australia). Her research aims to support the long-term success of Wolbachia-based biocontrol programs that are being utilised to reduce the incidence of Ae. aegypti-borne viral disease. Currently her team is working to define the risk of viral resistance developing towards Wolbachia, and to describe the mechanisms underpinning Wolbachia's antiviral activity.

Dr. Fraser's team uses a range of molecular techniques including fluorescent and transmission electron microscopy, viral genomics, and transcriptomics to better understand the interactions between viruses, Wolbachia and mosquito host cells.

DEFINING THE ANTIVIRAL MECHANISMS OF WOLBACHIA; THE BACTERIUM PROTECTING COMMUNITIES FROM MOSQUITO-BORNE VIRUSES

Abstract

The endosymbiotic bacterium, Wolbachia, has been developed as a biocontrol tool to limit transmission of human pathogenic viruses by Aedes aegypti. Wolbachia has now been established in Ae. aegypti populations at sites in >11 countries and field trials have demonstrated its efficacy. This includes a randomised controlled trial in Indonesia, which reported a 77% reduction in dengue incidence in regions where Wolbachia-infected Ae. aegypti were established (Utarini et al., NEJM 2021).

Despite this success, the mechanisms underpinning Wolbachia's antiviral activity in mosquitoes are not well defined. To address this we have developed a panel of Ae. aegypti-derived cell lines infected with genetically diverse Wolbachia strains with varying antiviral activity. We probed how these Wolbachia strains associated with host cell organelles and identified specific impacts on the endoplasmic reticulum and lipid droplets contributing to viral restriction.

INVITED SPEAKERS

Dr Jamal I-Ching Sam

Dr Sam is a medical graduate from the University of Nottingham in the UK, and completed his postgraduate training in Medical Microbiology in London. He is head of the diagnostic virology and advanced (molecular) diagnostics units in the University of Malaya Medical Centre, a 1000-bed tertiary referral centre in Kuala Lumpur. He is also involved in teaching at both undergraduate and postgraduate levels. His research interests cover clinical, epidemiological, diagnostic and pathogenesis aspects of chikungunya and other arboviruses, respiratory viruses, and enteroviruses.

CIRCULATING CHIKUNGUNYA VIRUS VARIANTS IN MALAYSIA AND POTENTIAL IMPLICATIONS FOR MOSQUITO VECTORS AND HUMANS

Abstract

Chikungunya virus (CHIKV) is transmitted mainly by Aedes aegypti and Ae. albopictus mosquitoes, and causes epidemic fever, rash and joint pains. Since the first documented CHIKV outbreak in Malaysia in 1998, there have been changes in the predominant circulating genetic variant: from the previously endemic Asian genotype, prior to mid-2006; to the East/Central/South African (ECSA) epidemic strains carrying the E1 glycoprotein A226V mutation, which caused nationwide outbreaks in 2008-2010; to the resurgence of the ECSA E1-226A strains causing outbreaks after 2017. These variant differences impact vector competence to different Aedes species and spatial (rural/urban) distribution of human cases. They may also possibly affect immunological responses and severity of clinical manifestations including arthritis and neurological involvement, as well as effectiveness of Wolbachia biocontrol in Malaysia. Genomic surveillance of circulating arboviruses is thus important for monitoring variants which may change disease epidemiology.

INVITED SPEAKERS

Dr Indra Vythilingam

Indra Vythilingam (PhD) is currently a Professor in the Department of Parasitology, Universiti Malaya (UM). She worked as a Principal Research Scientist, in Environmental Health Institute, Singapore prior to her appointment to UM. Indra has contributed vastly to the field of vector biology and control for the past 30 years when she worked in the Institute for Medical Research (IMR) in Kuala Lumpur. She incriminated the vectors of simian malaria in Malaysia. She has published more than 160 articles in peer reviewed International and local journals. Indra has served as a WHO consultant on many occasions. She was awarded the Sandosham Gold medal in 2007 by the Malaysian Society of Parasitology and Tropical Medicine for her contribution towards parasitology and Tropical Medicine and Malaysia's Star Research Award 2017, for outstanding national research in tropical diseases by the Ministry of Higher Education, Malaysia. She was the Editor of Journal Tropical Biomedicine from 2006-2014 and subject Editor for Parasites and Vectors from 2016-2020.

CURRENT STATUS OF SIMIAN MALARIA AND ITS VECTORS IN SOUTHEAST ASIA

Abstract

Simian malaria from nonhuman primates is a public health threat to countries in Southeast Asia and is the predominant species affecting humans in Malaysia. Malaysia reported a fair number of Plasmodium knowlesi cases in 2004 and from that year cases of knolwesi malaria have been on the increase in the country. Currently Malaysia is the first country that failed to obtain malaria elimination status due to the occurrence of simian malaria in humans. Simian malaria has been reported in all countries in Southeast Asia. The Luecosphyrus Group of Anopheles mosquitoes have been incriminated as the vectors of simian malaria. These mosquitoes are biting outdoors in the early part of the night and thus current malaria control measures are not effective. With deforestation, the macaques are encroaching human habitats and thus the mosquitoes are able to transmit the parasites from macaques to humans and vice versa. Novel control strategies are required to control the spread of simian malaria to humans in order for countries in SEA to achieve malaria elimination status.

INVITED SPEAKERS

Dr Christopher Ang

Christopher Ang is a senior research officer at the National Environment Agency's Environmental Health Institute (EHI). After obtaining his Bachelor of Science with Honours (Distinction) from Nanyang Technological University in 2021, Christopher embarked on his journey into virology, where he works with insect-specific and medically-important flaviviruses. His current research interests include the detection, isolation and characterisation of novel viruses, as well as understanding the molecular determinants of dengue virus virulence.

DETECTION AND CHARACTERISATION OF THE LINEAGE I INSECT-SPECIFIC FLAVIVIRUS, QUANG BINH VIRUS, FROM RURAL CAUGHT MOSQUITOES IN SINGAPORE

Abstract

Insect-specific flaviviruses (ISFs) replicate efficiently in arthropods but not in vertebrate hosts, distinguishing them from medically-important flaviviruses. Although non-pathogenic to humans, ISFs provide insights into flavivirus evolution, virus-host transmission mechanisms and various biotechnological applications. Using the MAVRIC (monoclonal antibody against viral RNA intermediates in cells) assay, we isolated an ISF in Singapore from Culex gelidus mosquitoes, sharing a 95% partial NS5 sequence homology with Quảng Bình virus (QBV), first discovered in Vietnam. Screening 721 mosquito pools across 17 locations revealed 37 QBV-positive mosquito pools with recurrent detections in northwest and western Singapore. Three QBV isolates were obtained from Culex gelidus mosquitoes, showing efficient growth in C6/36 cells but no replication in Vero cells. Notably, QBV inhibited dengue (DENV) and Kunjin (WNVKUN) viruses in C6/36 cells by 2.9-log and 1.8-log, respectively. This report represents the first spatiotemporal study of an ISF in Singapore and highlights QBV's potential as a biological control against medically-important flaviviruses.

INVITED SPEAKERS

Dr Sazaly Bin Abu Bakar

Sazaly ABUBAKAR, Ph.D., received his training in Virology from the University of Texas Medical Branch, USA. He is currently a Professor of Virology and the Director of the Tropical Infectious Diseases Research and Education Center (TIDREC), the Ministry of Higher Education Malaysia Center of Excellence (HICoE) in infectious diseases, at Universiti Malaya. He is also the director of the WHO Collaborating Center for Arboviruses Reference and Research (MAA-12). His research interest is in vector-borne infectious diseases and the highly virulent emerging infectious disease pathogens. His research team is actively undertaking zoonotic pathogen surveillance activities, developing diagnostics, antivirals, and vaccines against several of these pathogens.

DENGUE VIRUS, MOSQUITOES AND HOST IN SHAPING MAJOR DENGUE OUTBREAKS

Abstract

Post COVID-19 pandemic saw a resurgence in the number of reported dengue cases in most dengue-endemic regions. While factors attributed to COVID-19 mitigation measures have been credited with significantly reducing the number of expected dengue cases, the drivers contributing to its resurgence are less understood. Dengue transmission dynamics involve complex interactions between the virus, host, and vector. The potential roles of the primary dengue virus vectors; Aedes aegypti and Aedes albopictus and virus genetics during dengue outbreaks have remained unclear. A study to investigate the potential of intrinsic differences in the replication properties of DENV-1 genotypes recovered from major outbreaks against that not associated with any outbreak was undertaken using an in vitro and in vivo replication systems. Understanding the influence of genetics-phenotypic relationships of the virus and vectors may shed light on the mechanisms underlying recurrences of dengue outbreaks. This insight could contribute to improved outbreak prediction, preparedness, and control strategies.

INVITED SPEAKERS

Dr Nalini Puniamoorthy

Dr. Nalini Puniamoorthy leads the research at the Reproductive Evolution Lab at National University of Singapore, where they study biodiversity, sexual selection, and speciation. They focus on widespread insect species and use experimental methods involving fieldwork, geometric morphometrics as well as several '-omics techniques to study macro-evolutionary patterns as well as micro-evolutionary processes involved in reproduction. They also focus on ecologically relevant insect models to seek solutions to diverse problems: From estimating polyandry and gene flow in mosquito vectors to studying reproductive diversification ecosystem service providers like dung beetles and even to engineering black soldier fly reproduction for sustainable food waste management.

POLYANDRY, POPULATION STRUCTURE AND WOLBACHIA INFECTIONS IN AEDES ALBOPICTUS ACROSS SINGAPORE

Abstract

Aedes aegypti and Ae. albopictus are major mosquito vectors of deadly pathogens. Vector control programs worldwide release Wolbachia-infected males to suppress wild Ae. aegypti population by inducing cytoplasmic incompatibility in eggs. However, female remating frequency or polyandry in natural Aedes populations can influence the effectiveness of such vector programs because female fertility may be rescued by mating with non-infected males. Additionally, when they co-occur, the environmentally resilient Ae. albopictus, often naturally infected with Wolbachia, may take over niches as Ae. aegypti is suppressed. There are gaps in knowledge about polyandry in natural mosquito populations, especially in the tropics. We estimate female remating by genotyping sperm dissected from spermathecae of Aedes albopictus mosquitos in tropical Singapore, a dengue-endemic, urban city-state currently employing Wolbachia vector control. Despite using conservative approaches, we report extremely high polyandry in natural populations (Ae. albopictus – 83.9%). Notably, we find strong female-biased sexual size dimorphism, with female body size strongly predicting female re-mating frequencies but little evidence for selection on sperm length as a function of body size in males.

INVITED SPEAKERS

Dr Jingwen Wang

Dr. Jingwen Wang is a professor at Fudan University, where she received her PhD. Following postgraduate and postdoctoral training with Professor Serap Aksoy at Yale School of Public Health, she established her laboratory at Fudan University in 2014. In her lab, she examines vector symbiosis (mosquitoes, ticks), investigating how microbiota regulates vector metabolism and immunity. Her lab also aims to understand how these interactions influence pathogen transmission, paving the way for novel vector control strategies.

THE INFLUENCE OF TRYPTOPHAN METABOLISM ON PLASMODIUM TRANSMISSION IN MOSQUITOES

Abstract

Malaria parasites hijack the metabolism of their mammalian host during the blood-stage cycle. Anopheles mosquitoes rely on mammalian blood for sustenance and as a means of transmitting malaria parasites. However, it remains unclear if changes to blood metabolites affect parasite transmission by mosquitoes. We found Plasmodium infection significantly reduced levels of the tryptophan metabolite 5-hydroxytryptamine (5-HT) in humans, mice and mosquitoes. Oral 5-HT supplementation enhanced Anopheles stephensi resistance to Plasmodium berghei by promoting mitochondrial reactive oxygen species generation. Accumulation of dysfunctional mitochondria, due to 5-HT's inhibitory effect on mitophagy, caused this effect. Elevating mouse serum 5-HT levels restored mosquito 5-HT and significantly suppressed parasite infection. In summary, our data highlight the critical role of tryptophan metabolism in determining the capacity of mosquitoes to control parasite infection.

INVITED SPEAKERS

Dr Leen Delang

Leen Delang is an assistant professor at the University of Leuven in Belgium. She received her PhD in Pharmaceutical Sciences from the University of Leuven in 2011, working on new antivirals for hepatitis C virus. As a postdoc, she characterized new antiviral drugs for the chikungunya virus. In 2016, she was a visiting researcher at the Pasteur Institute in Paris, where she studied transmission of drug-resistant chikungunya viruses by mosquitoes. In 2019, Leen started her own research group in Leuven, focusing on understanding interactions between arboviruses, their mosquito vectors and the mammalian host, and translating this work into new antiviral strategies.

ANTIVIRAL STRATEGIES FOR MOSQUITO-BORNE VIRUSES: A 'BUZZING' ROLE FOR THE MOSQUITO VECTOR?

Abstract

Over the past 20 years, the world has experienced multiple significant epidemics of mosquito-borne virus infections. Mosquito-borne viruses can cause severe diseases such as hemorrhagic fever, encephalitis and chronic arthritis. Despite their significant disease burden and their worldwide presence, there are currently no antiviral drugs available for treatment. In this presentation, Leen Delang will discuss the development of small-molecule antiviral drugs for the chikungunya virus. She will also talk about new strategies that could complement traditional antiviral therapies and mosquito control methods. Such new approach could be the inhibition of virus replication in the mosquito by antiviral drugs. A possible route by which an adult mosquito can take up an antiviral drug, is through blood ingestion from a patient who is being treated with the drug. Antiviral activity in the mosquito could be a favorable drug characteristic, since this might significantly reduce virus transmission to new hosts.

INVITED SPEAKERS

Dr Claudia Rückert

Dr. Rückert discovered her interest in arboviruses during an internship in Dr. Alain Kohl's lab in 2009. She earned her PhD from the University of Edinburgh in 2014 where she worked on antiviral responses of tick cells in Dr. John Fazakerley's lab at the Roslin Institute and the Pirbright Institute. In 2015, she joined Dr. Greg Ebel's lab at Colorado State University to study antiviral responses of mosquitoes, co-infection of mosquitoes, and arbovirus evolution. Currently, Dr. Rückert's lab at the University of Nevada, Reno, focuses on antiviral responses of mosquitoes with a focus on Culex mosquitoes and molecular tool development.

DEFINING MECHANISMS OF VIRAL DSRNA SENSING IN VECTOR MOSQUITOES

Abstract

The prevention of virus transmission at the vector level is a promising avenue of research to reduce arboviral disease burden. Improving our understanding of mosquito immune pathways may ultimately translate into novel vector control strategies. The first step in mounting an antiviral immune response is recognizing the presence of infecting viruses. Long dsRNA generated during virus replication is generally foreign to animal cells and acts as a pathogen associated molecular pattern in many organisms. In mosquitoes, our hypothesis is that dsRNA is sensed predominantly by two proteins: Dicer-2 and Toll-6. Here, we introduce these two proteins, what role they may play during virus replication, and what tools we have developed to study these proteins in mosquito cells. We also highlight other dsRNA binding proteins that may be involved in controlling or facilitating virus replication, increasing our repertoire of targets for future generation of transgenic mosquitoes.

INVITED SPEAKERS

Dr Cheng Gong

Dr Cheng's studies focus on the molecular dissection of the mosquito-virus-host interphase, which intend to identify key factors involved in viral pathogenesis, transmission, and immunity in mosquitoes/hosts, thus developing novel approaches to control these viral diseases spreading in nature. Dr. Cheng has identified multiple key factors in both host blood and mosquito to determine the effectiveness of flavivirus acquisition from infected hosts to fed mosquitoes. Besides, Dr. Cheng's studies aim at understanding the molecular basis of flavivirus infection in mosquitoes and the viral transmission from infected mosquitoes to naïve hosts. These pioneer works offer an insight into the emergence and re-emergence of flaviviruses in nature, thus providing an avenue for disease prevention.

SKIN MICROBIOTA, HOST VOLATILES AND VIRAL TRANSMISSION BY MOSQUITOES

Abstract

Host-seeking activity of hematophagous arthropods is essential for arboviral transmission. Here, we demonstrate that mosquito-transmitted flaviviruses can manipulate host skin microbiota to produce a scent that attracts mosquitoes. We observed that Aedes mosquitoes preferred to seek and feed on mice infected by dengue and Zika viruses. Acetophenone, a volatile compound that is predominantly produced by the skin microbiota, was enriched in the volatiles from the infected hosts to potently stimulate mosquito olfaction for attractiveness. Of note, acetophenone emission was higher in dengue patients than in healthy people. Mechanistically, flaviviruses infection suppressed the expression of RELMα, an essential antimicrobial protein on host skin, thereby leading to expansion of acetophenone-producing commensal bacteria and consequently a high acetophenone level. Given that RELMα can be specifically induced by a vitamin A derivative, dietary administration of isotretinoin to flavivirus-infected animals interrupted flavivirus lifecycle by reducing mosquito host-seeking activity, thus providing a strategy of arboviral control.

INVITED SPEAKERS

Dr Emilie Pondeville

Dr Pondeville is an expert in mosquito biology and interactions with pathogens. After her PhD studies on mosquito reproductive processes at UPMC (Paris, France), she moved to the Institut Pasteur as a postdoctoral fellow where she developed mosquito genetic transformation and genetic tools to study mosquito-pathogen interactions. She is now Senior Research Fellow and head of the mosquito research infrastructures that she established at the MRC-University of Glasgow Centre for Virus Research. Her research interests focus on understanding how mosquito biology influences the spread of mosquito-borne pathogens to inform the design of vector control strategies to tackle mosquito-borne diseases. V

MICROBIOTA-NUTRITION-PHYSIOLOGY INTERACTIONS IN MOSQUITOES: TREAT AND TRICK?

Abstract

Trade-offs exist in many aspects of our daily life. In biology, as previously well understood and described in other words by Darwin, a trade-off exists when a choice must be made between two incompatible traits or when one trait cannot increase without a decrease in another. These negative relationships occur because costly traits influencing fitness, such as survival, reproduction, or immunity cannot be optimized simultaneously beyond certain limits. I will present data showing that the reproductive strategy of mosquitoes has led to a trade-off between reproduction and immunity, governed by the peculiar nutrition mode of mosquitoes - alternating between sugar and blood feeding - as well as their microbiota. Our findings highlight the implications of trade-offs in the processes governing mosquito susceptibility to arbovirus infection and spread and this may ultimately inform the design of vector control strategies to tackle mosquito-borne diseases.

INVITED SPEAKERS

Dr Wang Si Bao

Dr. Sibao WANG is a professor at CAS Center for Excellence in Molecular Plant Sciences, Institute of Plant Physiology & Ecology, Chinese Academy of Sciences (CAS), and the director of the CAS Key Laboratory of Insect Developmental and Evolutionary. He received Ph.D. degree from Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences in 2007. After carrying out postdoc studies at University of Maryland (2007-2009) and Johns Hopkins University School of Public Health (2009-2012), he was appointed as a Principal Investigator and research group leader in the Institute of Plant Physiology & Ecology, CAS in 2013.

Professor Wang's research focuses on unraveling molecular interactions between insects, pathogens, and microbiota, and developing innovative approaches to control insect pests and prevent mosquito-borne disease transmission. Prof. Wang has published papers in prestigious peer-reviewed journals, such as Science (2017, 2021), Cell Host & Microbe (2023), Nature Microbiology (2021), Science Advances (2020), Nature Communications (2019, 2023), PNAS (2011, 2012, 2014, 2017, 2021, 2023), Cell Reports (2022), PLoS Pathogens (2011), Sci. China Life Sci.(2017), Trends in Parasitology (2020), Trends in Biotechnology (2013), etc.

INVITED SPEAKERS

Dr Wang Si Bao

MOSQUITO MICROBIOTA AND IMPLICATIONS FOR DISEASE CONTROL

Abstract

The stalling global progress in the fight against malaria prompts the urgent need to develop new intervention strategies. Blocking malaria parasites in the vector mosquito before they are transmitted to humans is a promising strategy to prevent malaria transmission. As part of this effort, we have been developing a promising strategy for blocking the transmission of mosquito-transmitted diseases via populating mosquitoes with anti-pathogen bacteria, known as paratransgenesis or symbiont-based transmission blocking strategy. We demonstrated that engineered symbiotic bacterium Serratia AS1 that secretes anti-Plasmodium effector molecules effectively render mosquitoes resistant to Plasmodium infection. More recently, we identified a natural Plasmodium-blocking symbiotic bacterium, Serratia ureilytica Su_YN1, isolated from the midgut of wild Anopheles sinensis in China that directly inhibits Plasmodium falciparum via secretion of a lipase. Importantly, Su_YN1 rapidly disseminates through mosquito populations by vertical and horizontal transmission, providing a potential tool for blocking malaria transmission in the field. We further found Su_YN1 delivers the effector lipase AmLip to Plasmodium parasites via outer membrane vesicles (OMVs), leading to targeted killing of the parasites. Notably, Su_YN1 OMVs incorporate certain serum-derived phospholipids that are important for OMV uptake by Plasmodium parasites via the phosphatidylcholine scavenging pathway, uncovering a novel mechanism by which gut commensal bacteria deliver effector molecules via OMVs to selectively attack the parasites and thus render mosquitoes refractory to malaria parasite infection. We also found that blood meal activates the mosquito symbiotic bacterium Su_YN1 quorum sensing system, inducing the synthesis of C6-HSL molecules that drive OMV biogenesis by activating phenylalanine metabolism. The abundant OMVs facilitate bacterial biofilm-like aggregation and promote Serratia survival and persistence in the gut of blood-fed mosquitoes, identifying a powerful strategy for enhancing commensal resistance to pathogens. These findings show that Su_YN1 provides a potential tool for driving mosquito refractoriness to Plasmodium infection and thus blocking malaria transmission in the field.

INVITED SPEAKERS

Dr Julien Pompon

Julien Pompon is a team leader at IRD in France. His research focuses on the triangular interactions between viruses, mosquitoes and hosts that takes place at the bite site and results in transmission. His research objective is to develop novel interventions by targeting molecular factors responsible for transmission.

LIPIDS IN MOSQUITO SALIVA ENHANCE TRANSMISSION FOR MULTIPLE FLAVIVIRUSES

Abstract

During biting, flaviviruses are secreted in mosquito saliva, resulting in skin infection and transmission. Salivary proteins have been implicated in modulating transmission. Here, we discovered that lipids contained in mosquito salivary extracellular vesicles (EV) enhance transmission. We showed that supplementation with mosquito lipids increases infection for multiple flaviviruses in different cellular models and in vivo. We determined that salivary lipids increase viral translation by regulating mammalian intracellular lipidome. We identified that mosquito sphingomyelin was responsible for the increased infection and used sphingomyelinase to develop a treatment that inhibits the salivary lipid enhancement of flavivirus transmission. Altogether, we revealed that mosquito EV lipids are a new type of salivary components that increase flavivirus transmission and identified the lipid class at play to develop a novel intervention.

INVITED SPEAKERS

Dr Guann-Yi Yu

Dr. Guann-Yi Yu is a virologist with expertise in virology and viral pathogenesis. Dr. Yu has more than 20 years of experience investigating RNA viruses, including Hepatitis C Virus, Zika Virus, Dengue Virus, and SARS-CoV-2. Dr. Yu has established several small animal models to investigate virus-host interaction and pathogenesis. Her research interests also have been extended to innate immune responses and inflammation in liver cancer. Furthermore, Dr. Yu's dedicated team is actively involved in the establishment of viral collections for the National Infectious Diseases Bank in Taiwan, aiming to meet the academic and industrial requirements in this crucial field.

HIGH PATHOGENIC DENV-2 STRAIN IN MOSQUITOES AND MOUSE MODELS

Abstract

Dengue virus (DENV) causes dengue fever and severe hemorrhagic fever in humans and is primarily transmitted by Aedes aegypti and A. albopictus mosquitoes. The DENV serotype 2 (DENV-2), which caused a widespread outbreak in Taiwan in 2015 (TW2015), is of the Cosmopolitan genotype and is phylogenetically related to the virus strain linked to another large outbreak in Indonesia in 2015. We found that the TW2015 virus exhibits high virulence in type I and type II interferon-deficient mice, with robust replication observed in the spleen, lung, and intestine. The TW2015 virus demonstrates a high level of transmissibility to Aedes mosquitoes and can efficiently propagate within a continuous mosquitoes-mouse-mosquitoes-mouse transmission cycle. This transmission mouse model serves as a valuable platform for the development of new strategies to combat dengue outbreaks.

INVITED SPEAKERS

Dr Pablo Bifani

Pablo obtained his PhD from the New York University, USA on the molecular epidemiology and drug resistance of Mycobacterium tuberculosis. He continued working on tuberculosis at the Pasteur Institute of Lille, France and the Pasteur Institute of Brussels, Belgium (now Institute of Public Health). In 2008, he joined the Novartis Institute for Tropical Diseases, Singapore, first as lead in TB drug discovery and subsequently in 2011 he established and headed the Malaria Biology team until 2017. He holds a joint Professorships with the Department of Microbiology and Immunology, YLLSoM, National University of Singapore, the Infectious Diseases Labs at A*STAR, and the London School of Hygiene and Tropical Medicine (LSHTM), U.K

FROM STRUCTURAL BIOLOGY TO EPIDEMIOLOGY

Abstract

In recent years, there has been shift and resurgence in the drug discovery field towards the selection of novel compounds based on phenotype screens. However, these are hindered by the time-consuming process of target deconvolution. There is a need to develop a system that rapidly enables determination of a drug targets or mechanism of resistance. Here, we apply forward genetics and borrow methods used bacteriophage biology and bacteriology with the aim to swiftly identifying viral drug targets and mechanisms of resistance. We show that, using these methods, we can determine the DENV gene targeted by novel antiviral drugs based on the mutation profile of multiple resistant mutants.

INVITED SPEAKERS

Dr Marco Vignuzzi

Marco Vignuzzi obtained his B.Sc from McGill University, and MSc and PhD from University of Paris. Following 7 years of postdoctoral studies in Raul Andino's lab at UCSF, he founded his own laboratory at Institut Pasteur in 2008. Since September 2022, he is a Senior Principal Investigator at A*STAR ID Labs, and an adjunct Associate Professor at NUS and NTU medical schools.

FROM STRUCTURAL BIOLOGY TO EPIDEMIOLOGY

Abstract

RNA viruses are the fastest evolving organisms, with high mutation frequencies, small genomes, and fast replication rates. Despite their simplicity, they interact with each other through complementation, competition and other collective behaviours in complex population dynamics. In this talk, I describe our recent work on flavi- and alpha-virus defective genomes that can either promote or hinder virus infection and evolution.

INVITED SPEAKERS

Dr Amit Sharma

Dr Sharma is a Group leader at the International Centre for Genetic Engineering and Biotechnology. He is also Former Director, National Institute of Malaria Research, New Delhi (2019-2022), in addition to Research and teaching fellow at St Johns and Trinity Colleges, Oxford Univ, 1996-2000. Dr Sharma works at Structural Parasitology, Molecular Medicine Group, International Centre for Genetic Engineering and Biotechnology, New Delhi

FROM STRUCTURAL BIOLOGY TO EPIDEMIOLOGY

Abstract

Our work on public health research and policies can take India towards elimination of malaria. India has sustained a decline in the overall malaria burden, but the epidemiological picture of the disease remains varied. Several challenges need to be addressed including insufficient surveillance, climate change and data collation. We have proposed that surveillance, data visualization, and analysis be supported through over-the-counter availability of rapid diagnostics, adoption of molecular tools like PCR, mobile applications for data capture, and use of a dedicated malaria data dashboard. We have developed a digital dashboard interface that allows prompt and interactive analyses of malaria epidemiological data. This will greatly facilitate transparent and evidence-based formulation of malaria control and elimination policies. It can be used by all malaria endemic countries with their epidemiological data. It can include vector surveillance and vector resistance data in it.

INVITED SPEAKERS

Dr Jody Peters

Dr Jody 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. She has focused on strategies to detect emerging viruses and benign mosquito symbionts, the latter of which have been exploited to generate innovative vaccine and diagnostic candidates against numerous mosquito-borne diseases caused by viruses such as Japanese encephalitis, West Nile and chikungunya viruses.

HARNESSING RECOMBINANT MOSQUITO-SPECIFIC VIRUSES TO TACKLE EMERGING ONE HEALTH VIRAL DISEASES

Abstract

We have developed recombinant mosquito-specific virus platforms for the manufacture of chimeric virus particles for major One Health viral diseases such as Japanese encephalitis and West Nile. One platform, based on the Australian insect-specific flavivirus, Binjari virus (BinJV) is remarkably versatile, facilitating the production of vaccine and diagnostic antigens for a multitude of flaviviruses, including dengue. The chimeric virions are structurally and antigenically indistinguishable from pathogenic flaviviruses, are replication-deficient in vertebrate cells, but replicate efficiency in mosquito cells. Our recent vaccine trials have extended beyond the lab, providing protection against disease in two Livestock species, pigs and crocodiles. During translation, we are adopting using industry-standard protocols for chimeric antigen production. As diagnostic antigens, the chimeric particles have been applied to a variety of platforms, including rapid lateral flow assays, the design of which will form a blueprint for the optimisation of similar point-of-care tests for flavivirus infection detection in both humans and animals.

INVITED SPEAKERS

Prof Julien Lescar

Prof. Julien Lescar is a biochemist and structural biologist with extensive experience in using X-ray crystallography and cryo-electron microscopy as a main tool for protein structure-function studies especially in the field of infectious diseases. He has determined the 3D structures of numerous viral proteins involved in RNA virus entry and virus replication for several major human pathogens (flaviviruses such as dengue virus or Zika virus, alphaviruses such as chikungunya virus, human metapneumovirus). He is collaborating with Professors Bozdech and Preiser on identifying novel targets for the malaria parasite.

IDENTIFICATION AND STRUCTURAL VALIDATION OF PURINE NUCLEOSIDE PHOSPHORYLASE FROM PLASMODIUM FALCIPARUM AS A TARGET OF MMV00848

Abstract

In the absence of efficacious vaccines, chemotherapy remains crucial to prevent, treat and contain malaria. The efficacy of current drugs will suffer from the emergence of resistant parasites. Efforts to identify lead compounds led to several initiatives such as the Medicine for Malaria Ventures (MMV), a repository of compounds able to kill the parasite in cell-based assays. We used mass spectrometry coupled with cellular thermal shift assay (MS-CETSA) to identify protein targets of MMV000848, a drug candidate against the parasite. Thermal shift assays showed a strong increase of P. falciparum purine nucleoside phosphorylase (PfPNP) melting temperature upon incubation with MMV000848. Binding and enzymatic assays showed that the inhibition is competitive with respect to the substrate, as confirmed by a cocrystal structure of PfPNP bound with MMV000848 at the active site. These results point to PfPNP as a promising antimalarial target and suggest avenues to improve inhibitor potency.

SELECTED SPEAKERS

Dr Piyatida Leelagud

Piyatida Leelagud, a Thai PhD candidate at the Department of Entomology at National Chung Hsing University, Taiwan. I am focusing on biological control, specifically utilizing microbial methods to control Aedes aegypti mosquitoes. My research also involves histological studies of Aedes aegypti larvae.

PSEUDOMONAS ENTOMOPHILA: A POTENTIAL ALTERNATIVE FOR THE MANAGEMENT OF PYRETHROID-RESISTANT AEDES AEGYPTI

Abstract

Aedes aegypti is widespread in tropical and subtropical regions, transmitting dengue fever and Zika virus that causes significant human mortality and morbidity. Synthetic insecticides like pyrethroids have been used for controlling Ae. aegypti. However, they also affect non-target organisms and cause environmental contamination. This study investigated the mosquitocidal activity of Pseudomonas entomophila, an entomopathogenic bacteria, against Ae. aegypti larvae. The results showed that the supernatant of the bacterial culture possessed a similar time-course profile of mosquitocidal activity as the culture, and the pellet resuspended in the LB medium showed delayed toxicity. These results imply that the toxic component can be released into the medium from live bacteria. Upon further investigation, results showed that the toxic component appeared in supernatant about 4 h after culturing in LB medium. P. entomophila culture stored at 28°C has the best stability while supernatant showed its best stability at 4°C. Moreover, bacterial culture and supernatant were toxic to the pyrethroid-resistant (Per-R) strain with LT50 values of 4.87 and 5.13 h, respectively, which were similar to those of susceptible strains. These results further indicate that P. entomophila can be used as an alternative insecticide to control field pyrethroid-resistant Ae. aegypti.

SELECTED SPEAKERS

Dr Kelvin Ho

Kelvin Ho trained as a veterinarian at the University College Dublin Veterinary School and attained professional qualification through the Australian and New Zealand College of Veterinary Scientists (MANZCVS (Veterinary Epidemiology)). He joined the Agri-Food and Veterinary Authority in 2016 and was previously involved in shelter medicine and animal population management. He currently works within the Biorisk and Biosurveillance Branch of the Animal & Veterinary Service, National Parks Board, which oversees the planning and coordination of animal health biosurveillance, risk assessment, disease investigation, and outreach programmes to improve health in animal populations.

TICK AND CANINE TICK-BORNE DISEASE BIOSURVEILLANCEIN FREE ROAMING DOGS AND ANIMAL ESTABLISHMENTS IN SINGAPORE: 2019-2023

Abstract

We characterise biosurveillance for ticks and canine tick-borne diseases (CTBDs) in Singapore from 2019 to 2023. Over 5 years, 1111 ticks were collected from animal establishment environment and identified via morphological and molecular methods as Rhipicephalus linnaei, the tropical lineage of Rhipicephalus sanguineus. These ticks were pooled into 205 pools for pathogen analysis, of which 14 pools (6.83%), 7 pools (3.41%), and 29 pools (14.1%) had detections for Babesia gibsoni, Ehrlichia canis and Anaplasma phagocytophilum, respectively. A survey was conducted in 119 dogs from some of these establishments – 15.13% and 10.92% had antibodies against Ehrlichia sp. and Anaplasma sp. respectively, while 6.72% had detections of Babesia gibsoni by PCR; none had detections for Ehrlichia sp. and Anaplasma sp. by PCR. Of the free-roaming dogs (FRDs) sampled from 2020 to 2022, 4.50% (5/111) had antibodies against Ehrlichia sp., while 50.00% (15/30) had detections for Babesia gibsoni by PCR. None (n=111) had detectable antibodies against Anaplasma sp. We demonstrate continuous risk of CTBDs in host and vectors particularly in high-density settings, warranting year-round tick management. Despite the emerging role of R. linnaei in vectoring zoonotic A. phagocytophilum, the prevalence in FRDs appears low. Ongoing monitoring is required to assess human spillover risk.

SELECTED SPEAKERS

Dr Zhen Yuan Yeo

Yeo Zhen Yuan, with a Master's in Physics from the National University of Singapore in 2021, has been exploring the applications of unsupervised machine learning with a keen interest in epidemiology. He has worked on network reconstruction techniques, aiming to shed light on transmission networks that are not directly observable.
In a notable project, Zhen Yuan applied a coarse-grain model to dengue transmission, adapting it to work with the infection data that is often the only information available in real-world scenarios.

INFERRING THE HIDDEN AND LONG-RANGE DENGUE TRANSMISSION ROUTES IN SINGAPORE

Abstract

Dengue is recognized as a significant health threat in tropical areas, particularly in Singapore, where it is primarily transmitted by the Aedes aegypti mosquito. In this study, a novel model is introduced, depicting dengue transmission as a direct host-to-host interaction, bypassing the traditional host-vector-host model.
Under this assumption, dengue infections were simulated on a small-world network with realistic spatiotemporal properties. By the use of geotagged and time-tagged infection data, we reformulated the infections as independent cascades and its underlying network could be reconstructed with a network inference algorithm. When this approach was applied to data from Singapore from 2014 and 2016, different transmission patterns were observed between the years. This network inference methodology was found to have 10-100x more Positive Predictive Value (PPV) than random methods. Enhanced genetic tracking of the dengue virus further authenticated transmission routes.
In conclusion, the proposed host-to-host transmission model, based on geotagged and time-tagged data, offers a novel approach to understanding dengue transmission dynamics. The adaptability of this methodology to other diseases with comparable datasets and the observed variations in transmission patterns highlight its potential impact and relevance for broader disease control strategies.

SELECTED SPEAKERS

Dr Julie Reveillaud

Julie Reveillaud was trained in molecular evolution at the University of Gent in Belgium and in microbial ecology at the MBL in Woods Hole (MA, USA). She is broadly interested in how animals, bacteria and viruses interact between each other. Currently, she investigates the molecular dialog between Wolbachia and its mobilome, commensal microbial communities and pathogens in the different body compartments of naturally infected Culex mosquitoes. Her team uses wet lab and in silico approaches including genetics, 16S amplicon sequencing, metagenomics and advanced binning together with metatranscriptomics to better understand intimate host-microbe interactions and potentially develop novel vector biocontrol strategies

WOLBACHIA PLASMID PWCP IS WIDELY DISTRIBUTED AND HIGHLY CONSERVED IN CULEX PIPIENS AND CULEX QUINQUEFASCIATUS MOSQUITOES WORLDWIDE

Abstract

Mosquitoes represent the most important pathogen vectors and are responsible for the spread of a wide variety of poorly treatable diseases. The widely distributed Wolbachia bacterium, which can block pathogen transmission and dramatically manipulate host reproduction, represents one of the most promising solutions for vector control. Yet, due to its endosymbiotic nature, Wolbachia is not easily amenable to genetic manipulation, which imposes strong constraints on dissecting its mechanisms of action. Recently, several Wolbachia plasmids, carrying phage WO-like genes and Insertion Sequences, have been discovered. Here, we investigated the diversity and distribution of the first described plasmid of Wolbachia in Culex pipiens (pWCP) in several islands and continental countries around the world—including Cambodia, Guadeloupe, Martinique, Thailand, and Mexico—together with mosquito strains from colonies that evolved for 2 to 30 years in the laboratory. We used (q)PCR to screen for the presence and abundance of pWCP in both the germline and somatic tissues of individual mosquitoes, and highly accurate Sanger sequencing to evaluate potential variations. Our results show that pWCP is omnipresent and strikingly conserved among Wolbachia populations within mosquitoes from distant geographies and environmental conditions.

SELECTED SPEAKERS

Dr Milly Ming-Ju Choy

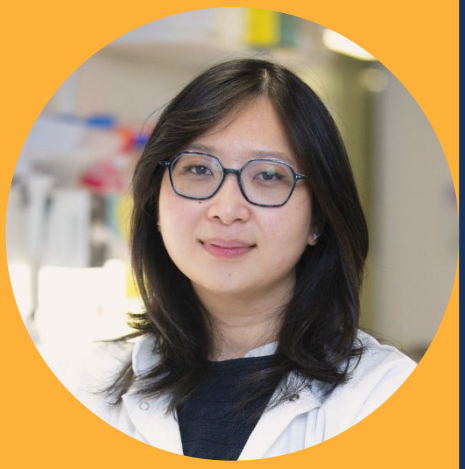
I am a Principal Research Scientist in the Programme in Emerging Infectious Diseases at Duke-NUS Medical School. I run the Arthropod Containment Level 2 Insectary Core Facility. I am also affiliated to the J&J Center of Global Health Discovery for flavivirus research. My research interest lies in the use of genomics and next generation sequencing to study flavivirus-host interaction so that this body of knowledge can be applied to the development of effective vaccines and antiviral therapeutics.

SPECIES- AND TISSUE-SPECIFIC MICRO-EVOLUTION OF DENGUE VIRUS IN AEDES AEGYPTI AND AEDES ALBOPICTUS MOSQUITOES

Abstract

DENV is transmitted in an urban cycle between humans and Ae. aegypti or Ae. albopictus, both of which are present in most Asian cities. While Ae. albopictus has been associated with a few dengue epidemics over the past decades, almost all major epidemics of dengue haemorrhagic fever have occurred in areas where Ae. aegypti is present. One plausible explanation is that the development of intra-host variants of DENVs in Ae. aegypti and Ae. albopictus is different in potential for epidemic transmission. To this end, we performed next- generation sequencing of DENV2-populations isolated from the midguts and heads/thoraces of infected mosquitoes. Whilst Ae. aegypti and Ae. albopictus share consensus changes in the dengue genome, higher DENV genome diversity were observed in both midguts and heads/thoraces of Ae. albopictus compared to Ae. aegypti. We show that the differences in the micro-evolution of DENV between Ae. aegypti and Ae. albopictus occurs primarily in the midgut, the main anatomical and physiological barrier of virus infection. DENVs transmitted predominantly in an Ae. aegypti-human cycle may produce viruses genetically distinct from those in an Ae. albopictus-human cycle. Future studies on the emergence of virulent strains evolving out of species-specific selective pressure on the DENV genome may prove insightful.

SELECTED SPEAKERS



Dr Cassandra Koh

Cassandra Koh is a Postdoctoral Research Fellow in the Viruses and RNA Interference Unit at Institut Pasteur, France. She obtained her Doctorate degree in 2019 at Monash University, Australia, investigating the vector biology of the Aedes aegypti mosquito from several angles, including the influence of the antiviral Wolbachia endosymbiont. Her cu rrent research focuses on the mosquito virome, seeking to parse the role of mosquito-specific viruses within the arboviral disease ecology. Understanding the interplay between mosquito viruses and their impact on the transmission of arboviruses will lead to new insights into mosquito-virus interactions, as well as novel interventions for the management of mosquito-borne disease epidemics.

EXPLORING THE VIROMEOF FIVE MOSQUITO GENERA ACROSS DIVERSE GEOGRAPHIC REGIONS

Abstract

The mosquito viral microbiota plays an important role in the disease ecology of mosquito-borne viruses due to their influence on vector competence. They have consequently garnered great research interest in their use to comprehend and manage arboviral disease outbreaks. Although recent metaviromics studies have uncovered a remarkable number and diversity of novel mosquito-specific viruses, these are often limited to a narrow range of mosquito species. In addition, investigations across distant geographical locations are rare and methodological discrepancies complicate cross-study comparisons, hindering our understanding of the diversity of global mosquito viromes. To bridge this gap, we conducted a longitudinal study of 21 mosquito species from the genera Aedes, Culex, Anopheles, Mansonia, and Coquillettidia to examine the factors shaping mosquito virome diversity. Mosquito populations from Cambodia, Madagascar, the Central African Republic, and French Guiana were sampled from 2019 to 2021. Our metagenomics study revealed virus distribution patterns that bring additional insights into the notion of a species-specific ‘core’ virome. Notably, we found ‘super host’ mosquito species and viruses with broad mosquito host ranges, reshaping our view of mosquito-virus interactions and highlighting the mosquito-specific viruses deserving further research attention for improved arboviral disease management through a One Health perspective.

SELECTED SPEAKERS

Dr Hong-Guan Tee

Specializing in the study of mosquito behavior and the circadian clock. I have pioneered ground breaking experiments that unravel the mysteries of how mosquitoes operate and their temporal rhythms. These endeavours have significantly enhanced our understanding of these crucial aspects, paving the way for advancements in pest control and chronobiology.

CRYPTOCHROME-1 INFLUENCES CIRCADIAN CLOCK RESETTING AND MORNING ACTIVITY LEVELS IN AEDES AEGYPTI

Abstract

The circadian clock of Aedes aegypti is significantly modulated by the environmental photoperiod, which impacts the timing and duration of essential behaviors including host-seeking. Whilst cryptochromes are known to play a role in transmitting light signalling information to the core clock machinery, it remains unclear how these flavoproteins operate in Aedes mosquitoes. Here, we investigated the influence of Aedes aegypti cryptochrome1 (CRY1) and cryptochrome2 (CRY2) on mosquito behaviors by generating CRISPR/Cas9 knockout lines for use in molecular and behavioral assays. Firstly, we examined rhythmic changes in the expression of core clock genes at both RNA and protein levels, revealing significant differences in the cycling of circadian clock-relevant proteins between CRY1 KO adults and controls. Next, we conducted a locomotor monitoring assay to assess changes in activity under different light:dark (LD) regimes. Intriguingly, CRY1 KO mutants displayed distinct locomotor profiles and activity indexes compared to controls, especially during the transition from the dark phase to light (denoted as morning activity). Via brain immunostaining, we observed reduced expression of the important circadian transmitter pdf in clock neurons in CRY1 KO adults at specific time points, implicating these neurons in determining morning activity levels. These findings suggest that the morning activity of Aedes aegypti is regulated through the action of CRY1 within specific pdf-positive clock neurons.

SELECTED SPEAKERS

Dr Yueh Hsin Ping

Dr Ping who received his Ph.D. in Molecular and Cellular Pharmacology from Rutgers University in the United States is currently an associate professor at the Department and Institute of Pharmacology and an adjunct associate professor at the Institute of Biophotonics at National Yang Ming Chiao Tung University, Taipei, Taiwan. He also serves as the Vice Chairman of the School of Medicine and the Director of the Physician Scientist Program. At the forefront of virological research, Dr. Ping's laboratory is dedicated to the study of critical reemerging viruses, such as the Dengue virus (DENV), Zika virus (ZIKV), and SARS-CoV-2.

UNCOVERING NOVEL ROLES OF DENGUE VIRUS-INDUCED AUTOPHAGY DURING THE EARLY INFECTION STAGE BY SINGLE-VIRUS TRACKING

Abstract

Virus-induced activation of autophagy, termed pro-viral autophagy, is linked to Dengue virus (DENV) replication. However, the precise molecular mechanism underlying DENV-induced autophagy and its functions at the early stage of infection remain unclear. Utilizing a single-virus tracking approach, our study unveiled that DENV swiftly activated the formation of GFP-LC3 puncta, with DENV particles engulfed by autophagosomes within 15 minutes of infection. Notably, we identified the T-cell immunoglobulin and mucin domain 1 (TIM-1) receptor as a novel factor triggering autophagy during DENV infection, alongside its role as a DENV receptor. Knocking down TIM-1 and associated factors by siRNA revealed the involvement of the TIM-1-p85 axis in autophagy induction. Furthermore, employing single-virus tracking in conjunction with pH sensor and FRET imaging, we observed the co-localization of DENV with autophagic vesicles, leading to vesicle acidification and membrane fusion. This facilitated the release of DENV RNA for replication. Quantitative analysis confirmed that 43% of DENV particles translocated from endosomes to autophagic vesicles post internalization. In summary, our findings elucidate an autophagy-dependent uncoating process as a fundamental intracellular trafficking route in DENV infection.

SELECTED SPEAKERS

Dr Ruyue Liu

In 2016, Zika virus (ZIKV) caused a global pandemic involving millions of infections with instances of neurological complications and congenital deformities. ZIKV, like most RNA viruses, has an error-prone RNA-dependent RNA polymerase (RdRp) giving rise to numerous mutations over the course of a single infection. Detailed characterization of these mutations can inform their macroevolution trends plus provide unique insight into their pathogenic potential.. Herein, we have identified several common intrahost mutations from a well-characterized Nicaraguan pediatric cohort during the ZIKV epidemic. Each of these mutations were evaluated using a reverse genetics system for their replicative potential in human cells and mosquitoes. Our results show that three of the identified mutations exhibit growth advantages in one or both hosts. We then examined the underlying mechanisms at the cellular transcriptome level, namely immune downregulation and physiological disturbance. Two of the mutants may also represent an increased neuropathogenesis risk. Finally, we illustrated these mutations' roles beyond ZIKV alone as they also changed the growth phenotype of the closely related dengue virus (DENV). Together, by combining epidemiological data and reverse genetic systems, we demonstrated the enormous potential of intrahost microevolution with single amino acid mutations, which might be a promising area for future studies.

CHARACTERIZATION OF NATURALLY OCCURRING FLAVIVIRUS HOST-SPECIFIC MUTATIONS

Abstract

RNA viruses are the fastest evolving organisms, with high mutation frequencies, small genomes, and fast replication rates. Despite their simplicity, they interact with each other through complementation, competition and other collective behaviours in complex population dynamics. In this talk, I describe our recent work on flavi- and alpha-virus defective genomes that can either promote or hinder virus infection and evolution.

SELECTED SPEAKERS

Dr Carla Bianca L. Victorio

Dr. Bianca Victorio is a native of Manila, Philippines and moved to Singapore to pursue her passion for Virology and Infectious Diseases. After obtaining her Ph.D. in Microbiology and Immunology at NUS, while working on molecular virology and animal model development for enterovirus 71, she subsequently trained as a Molecular Imaging Scientist at Duke-NUS with A/Prof. Ann-Marie Chacko at the Laboratory for Translational and Molecular Imaging (LTMI). She specializes in optical (bioluminescence) and nuclear (PET/SPECT/CT) imaging in preclinical models of viral infections (dengue, Zika, influenza, and common colds) and cancers (glioblastoma, head & neck cancer, lung cancer).

POSITRON EMISSION TOMOGRAPHY (PET) IMAGING BIOMARKERS OF DENGUE AND ZIKA DISEASE IN MOUSE MODELS

Abstract

Dengue and Zika are viral inflammatory diseases prevalent in the Tropics and currently without effective vaccines and antivirals. Our goal is to expedite preclinical evaluation of candidate therapeutics using non-invasive imaging biomarkers (I.B) that are surrogates of in situ tissue disease and inflammation status. We performed positron emission tomography/ Computed Tomography (PET/CT) imaging with PET probes [18F]FDG (fluoro-deoxy-glucose) and [18F]FEPPA (fluoroethoxybenzylphenoxypyridinylacetamide) in dengue and Zika AG129 mouse models at different disease stages. We also performed ex vivo assays to measure viral load and expression of IL-6 and TNF-α in tissues of interest. Zika is characterized by elevated [18F]FEPPA brain uptake at late disease and transiently increased [18F]FDG spleen uptake at mid disease. Meanwhile, dengue is characterized by prominently high intestinal [18F]FDG uptake and liver [18F]FEPPA uptake at late disease. These Zika and dengue I.B. strongly correlated with viral burden and cytokine expression. In addition, dengue I.B. diminished when disease was ameliorated by treatment with celgosivir or anti-TNFα treatment and could distinguish infected mice with active disease from those successfully treated with drugs as early as day 3 post-infection. Thus, dengue I.B. can also be used as early predictors of successful response to experimental therapeutics.

SELECTED SPEAKERS

Dr Amanda Leow

TNFAPROMOTES SEXUAL CONVERSION OF PLASMODIUM FALCIPARUM VIA A SERINE/THREONINE KINASE.

Abstract

Gametocytes are essential for malaria transmission. Gametocytogenesis has been known to be triggered by unfavorable growth conditions but the parasite proteins that facilitate the transduction of host pro-gametocytogenesis signals from host to parasite are poorly understood. In this study, we show that TNFα promotes gametocytogenesis via TNFR1 and downstream signalling through MAPKs p38 and JNK. One of the exported FIKK kinases has been identified to transmit the TNFα signals into the parasite to initiate gametocyte formation. The inhibition of this kinase abolishes both TNFα- and nutrient depletion-induced gametocytogenesis as well as the transcriptional activation of Pfap2-g, the master transcription factor for gametocytogenesis. These findings identify TNFα as a host factor involved in pro-gametocytogenesis signalling, highlighting how the host immune response could modulate parasite transmission and how the parasite could adapt to host signalling pathways for its own survival.

SELECTED SPEAKERS

Dr Sebastien Nisole

Sébastien Nisole is a tenured INSERM researcher and head of the "Viral Trafficking, Restriction, and Innate Signaling" (VTRIS) team at the Research Institute on infectious diseases of Montpellier, France. His team's research is dedicated to virus-cell interactions and innate antiviral immunity. In particular, his work aims to identify cellular factors that control viral replication in human cells and to characterize the molecular mechanisms involved, with a particular focus on mosquito-borne flaviviruses

IDENTIFICATION OF INTERFERON-STIMULATED GENES THAT INTERFERE WITH THE REPLICATION OF WEST NILE AND USUTU VIRUS.

Abstract

West Nile virus (WNV) and Usutu virus (WNV) are two phylogenetically related emerging mosquito-borne flaviviruses. They share the same enzootic transmission cycle that involves Culex mosquitoes as vectors, birds as amplifying hosts, and mammals as dead-end hosts. While WNV is one of the most widely distributed flaviviruses worldwide, USUV is currently limited to Africa and Europe. Since both can cause serious neurological complications, particularly in birds but also in humans, WNV and USUV are considered as serious potential threats to human and animal health.

In vitro, viral replication can be potently inhibited by interferon, a cytokine that has no antiviral activity per se, but acts through the induction of hundreds of interferon-stimulated genes (ISGs), whose products interfere with viral replication. While only a few ISGs are known to impair WNV replication, no studies have ever been undertaken for USUV. To identify the effectors of the antiviral effect of interferon on WNV and USUV, we screened a library of more than 1500 ISGs. We identified several ISGs with potent antiviral activity, among which some had never been described before. Moreover, despite their close genetic proximity, WNV and USUV exhibited major differences in their susceptibility to certain ISGs.

SCIENTIFIC POSTER

Mr Adrian Abarientos

COMPARING THE NEUTRALIZING ACTIVITY OF A POTENT ANTI-FLAVIVIRUS HUMAN MONOCLONAL ANTIBODY EXPRESSED AS IGG1 AND IGG3

A broadly neutralizing anti-flavivirus human monoclonal antibody (huMAb) from a dengue patient with prior exposure to JEV was isolated in our lab. We observed that huMAb K8b, naturally IgG1 isotype, has potent neutralization activities against DENV-1, DENV-2, DENV-4, JEV, and ZIKV, but has moderate neutralization against DENV-3. We hypothesized that the neutralizing activity against DENV-3 could be enhanced if K8b-IgG1 was expressed as IgG3, a more potent IgG subclass due to its longer hinge region that mediates greater molecular flexibility. First, we constructed our expression plasmid by cloning the constant heavy chain of human IgG3 into our in-house expression plasmid of K8b. Next, we expressed the proteins by co-transfection of the heavy chain and light chain plasmids using PEI into HEK293T cells followed by protein purification. We tested the binding reactivity by performing an antigen-capture ELISA using our in-house generated DENV-1, DENV-2, DENV-3, DENV-4, JEV, and ZIKV virus-like particles (VLPs). Lastly, we compared the neutralization activities of K8b-IgG1 and K8b-IgG3 against prototype virions by performing an in-house optimized microneutralization-ELISA (MNT-ELISA). Our initial results showed no statistically significant difference on the binding and neutralization activities of huMAb K8b expressed as IgG1 and IgG3, thus, further investigation is warranted.

SCIENTIFIC POSTER

Dr Benoit Malleret

SYNTHETIC CONTROL METHODS FOR INFECTIOUS DISEASE EPIDEMIOLOGY: APPLICATIONS TO WOLBACHIA INTERVENTIONS

Background: Large scale field trials to evaluate the effect of interventions are increasingly common. However, random assignment of interventions is often difficult to achieve. Here, we present the development and application of synthetic control methods (SCM) in evaluating the efficacies of interventions. We use Project Wolbachia, Singapore as the key example, where incompatible-insect technique coupled with sterile insect technique was employed to suppress Aedes mosquito populations and consequentially, dengue transmission.

Methods & results: Spatially resolved dengue incidence and/or adult Aedes abundance data from Singapore were used, along with a high-dimensional set of spatio-temporal set of environmental and anthropogenic covariates. Donor pools consisting of control units which are never treated by Wolbachia interventions were used to construct synthetic controls using SCM. The canonical SCM was employed. We used different linear combinations of covariates to account for confounding. Intervention efficacies, defined as the percentage reduction in dengue incidence or mosquito abundance, was compared under different settings and methodologies.

Intervention efficacies depended on levels of coverage in release sites and ranged from 47 – 99% across all endpoints. Intervention efficacies were found to be consistent across different endpoints, subgroups and locations. Synthetic control methods were found to generate appropriate control groups as noted by good balance in the endpoint of interest and covariates between both intervention and synthetic control arms in the pre-intervention period. A further battery of robustness checks, such as placebo testing, confirm the validity of intervention efficacy estimates.

Implications: SCM can alleviate many problems which arise from non-randomized experimental settings. Alternatives can flexibly account for many confounders as well as staggered adoption settings where interventions were sequentially applied to different units across time. Our applications to Wolbachia releases demonstrate the high utility for this new class of vector control tools to stem both vector populations and dengue transmission across multiple setting.

SCIENTIFIC POSTER

Mr Bo-Yu Chen

INTERSPECIFIC MATING BIAS CONTRIBUTES TO THE GEOGRAPHIC DISTRIBUTION OF AEDES ALBOPICTUS AND AEDES AEGYPTI IN TAIWAN

Aedes albopictus and Aedes aegypti are important vectors of mosquito-borne diseases. Although the reasons for the differences in their distribution areas in Taiwan are still unclear, interspecific mating with reproductive interference may be a possible contributing factor. Field-collected Ae. albopictus and Ae. aegypti from the northern and southern regions of Taiwan were subjected to different crosses and sex-choice experiments. The results confirmed asymmetric interspecific mating between these two species, with Ae. aegypti having a competitive advantage in southern Taiwan and Ae. albopictus dominating in the northern region. This finding may explain the regional presence of these two mosquitoes in Taiwan. However, variations in distribution seemed unrelated to clasper length. These observations may provide data for public health authorities responsible for dengue fever prevention, potentially leading to more effective resource allocation, especially in mosquito vector control.

SCIENTIFIC POSTER

Mr Cavin Ker

MGI VECTOR AND MICROORGANISMS IDENTIFICATION SEQUENCING SOLUTION

With the globalization, the rapid spread of vectors and pathogens has contributed greatly to the emergence of Vector-borne diseases (VBDs). Due to the limitations of morphological identification, such as the inability to identify non-adult insect stages or incomplete limbs, while the DNA barcoding identification based on Sanger sequencing is time-consuming and labor-intensive and hard to distinguish mixture samples, furthermore, the conventional pathogens identification has the problems of selected detection and unable to detect novel pathogens, which poses challenges for rapid and precise identification and prevention of VBDs.

To solve these problems, MGI recently developed a “trinity” intelligent identification solution from nucleic acid to final report based on high-throughput sequencing (HTS), covering the automated sample preparation, HTS and Vector and Microorganism Identification (VMI) software for data analysis. VMI contains a DNA barcoding database of nine categories of vectors (mosquitoes, flies, mice, cockroaches, shrews, fleas, ticks, mites, and midges) and a microbial database covering over 20,000 species of bacteria, viruses, parasites etc., enabling researchers to simultaneously detect multiple vectors and microorganisms from one nucleic acid sample. In conclusion, the MGI Vector and Microorganisms Identification Sequencing Solution paves the way to facilitate the entry-exit inspection and quarantine, benefiting the prevention of VBDs.

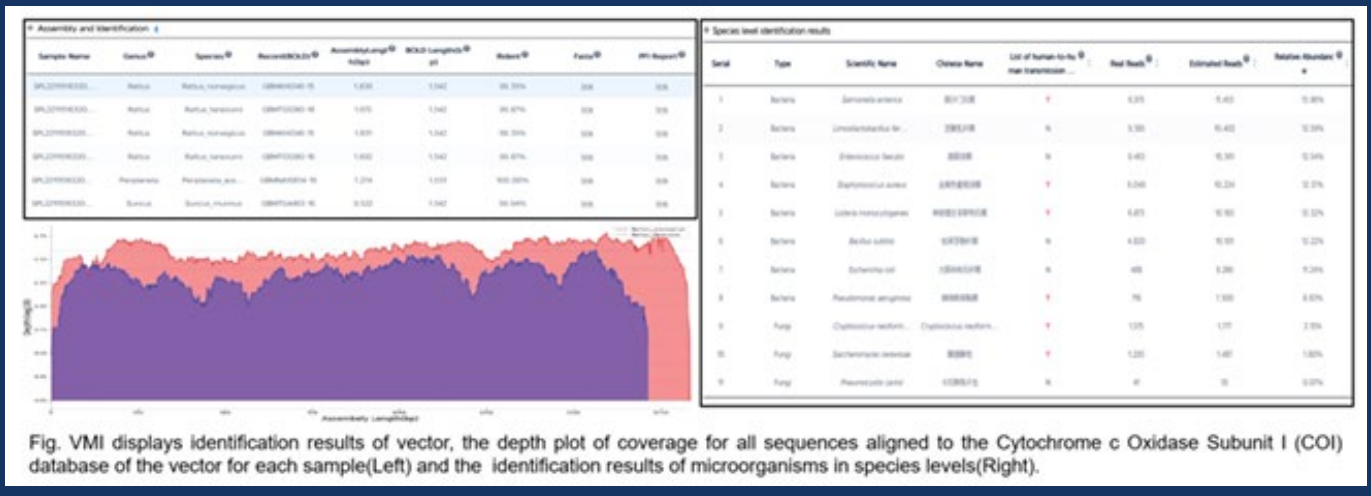


Fig. VMI displays identification results of vector, the depth plot of coverage for all sequences aligned to the Cytochrome c Oxidase Subunit I (COI) database of the vector for each sample(Left) and the identification results of microorganisms in species levels(Right).

SCIENTIFIC POSTER

Dr Chia-Chen Chang

A SHORT-TERM REAL-TIME DENGUE FORECAST MODEL IN SINGAPORE

Dengue is a major public health challenge in Singapore. Vector control program to mitigate outbreak risk has been one of key focus in Singapore. To facilitate resource allocation and planning, a short-term (3 month) dengue forecast model is critical. The first operationalized dengue forecast model, least absolute shrinkage and selection operator (LASSO) model, was developed about 10 years ago. However, due to concept and data drift, the forecast performance of the LASSO model has reduced, so that upgrading the forecast model is upmost important. In this study, we developed an ensemble model by integrating both LASSO and random forest models as well as incorporating additional parameters, such as sub-seasonal weather forecast, serotypes, and effective reproduction value. The ensemble model trained on data from 2010 to 2022 and tested in 2023 provided more accurate forecasts than the original model by reducing the mean average percentage error around 50%. The forecast model can be used to raise public awareness and provide recommendations on the vector control programs.

SCIENTIFIC POSTER

Dr Chun-Hong Chen

MECHANICAL TRANSMISSION OF DENGUE VIRUS BY AEDES AEGYPTI MAY INFLUENCE DISEASE TRANSMISSION DYNAMICS DURING OUTBREAKS

National Mosquito-Borne Disease Control Research Center, National Institute of Infectious Diseases and Vaccinology, NHRI, Taiwan; Electronic address: chunhong@gmail.com. The escalating number of dengue virus (DENV) outbreaks and their worldwide spread pose a major threat to global public health. DENV transmission dynamics significantly influence outbreak duration and magnitude. Conventional DENV transmission requires an incubation period between mosquitoes biting infected humans and the mosquitoes becoming infectious. However, the possibility of immediate, mechanical transmission of DENV without viral replication in the mosquito has received little attention despite its potential importance. Here, we show that Aedes aegypti mosquitoes can mechanically transmit DENV to susceptible mice immediately after biting infected mice without the need for an incubation period. By incorporating parameters from our experiments into a newly developed mathematical model, we found a significant impact on DENV outbreak characteristics. Mechanical transmission may amplify existing disease transmission routes and influence outbreak dynamics. Our findings have implications for vector control strategies that target mosquito lifespan and suggest the possibility of similar mechanical transmission routes in other disease-carrying mosquitoes.

SCIENTIFIC POSTER

Dr Donald Tay

HIGHLY EFFECTIVE MULTISTAGE COMPOUND AGAINST P. FALCIPARUM BINDS TO THE EXOCITE OF FALCILYSIN

Widespread multidrug-resistance threatens to derail plans for the malaria eradication. Therapeutic failure has been reported in almost every clinically approved antimalarial, and novel antimalarials with unique mechanisms of action are of great need. However, this is hindered by the lack of target candidates which therapies can be designed upon. We aim to supplement the antimalarial drug discovery pipeline in both these aspects. Here, we report a novel small molecule, A1 as well as its target. A1 exhibits multiple traits of an ideal antimalarial candidate, with a good selectivity, being active against multiple stages of the parasite's life cycle, while also proving to have a low propensity for resistance. We identified the M16 metalloprotease, Falcilysin as its intracellular protein target in both rings and gametocyte stages. This was subsequently validated biophysically and structurally, with the latter identifying interacting amino acid residues involved in the binding. This information enabled the exploration of the chemical space around the molecule to obtain a panel of analogues with improved efficacy. Our findings look not only to have delivered a chemical scaffold of a next-generation antimalarial, but also potentially opened a new avenue in chemotherapeutic design against a critical enzyme of the parasite as well.

SCIENTIFIC POSTER

Mr Donald Heng Rong Ting

THE N153-LINKED GLYCANS ON ENVELOPE PROTEIN PROTECT DENGUE VIRUS FROM EARLY ANTIBODY-MEDIATED CLEARANCE

Dengue virus (DENV) poses a huge disease burden globally with an estimated 390 million infections annually. The main viral structural protein, envelope protein (E) is glycosylated at two asparagine (N) sites (N67 and N153), but its glycosylated variants and their biological importance have been largely overlooked.

Using reverse genetic, we have generated a partially deglycosylated DENV mutant that lacks glycan structures at N153 (N153Q). The in vitro and in vivo fitness of the mutant was studied. Our data show that the N153Q mutant was slightly impaired in some mammalian cell line. In contrast, N153Q mutant was greatly attenuated in mice, as evidenced by significantly milder clinical manifestations and accelerated viral clearance in circulation. Whole blood transcriptomic and cytokine profiling suggested that there was no difference in the host responses to infection with WT and N153Q strains. B cells depletion and knockout in mouse model restored N153Q parental virulence, suggesting the involvement of B cells in N153Q attenuation. Passive transfer of serum from infected mice into B cells knockout mice cleared N153Q but not WT from blood circulation, hence supporting a role for antibodies in N153Q attenuation.

In conclusion, our findings provide novel insights on the role of N153-linked glycan in protecting DENV from antibody-mediated viral clearance, with potential implications for the development of effective therapeutic antibodies, live attenuated vaccine candidates and anti-viral drugs.

SCIENTIFIC POSTER

Mr Eugene Tan

A STUDY ON CROSS-REACTIVITY OF SARS-COV-2 ANTIBODIES WITH DENGUE IGM TEST KITS

Background: COVID-19 and dengue fever share similar clinical symptoms but have different follow-up regimes. Therefore, reliable diagnostic tests are needed to provide accurate diagnosis, particularly in dengue-endemic countries. As several reports have suggested crossreactivity between SARS-CoV-2 antibodies and dengue IgM kits, this study aimed to evaluate SARS-CoV-2 cross-reactivity of three dengue IgM kits – SD Bioline Dengue Duo Rapid Diagnostic Test (BL-RDT), SD Biosensor Dengue Duo RDT (BS-RDT), and Panbio Dengue IgM ELISA (PB-ELISA).

Methods: SARS-CoV-2 antibody-positive serum samples (n=130) collected between 20202022 were tested using the dengue IgM assays. BL-RDT dengue IgM-positive and -negative serum samples collected between Jan-Oct 2021 were also tested for SARS-CoV-2 antibodies and compared. All serum samples used were anonymized residual clinical diagnostic samples.

Results: Among SARS-CoV-2 positive samples, dengue IgM was detected in 0.7% and 1.5% of the samples for PB-ELISA and BS-RDT, respectively. For BL-RDT, 16.9% of the samples were positive for dengue IgM. Among BL-RDT dengue IgM-positive and -negative samples, 28.5% (37/130) and 36.2% (47/130) were SARS-CoV-2 antibody-positive, respectively, and were not significantly different (p-value <0.05).

Conclusion: Collectively, results suggest minimal cross-reactivity with SARS-CoV-2 antibodies for the three dengue IgM assays. However, the poor specificity of BL-RDT warrants further investigation.

SCIENTIFIC POSTER

Ms Eunice Tan

DENGUE VIRUS PRECURSOR MEMBRANE/ENVELOPE PROTEIN INFLUENCES IN VIVO VIRULENCE

Previously, our lab showed that dengue virus (DENV) precursor-membrane and envelope protein (prME) plays a critical role in driving the in vivo fitness of D2Y98P, a representative DENV2 strain in Southeast Asia. To further characterise the role of prME in DENV virulence and pathogenesis, we adopted a chimerisation approach to replace prME from D2Y98P with that from non-virulent DENV2 NGC strain (NGC-D2Y chimera). NGC-D2Y was strongly attenuated, as evidenced by lower viral loads and mild symptoms, confirming the role of prME in D2Y98P in vivo fitness. Seven selected amino acid substitutions were then introduced in NGC-D2Y to partially revert NGC prME sequence to D2Y98P sequence (NGC7-D2Y). Partial restoration of virulence was observed whereby NGC7-D2Y infected mice displayed initial viremia titers that were comparable to D2Y98P-infected mice. However, NGC7-D2Y virus was cleared faster from the circulation than WT D2Y98P. RNA-sequencing of white blood cells revealed that B and T cell activation was significantly more down-regulated in mice infected with D2Y98P compared to NGC7-D2Y, suggesting a possible role for prME in the suppression of adaptive immunity. Our results highlight that prME drives in vivo virulence through interaction with host immune system and that prME amino acid sequence is crucial for virulence.

SCIENTIFIC POSTER

Dr Feng Guang Goh

UNDERSTANDING THE ROLE OF TRANSFORMER 2 BETA IN AEDES AEGYPTI

Transformer 2 (Tra2) is a highly conserved pre-mRNA binding protein that plays a role in mRNA processing, alternative splicing, and gene expression. In Drosophila, Tra2 is essential for female sex determination and male fertility. Aedes aegypti genome harbours four Tra2 homologs with unknown functions. In this study, we investigated the role of Tra2-β (Aaetra2-β) during Aedes development. Using the CRIPSR-Cas9 technique, several knock-in mutants of Aaetra2-βKI were generated. Phenotypic analyses of these mutants showed that differing from its Drosophila homolog, Aaetra2-β is not involve female sex determination. However, Aaetra2-βKI is male sterile and exhibits defective spermatogenesis. Consistently, antibody staining and knock-in reporter assay showed that Aaetra2-β expresses specifically in testis. Detailed analyses showed that Aaetra2-βKI spermatids do not elongate properly and break down into fragments, which is likely due to defect in the basal body, the microtubule organization center essential for nuclear elongation of spermatids. RNA-sequencing experiments identified several potential targets, among which is one gamma-tubulin ring protein. In Drosophila, testis with a mutation in this homolog also exhibits defects in spermatogenesis. Further works are planned to address this causal relation. Understanding the specific function of Tra2-β during spermatogenesis might help to generate a male-biased mosquito population for vector control.

SCIENTIFIC POSTER

Ms Geraldine Nadya Putri

IDENTIFICATION OF A BAICALEIN-DERIVED COMPOUND WITH POTENT PAN-SEROTYPE DENV AND PAN-ZIKV ANTIVIRAL ACTIVITY

Despite dengue's potential to manifest as a severe disease and the economic burden it imposes on endemic countries, there is a lack of approved antiviral agents to treat the infection. Flavonoids such as baicalein have been studied for their antiviral properties against a myriad of viruses. Baicalein has been reported to be active against DENV infection and ZKV infection, with in vitro efficacy in the micromolar range. Baicalein-derived compounds were generated through systematic and iterative chemistry optimization. The generated compounds were then screened based on their anti-DENV activity and low cytotoxicity. The IC50 and selective indices of the lead compound, Compound 11064, was determined against DENV and ZIKV. Mode of action studies were conducted through time-of-addition assay, entry bypass assay, and viral translation reporter assay. Compound 11064 displayed pan-serotype DENV and pan-strain ZIKV antiviral activity in vitro with excellent selectivity indices in multiple cell lines, as well as improved antiviral efficacy as compared to baicalein. Compound 11064 does not inhibit viral RNA synthesis or viral protein translation, and targets multiple steps in the DENV replication cycle, namely in the late entry and post-entry steps. Compound 11064 has the potential to be a broad-spectrum anti-flaviviral drug.

SCIENTIFIC POSTER

Ms Gielenny Salem

INTERDISCIPLINARY APPROACHES TO GENERATING BROADLY NEUTRALIZING ANTIBODIES AGAINST VECTOR-BORNE FLAVIVIRUSES

In Asia, exposure to multiple mosquito-borne flaviviruses, including dengue virus (DENV), Japanese encephalitis virus (JEV), and the Zika virus (ZIKV) within a lifetime is not uncommon due to their high endemicity and geographic co-circulation in most territories. While efforts to develop effective pan-flavivirus vaccines or immunotherapeutics are underway, strategies to elicit strong and broadly protective immune responses remain elusive. Here, we purport novel insights for generating broadly neutralizing antibodies against flaviviruses using interdisciplinary approaches, such as epidemiology, immunology, and murine vaccination strategy. First, using a well-established and clearly defined Taiwan cohort of JEV-immune donors with recent dengue infection, we provided the first serological evidence of a robust anti-ZIKV antibody response elicited by JEVprimed individuals with a subsequent natural DENV infection. Second, we discovered a rare class of naturally occurring human antibodies with superior breadth, potency, and hypermutated variable immunoglobulin genes from one of the JEV-primed and dengue-infected volunteers. Third, a heterologous JEV-DENV virus-like particle (VLP) prime-boost stimulation in mice established a long-lived, potently neutralizing, and IgG3-focused heterotypic response and confirmed our initial observations in humans. Our findings highlight the role of flavivirus pre-immunity in the breadth of humoral response in the context of the Japanese encephalitis virus and provide novel insights for future vaccination strategies in flavivirus-endemic countries.

SCIENTIFIC POSTER

Ms Guan Hua Chen

THE ROLE OF AAMUCIN-11 IN GUT BARRIER INTEGRITY AND FEMALE MOSQUITOES' DEVELOPMENT IN AEDES AEGYPTI

Mucin-11 is a mucin protein present in the midgut of Aedes Aegypti, which is expressed at a higher level in the midgut and has a transmembrane region. Highly expressed after a blood meal, potentially playing a role in forming the mucin layer. This study used CRISPR/Cas9 to knock out Aamucin-11 in Aedes Aegypti, resulting in mutant mosquitoes (Mucin11-/-) unable to produce the mucin-11 protein. We demonstrated the timing of mucin11 protein production and the mutants were shown to slower ovary development and affect the number of female mosquitoes. In the midgut of females, the absence of Aamucin-11 causes bigger lipid droplets in epithelial cells and an abnormal arrangement of midgut epithelial cells. After blood feeding, Mucin11-/- shows different peritrophic matrix (PM) thickness and higher gut permeability. Together, mucin-11 supports the gut barrier integrity in Aedes Aegypti.

SCIENTIFIC POSTER

Mr Han Jie, Jonathan Ong

CHARACTERISATION AND TARGET DECONVOLUTION OF A POTENTIAL NOVEL ANTIMALARIAL COMPOUND

Malaria is caused by protozoan parasites of the Plasmodium genus, which causes over half a million deaths every year. The spread of drug resistance has highlighted the need for new antimalarial drugs. The aim of my project is to identify novel drug targets against P. falciparum and expand the druggable landscape against malaria. We have previously identified a compound that has demonstrated good parasite killing activity against P. falciparum in vitro with lownanomolar IC50. We show that this compound targets early trophozoite to early schizont stages of the parasite, has no indication of resistance in existing lab-grown lines as well as clinical isolates, and does not easily spontaneously generate resistance mutants. We performed Cellular Thermal Shift Assay coupled with Mass Spectrometry to determine the target of this compound and identified 3 potential targets in the parasite – cGMP-protein kinase, protein kinase 6, and calcium-dependent protein kinase 2. We are now evaluating whether one or all of these kinases are actively inhibited by our compound.

SCIENTIFIC POSTER

Ms Hui Ying Yu

THE ROLE OF ALTERNATIVE SPLICING FACTOR TRA2B DURING SPERMATOGENESIS IN AEDES AEGYPTI

Alternative splicing plays an important role in gene regulation during many developmental processes including spermatogenesis. Previous studies show that human and mouse exonspecific microarrays have detected testis and brain have a higher level of alternative splicing than other tissue. Sequence-specific RNA-binding protein Transformer 2 beta (tra2β) that participates in the control of pre-mRNA splicing. Previous studies show that Tra2β is a nuclear protein up-regulated at the onset of meiosis in mice male germ cells. To investigate the role of Tra2β during spermatogenesis, we generated tra2β knock-in and knock-out transgenic Ae. aegypti, respectively, by CRISPR/Cas9. The result showed that both tra2βKO and tra2βKI mutants cause male sterile similarly. Furthermore, the testis indirect immunofluorescence assay results demonstrate the tra2β mutation effect in meiotic cells suggested by partially post-meiotic cell identify phospho-histone H3 (Ser 10), the meta-phase marker in the cell cycle. In addition, these results prove that tra2β mutants affect the synchronous division characteristic of gametes. On the other hand, spermiogenesis is the transformation process consisting of spermatid elongation and individualization, but both are defective in tra2β mutation when the spermatocyte after completing meiosis occurs. Taken together, Tra2β is essential during and post-meiosis process, but not mitosis in germ cell development.

SCIENTIFIC POSTER

Mr Huicong Ding

FIRST RECORD OF PHLEBOTOMINE SANDFLIES (DIPTERA: PSYCHODIDAE) IN SINGAPORE AND THE IDENTIFICATION OF A NEW SPECIES, PHLEBOTOMUS SEOWPOHI

Phlebotomine sand flies (Diptera: Psychodidae) are small, blood-sucking insects that are of significant public and veterinary health importance for their role in the transmission of Leishmania parasites and arboviruses. Despite presence of sandflies in the region, there is no published record on their presence in Singapore. Here, we report the discovery of phlebotomine sandflies from Singapore including a species new to science. These sandflies were collected from routine vector surveillance activities carried out by the National Environment Agency. Using an integrated taxonomic workflow involving morphological review and DNA barcoding of the mitochondrial cytochrome b (cytb) gene, we identified 7 species of sandflies belonging to 2 genera, Phlebotomus and Sergentomyia. Phylogenetic analyses of the cytb gene suggest that the new species, Phlebotomus seowpohi, is closely related to Ph. argentipes, an important vector of Leishmania donovani from the South Asian region. The detection of sandflies in Singapore underscores the importance of continued monitoring and surveillance efforts. Data presented here will provide greater understanding of sandfly species diversity and distribution to identify high risk areas and contribute to the development of an early warning system. This is especially critical in the light of recent canine leishmaniasis detection in Singapore.

SCIENTIFIC POSTER

Dr Jonathan Liew

IT'S BLACK, IT'S WHITE: MODIFIED BLACK-BOTTOM CONTAINERS FOR MASS EGG COLLECTION OF WOLBACHIA-INFECTED AEDES AEGYPTI

Optimum collection of Wolbachia-infected Aedes aegypti eggs is important in a large-scale rearing/production setting, but it remains a logistic challenge. Often, less than ideal number of eggs are obtained in mass rearing cages. Furthermore, uneven distribution of eggs on oviposition substrates can negatively affect L1 hatchlings among the stacked eggs. Using a no-choice experimental setup, cages of mosquitoes were provided with visually different ovipots and the number of eggs collected per blood fed female was counted. The number of dead larvae among the stacked eggs was also determined. Prototypes of larger ovipots were evaluated for their ability to collect more and evenly distributed eggs. A black-bottom container, lined with white crepe paper collected the most eggs per blood fed female (9.6-13.7% more eggs vs. control). Within 48 hours, the black-bottom ovipots collected 91% of the eggs. A significantly higher percentage (0.96%) of dead L1 larvae were found among stacked eggs. A larger, black-bottom ovipot with white, crepe oviposition papers all vertically lined in the center of the container, was found to be suitable for use in the mass rearing cages, as it promoted better egg distribution and egg yield. This ovipot design can also be evaluated for field collection of eggs/mosquitoes.

SCIENTIFIC POSTER

Ms Katrina Tan

A VIRAL-CENTRIC IN VIVO APPROACH TO IDENTIFYING IMMUNOPATHOGENIC HOST FACTORS OF ALPHAVIRUS INFECTIONS

Recent advances have democratised high-throughput assays to identify key host factors dictating the outcomes of viral infections. While powerful techniques, genome-wide screens, RNAseq and unbiased proteomics still suffer from the limitations of in vitro cell lines. These consist of a low overlap with primary cell responses to infection and a lack of immune response interplay that neglects the consideration of host-driven immunopathogenic events dictating the clinical manifestations of disease, such as those of arthritogenic alphavirus infections. To address such issues, our lab has developed a novel selectable viral marker system coupled with an 'Omics-based in vivo approach to studying host-pathogen interactions. This has enabled us to conduct immunopathological comparisons of two closely related mosquitoborne alphaviruses that remain poorly distinguished from one another: Chikungunya and O'nyong-nyong. In this poster, we will present our in vivo approach and preliminary results from ongoing mechanistic investigations of several identified immune-related host factors that are potentially linked to the unique symptomatic differences of each viral infection.

SCIENTIFIC POSTER

Ms Kelly Ng

INSECTICIDE RESISTANCE MANAGEMENT OF AEDES MOSQUITOES IN SINGAPORE

Insecticide resistance in Aedes vector mosquitoes is a global threat to public health. Insecticide resistance management (IRM) is critical to ensure effective and efficient use of insecticides. The key elements of IRM include judicious use of insecticides, systematic rotation different classes of insecticide classes and adoption of appropriate innovative vector control tools. A sound IRM programme is crucial to limit and prevent the development of resistance especially to new classes of insecticides.

In Singapore, the use of insecticides is an integral component of the vector control programme, particularly in dengue outbreak management. To manage insecticide resistance and effective use of insecticides, regular review of the susceptibility status of local Aedes mosquitoes to insecticides and field assessment are important. Field efficacy assessments of formulated products using field mosquitoes are routinely conducted to ensure effective control and to guide operational use for local context. Being part of the Worldwide Insecticide Resistance Network also provides opportunity for knowledge exchange that would be essential in guiding decision-making on insecticide use and to manage insecticide resistance on the local and global scale.

SCIENTIFIC POSTER

Mr Kelvin Ho

INTEGRATED BIOSURVEILLANCE FOR EMERGING VECTOR-BORNE DISEASES: FIRST DETECTIONS OF CANINE LEISHMANIASIS IN SINGAPORE

Integrated biosurveillance for emerging vector-borne diseases in animal hosts and environment is critical for characterising the public health risk of such diseases, against the backdrop of climate change and land use changes. Using leishmaniasis as a case study, we outline cross-sectoral collaborations between public health agencies in this regard in Singapore. Over a three-year period (2020 to 2022), we report the first detections of leishmaniasis in two free-roaming dogs in Singapore enrolled under the national trap-neuterrelease/rehome-manage programme. One of these dogs presented with consistent clinicopathologic signs of leishmaniasis including renal failure. Prior to these detections, there were no known entomological records of sandfly in Singapore. To better assess the public health risk arising from any potential spillover to human populations, targeted surveys for phlebotomine vectors were initiated in the areas where the canine index cases were found. Despite our targeted approach, no sandflies were collected. This highlights the need to expand entomological surveillance to better understand the diversity and distribution of phlebotomine vectors across different green and grey spaces.

SCIENTIFIC POSTER

Ms Kirthana Radhakrishnan

CONSERVATION OF ERYTHROCYTE CALCIUM SIGNALLING IN PLASMODIUM INVASION

The invasion of erythrocytes by the malaria causing Plasmodium parasites is a critical step during its asexual cycle, which causes the clinical manifestations of the disease. In P. falciparum, the merozoite triggers Ca2+ signalling in the human erythrocyte prior to invasion through the interaction of PfRh5 with basigin on the erythrocyte surface, which ultimately leads to the modification of the erythrocyte cytoskeleton, which is indispensable for tight junction formation and parasite entry. This host Ca2+ signalling during invasion has been shown to be conserved in other species – including P. knowlesi invading monkey and human erythrocytes and P. yoelii invading mouse erythrocytes. P. knowlesi, unlike P. falciparum, does not require basigin interaction for invasion, suggesting that different species must have evolved different mechanisms to trigger host Ca2+ signalling for invasion. Here, we show that the rodent malaria, P. yoelii, also uses mouse basigin to trigger a similar signalling cascade, resembling P. falciparum despite not having RH5. This provides a starting point to identify the yoelii ligand. Since P. knowlesi also does not have Rh5, the identity of the yoelii protein which binds to basigin may also reveal possible candidates for the knowlesi ligand carrying out the same function.

SCIENTIFIC POSTER

Dr Lison Laroche

SAND FLY AND TOSCANA VIRUS: IMPACT ON VECTOR LIFE-HISTORY TRAITS AND POTENTIAL EFFECTS ON TRANSMISSION

Sand flies are hematophagous insects belonging to family Psychodidae. During blood meal taken by female sand flies, several pathogens such as Leishmania and Phleboviruses, including the Toscana virus (TOSV), can be transmitted to the host. The TOSV infects humans and can cause neuroinvasive infections in the Mediterranean region during the warm season. Currently, there is little information on Phleboviruses natural cycle in their sand fly vector. Thus, this study aims to determine, the TOSV infection dynamics in its major vector Phlebotomus perniciosus and the infection impact on vector life-history traits. Female sand flies are infected with TOSV via blood feeding under experimental conditions. We observed systemic dissemination around four days post infection, which could lead to a shorter extrinsic incubation period. Moreover, we showed an impact of infection on hatching time, which is longer for infected female eggs. Based on this result and the fact that TOSV can be transmitted by transovarial way in Ph. perniciosus, we hypothesize that this could have an impact on vectorial capacity and lead to an eco-epidemiological risk via the increase of the transmission risk period. These experimental results will help to better understand the virus maintenance in sand fly populations and its natural cycle.

SCIENTIFIC POSTER

Prof Mariangela Bonizzoni

DOES AEDES AEGYPTY GET SICK WHEN INFECTED WITH CELL FUSING AGENT VIRUS?

From their discovery, viruses have been linked to diseases. However, as our knowledge of viral diversity grew, we learned that most viruses do not cause disease, in other words that hosts are able to maintain their heath during infection. This defence strategy is called tolerance. Tolerance is evolutionary advantageous when its costs are constrained resulting in no effects on either the host or the pathogen fitness. As such the threshold between tolerance and susceptibility/resistance to infection is feeble and context dependent.

The arboviral vector Aedes aegypti hosts a large diversity of viruses ranging from human pathogenic viruses (arboviruses) to insect specific viruses (ISV), which are phylogenetically related to arboviruses, but unable to infect vertebrates. ISVs have been proposed as novel biological control agents against arboviruses based on results from co-infection experiments. However, the costs of ISV infection on mosquitoes have not been thoroughly investigated yet. Here we study if infection of the ISV Cell Fusing Agent Virus (CFAV) is tolerated by Ae. aegypti.

We build tolerance curves, look at mosquito fitness and evaluate their energy reserves after infection. We show that the CFAV can cause disease to Ae. aegypti and that this effect is strain specific.

SCIENTIFIC POSTER

Ms Meizhi Irene Li

CHARACTERISATION OF WPIP- TRANSINFECTED AEDES AEGYPTI IN A SINGAPORE GENETIC BACKGROUND REVEALS FITNESS COST OF WOLBACHIA ON QUIESCENT EGG VIABILITY AND THE ABSENCE OF ARBOVIRUS BLOCKING

The global resurgence of dengue and other Aedes-borne diseases underscores the limitations of current vector control strategies, highlighting the need to explore alternative approaches to bolster existing regime for the control of these arboviral diseases. One approach is the release of Wolbachia-transinfected Ae. aegypti into the community. This strategy is promising as Wolbachia can inhibit viral replication and reduce the reproductive capacity of mosquito vectors. The effectiveness of this approach depends on factors including the Wolbachia strain used, level of cytoplasmic incompatibility (CI) induced, maternal transmission, fitness effects and its ability to block virus transmission. In this study, we characterised local Aedes aegypti infected with the wPip strain of Wolbachia through backcrossing of wild-type Singapore mosquitoes with wPip-transinfected Ae. aegypti from China. Our study revealed that wPip- Ae. aegypti possesses desirable attributes such as perfect maternal transmission and strong CI induction in both wild-type and wAlbB-infected Ae. aegypti. However, the wPip infection has a fitness cost on Ae. aegypti eggs, resulting in a rapid loss in viability and Wolbachia infection in quiescent eggs. Furthermore, wPip did not inhibit dengue, chikungunya and zika virus replication and dissemination in Ae. aegypti. In conclusion, our study indicated that wPip-Sg has limited use in a Wolbachia-based biocontrol programme and highlighted the importance of evaluating the stability of introduced Wolbachia strains into Ae. aegypti and their impact on host's attributes which are pivotal for the effectiveness of such programme.

SCIENTIFIC POSTER

Dr Min Jie Alvin Tan

ZIKA VIRUS INDUCES AN NF-KB-DRIVEN INFLAMMATORY GENE SIGNATURE IN A CELL-TYPE SPECIFIC MANNER

Zika virus (ZIKV) induces inflammation in the central nervous system during the course of infection that has implications in virus pathogenesis and disease outcome. While the induction of an inflammatory response has been well documented, the molecular mechanism of its activation is not fully understood, together with the aspect(s) of ZIKV replication that triggers this response. We first demonstrate that the induction of an inflammatory gene signature by ZIKV infection occurs in cells and tissue from specific sites in a mouse model. In addition, ZIKV can persist in these cells and tissues even as the virus is being cleared systemically from the infected mice. Bioinformatic analysis of these stimulated inflammatory genes reveal an enrichment of genes that are regulated by the nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB) family of transcription factors. We confirmed this in silico analysis by demonstrating that this upregulation of inflammatory gene expression in response to ZIKV infection can be abrogated by small molecule inhibitors of the NF-κB signaling pathway. Finally we show that ZIKV RNA products during virus replication are sufficient to induce this response.

SCIENTIFIC POSTER

Mr Ming Hao Chua

NEXT GENERATION SEQUENCING-BASED ANALYSES ON POPULATION STRUCTURE AND DISPERSAL PATTERN OF AEDES AEGYPTI AT TWO WOLBACHIA-AEDES SUPPRESSION SITES IN SINGAPORE.

Singapore has deployed the Wolbachia-Aedes strategy to suppress Aedes aegypti population in selected areas. This strategy is fully effective in the absence of external intrusions of wild-type mosquitoes and the unintended leakage of Wolbachia-Aedes females in suppression sites, indicating the importance of understanding the genetic composition and migration patterns of local Ae. aegypti. Current study aimed to achieve this by analysing Ae. aegypti populations at suppression sites in Tampines and Yishun using Restriction site Associated DNA sequencing technology. The study included 215 field-collected Ae. aegypti females (Tampines=107 and Yishun=108) and generated ~60,000 variable sites across the genome of each Ae. aegypti. The findings indicated a restricted flight range of local Ae. aegypti adults (mean dispersal distance of ~50 m), and high population homogeneity within small geo-scales, such as residential estates. Two populations could be differentiated at an aerial distance of ~2 km. Suppression is strongest within a radius of at least ~100–130 m from the centre of each release area and was highly effective when combined with 250 m buffer-zone. Study outcomes assisted in strategizing the release of Wolbachia-carrying male Ae. aegypti at suppression sites and monitoring the potential sources of wild-type Ae. aegypti introductions into suppression sites.

SCIENTIFIC POSTER

Ms Moumita Jhara

CONSEQUENCES OF INSECTICIDE RESISTANCE HINDERING AEDES AEGYPTI CONTROL FOLLOWING DENGUE EPIDEMIC IN BANGLADESH

The number of cases and deaths reached the highest level in the history of dengue in Bangladesh. According to the Health Emergency Operation Center and Control Room of the Directorate General of Health Services (DGHS) of Bangladesh, the number of dengue cases has exceeded 200 thousand and the death toll has exceeded 1,000. The primary vector responsible for the transmission of dengue in Bangladesh is Aedes aegypti. Mosquito control in Bangladesh is prioritized with insecticides. However, the emergence of insecticide resistance (IR) causes a substantial challenge to effective control measures. This study aims to assess the extent of insecticide resistance in Ae. aegypti with an emphasis on insecticide of Pyrethroids, Organophosphates, and Carbamates groups that have previously been used in Bangladesh to control mosquitoes. We conducted this study on both laboratory (F1) and field-raised (F0) adult Ae. aegypti using a rigorous methodology of WHO susceptibility tube bioassay protocols. The recommended dose of Deltamethrin (0.05%) found as resistant both in F0 and F1 generation of Aedes aegypti. Among the 3 tested concentrations of Deltamethrin (0.05%, 0.25%, 0.5%) only a 10-fold higher concentration (0.5%) showed 99±0.25% knockdown after one hour. Other pyrethroid insecticides Etofenprox, Alphacypermethrin, and Permethrin in different concentrations were also found as resistant to F0 and F1 populations of Aedes aegypti. The carbamate group insecticide, Bendiocarb (0.1% & 0.5%) showed resistance in both generations. Conversely, Malathion 5% (organophosphates) was found as only susceptible (mortality 98>%). The findings of this study emphasize the use of Malathion or other susceptible insecticides for controlling the Aedes aegypti to reduce dengue. Furthermore, this study highlights the importance of the implementation of diversified vector-control strategies such as regular surveillance, public awareness, and breeding source management to combat the dengue burden in Bangladesh.

SCIENTIFIC POSTER

Mr Naim Che-Kamaruddin

ANTIBODIES AGAINST SARS-COV-2 CROSS-NEUTRALIZE DENGUE VIRUS

Co-endemicity of SARS-CoV-2 and dengue in endemic regions poses a higher risk of comorbidity in cases of co-infection. Transitioning into the endemic phase of COVID-19, booster doses of the SARS-CoV-2 vaccination are recommended to maintain protection against COVID-19. However, the implications of immunologic reactions through vaccination on the region's endemic virus remain unknown. The present study explores the crossneutralizing potential of different doses of the SARS-CoV-2-specific spike protein vaccine (BNT162b2) against Dengue Virus Type 2 (DENV-2). Human serum samples were collected pre-vaccination, on day 14 after the first vaccination dose, and on day 14 after the second vaccination dose to assess their potential to cross-neutralize DENV-2 in vitro. Dengue IgM/IgG monoclonal antibodies were detected using fluorescence immunoassay (FIA) and NS1 antigen ELISA to stratify the samples into individuals previously exposed to dengue and those unexposed. The serum samples were tested for neutralization with DENV-2 at MOI 0.1 using HuH7 cells. Preliminary results of the present study observed increasing inhibition activity in a dose-dependent manner, suggesting cross-neutralizing activity of anti-spike SARS-CoV-2 antibodies against DENV-2. Findings from the present study have implications for SARS-CoV2 vaccination strategies, especially in areas of high dengue endemicity.

SCIENTIFIC POSTER

Ms Qian Qi Hillary Yee

CHARACTERIZING DONOR HOST SPECIES TO DEVELOP A NOVEL WOLBACHIAAEDES LINE TO SUSTAIN INCOMPATIBLE INSECT TECHNIQUE

Dengue is a major global health threat that affects tropical and sub-tropical regions, causing high morbidity and mortality. Due to the absence of safe and effective vaccines, mitigation of such human arboviral infections currently relies on vector control strategies targeting Aedes aegypti. The incompatible insect technique (IIT) involves the release of Wolbachiatransinfected males into the community, inducing cytoplasmic incompatibility (CI) (and unviability of offspring) in mated wild-type females. Such strategies are often used as a complimentary approach to bolster existing dengue control regimes through population suppression. The need for novel Wolbachia-Aedes strains arises when secondary vectors are subsequently targeted and/or infection stability is threatened due to rising global temperatures brought upon by climate change. This study describes the identification of Ae. annandalei as a potential, Wolbachia-carrying (wAnn) donor host. Before use in a novel strain, wAnn must be optimized for stable maternal transmission, CI, and egg viability after microinjection into recipient. Before eventual mass production and release, fitness assays and risk assessment must also be performed. Additionally, we outline the steps taken to ensure the stable generation of Wolbachia-carrying eggs for strain development. This framework can be adapted for use in other IIT efforts within different geographical and epidemiological contexts.

SCIENTIFIC POSTER

Ms Saranya Jeevamani

ASSESSING THE EFFECTIVENESS OF ALL DENGUE INTERVENTION STRATEGIES IN THE SOUTHEAST ASIAN REGION: A SYSTEMATIC REVIEW

Despite ongoing vector control efforts in the region, Dengue remains endemic in all Southeast Asian (SEA) countries. While there is an approved vaccine (Dengvaxia), it has many limitations; thus, vector control remains the primary preventive and interventive method. According to WHO, the six intervention strategies are Chemical, Biological, Personal Protective Methods, Community Engagement (CE), Environmental Management, and Integrated Vector Management (IVM). Although previous systematic reviews have assessed individual strategies, this review is the first to evaluate all strategies individually and collectively to identify successes, failures, gaps, and areas for improvement. This review followed PRISMA guidelines. 36 published studies (a mix of research and field trials) were methodologically and rigorously analysed. A variety of approaches – “top-down” (national, government-driven) and “community, local and individual” were observed. Chemical, Biological and IVM interventions were the most successful – significantly reduced outcome measures (baseline to post-interventions). Biological interventions were the most sustainable and influential when combined with other strategies. Continued CE is necessary to observe extended impact and effectiveness of strategies. Study periods were generally short; thus, long-term effects remain to be evidenced. Fostering closer regional cross-collaboration, sharing of research findings, more focus on biological strategies, vector control capacity building and strengthening should be considered by countries. Furthermore, dengue surveillance and accurate diagnostic capabilities must be improved.

SCIENTIFIC POSTER

Dr Shih-Che Weng

EFFICIENT SEX SEPARATION BY EXPLOITING DIFFERENTIAL ALTERNATIVE SPLICING OF A DOMINANT MARKER IN MOSQUITOES

Female mosquitoes are the exclusive blood-feeders and carriers of dangerous human diseases. Hence, it's vital to eliminate females before implementing genetic biocontrol initiatives. We introduce SEPARATOR (Sexing Element Produced by Alternative RNA-splicing of A Transgenic Observable Reporter), a robust sex-sorting method that possesses the following key features: (i) Harnesses male-specific expression through sex-specific alternative splicing (SSAS) of a harmless, bright fluorescent marker. (ii) Facilitates sex-sorting from early larval development onwards. (iii) Adaptable for efficient high-throughput sorting. (iv) Independent of sexchromosome linkage. (v) Genetically stable, resilient against meiotic recombination or chromosomal rearrangements. (vi) Allows positive selection of males to enhance reliability. (vii) Easily transferable to different species via transposable elements, promoters, and markers. SEPARATOR reliably separates sexes during larval and pupal stages in Aedes aegypti. We demonstrate scalable high-throughput sex-selection of first instar larvae using the Complex Object Parametric Analyzer and Sorter (COPAS®). Furthermore, we employ this method to sequence the transcriptomes of early larval males and females, uncovering several sex-specific mosquito genes. SEPARATOR streamlines male production for release programs, offering cross-species adaptability to support genetic biocontrol initiatives.

SCIENTIFIC POSTER

Prof Shin-Hong Shiao

UNCOVERING DENGUE VIRUS HOST FACTORS: PAVING THE WAY FOR INNOVATIVE ANTIVIRAL STRATEGIES

Incidence of dengue virus (DENV) and Zika virus (ZIKV), two mosquito-borne flaviviruses, is increasing in large parts of the world. Vaccination and medication for these diseases are unsatisfactory. Here, we developed a novel antiviral approach, using a virus-inducible gene expression system, to block virus replication and transmission. Constructs containing the smallest replication units of dengue virus serotype 2 (DENV2) with negative-stranded DENV2 artificial genomes and genes of interest were established in an Aedes aegypti cell line, resulting in expression of target genes after DENV2 infection. Green fluorescent protein (GFP) assays confirmed the system was virus-inducible. When we used one of two apoptosis-related genes, A. aegypti michelob_x (AaMx) and inhibitor of apoptosis (IAP)-antagonist michelob_x-like protein (AaIMP) instead of GFP, the production of viral RNA and proteins were inhibited for all five viruses tested (DENV1–4 and ZIKV), and effector caspase activity was induced. The system thus inhibited the production of infectious virus particles in vitro, and in mosquitoes it did so after DENV2 infection. This is a novel broad-spectrum antiviral approach using a flavivirus-inducible gene-expression system, which could lead to new avenues for mosquito-borne disease control.

SCIENTIFIC POSTER

Prof Shu-Jen Tuan

EFFECTIVENESS OF BEAUVERIA BASSINA AND METARHIZIUM ANISOPLIAE ISOLATED FROM HERBIVORES AGAINST DIFFERENT STAGES OF AEDES AEGYPTI AND AE. ALBOPICTUS

Dengue fever has caused intense fear in Southeast Asian countries, the main control strategies for Aedes sp. are primarily based on synthetic insecticides. However, the increased applications of chemical insecticides not only led to an out of control resistance but also unfriendly impact on environment or food safety. Wild entomopathogenic fungi (EPF) might be a potential agent for suppressing the vectorborne-disease disaster. Two isolates, Beauveria bassina and Metarhizium anisopliae, were respectively collected from Spodoptera exigua and Odoiporus longicollis in crop plantations in central Taiwan. The mortalities of Aedes spp. larvae caused by EPF infection showed a positive relationship to the concentration of conidia spores. While, the infection rates decreased with aging, and the infection rate of male mosquitoes was much higher than that in female cohort. The pupation and emerging rate of adults were both increased with the concentrations of conidia spores. The improvement of control efficacy was contributed by using the conidia sporescontained nylon-mesh which could finally cause 100% lethality. However, the pathogenicity of these fungi to larvae and pupae varied with the timing of inoculation. The findings of this study inspired us a lot, hopefully, some isolates from agricultural pests may be selected as a high potential candidate for controlling Aedes spp. at lower concentration of fungi.

SCIENTIFIC POSTER

Prof Shu-Mei Dai

EFFECTIVENESS OF BEAUVERIA BASSINA AND METARHIZIUM ANISOPLIAE ISOLATED FROM HERBIVORES AGAINST DIFFERENT STAGES OF AEDES AEGYPTI AND AE. ALBOPICTUS

Dengue fever has caused intense fear in Southeast Asian countries, the main control strategies for Aedes sp. are primarily based on synthetic insecticides. However, the increased applications of chemical insecticides not only led to an out of control resistance but also unfriendly impact on environment or food safety. Wild entomopathogenic fungi (EPF) might be a potential agent for suppressing the vectorborne-disease disaster. Two isolates, Beauveria bassina and Metarhizium anisopliae, were respectively collected from Spodoptera exigua and Odoiporus longicollis in crop plantations in central Taiwan. The mortalities of Aedes spp. larvae caused by EPF infection showed a positive relationship to the concentration of conidia spores. While, the infection rates decreased with aging, and the infection rate of male mosquitoes was much higher than that in female cohort. The pupation and emerging rate of adults were both increased with the concentrations of conidia spores. The improvement of control efficacy was contributed by using the conidia sporescontained nylon-mesh which could finally cause 100% lethality. However, the pathogenicity of these fungi to larvae and pupae varied with the timing of inoculation. The findings of this study inspired us a lot, hopefully, some isolates from agricultural pests may be selected as a high potential candidate for controlling Aedes spp. at lower concentration of fungi.

SCIENTIFIC POSTER

Ms Somya Bansal

SYNTHETIC CONTROL METHODS FOR INFECTIOUS DISEASE EPIDEMIOLOGY: APPLICATIONS TO WOLBACHIA INTERVENTIONS

Background: Large scale field trials to evaluate the effect of interventions are increasingly common. However, random assignment of interventions is often difficult to achieve. Here, we present the development and application of synthetic control methods (SCM) in evaluating the efficacies of interventions. We use Project Wolbachia, Singapore as the key example, where incompatible-insect technique coupled with sterile insect technique was employed to suppress Aedes mosquito populations and consequentially, dengue transmission.

Methods & results: Spatially resolved dengue incidence and/or adult Aedes abundance data from Singapore were used, along with a high-dimensional set of spatio-temporal set of environmental and anthropogenic covariates. Donor pools consisting of control units which are never treated by Wolbachia interventions were used to construct synthetic controls using SCM. The canonical SCM was employed. We used different linear combinations of covariates to account for confounding. Intervention efficacies, defined as the percentage reduction in dengue incidence or mosquito abundance, was compared under different settings and methodologies. Intervention efficacies depended on levels of coverage in release sites and ranged from 47 – 99% across all endpoints. Intervention efficacies were found to be consistent across different endpoints, subgroups and locations. Synthetic control methods were found to generate appropriate control groups as noted by good balance in the endpoint of interest and covariates between both intervention and synthetic control arms in the pre-intervention period. A further battery of robustness checks, such as placebo testing, confirm the validity of intervention efficacy estimates.

Implications: SCM can alleviate many problems which arise from non-randomized experimental settings. Alternatives can flexibly account for many confounders as well as staggered adoption settings where interventions were sequentially applied to different units across time. Our applications to Wolbachia releases demonstrate the high utility for this new class of vector control tools to stem both vector populations and dengue transmission across multiple setting.

SCIENTIFIC POSTER

Dr Sook Yi Wong

DETERMINATION AND CHARACTERIZATION OF NS2B-NS3 INTERACTION AS A POTENTIAL DRUG TARGET

Flaviviruses are important arthropod-borne pathogens that are globally distributed, causing wide-spread mortality and morbidity every year. Dengue virus, a significant member of the flavivirus, was estimated to infect more than 390 million individuals annually. The flavivirus positive-strand RNA encodes for 3 structural and 7 non-structural proteins in a single polyprotein that is co- and post-translationally cleaved by host and viral proteases. The viral protease activity is accomplished by non-structural protein 3 (NS3), a multifunctional protein which consist of an N-terminal protease domain and a C-terminal helicase domain. Given the essential role in replication and protein processing, NS3 has been an attractive anti-viral target. NS3 requires NS2B as a co-factor for its proper folding and enzymatic activity. Previous study on DENV4 NS2B47NS3 protease observed an extensive interaction of S48 of NS2B to multiple residues of NS3 that was not previously observed in crystal structures and could be potentially targeted to inhibit the protease activity. In this study, we further characterize this interaction site on the full length NS3 with NS2B47 using biochemical and biophysical analysis. With additional mutagenesis studies on S48 and K55 of NS2B, we aim to elucidate the role of these highly conserved residues and their interaction with NS3.

SCIENTIFIC POSTER

Ms Sotheary Sann

PHENOTYPIC AND FUNCTIONAL EVALUATION OF REGULATORY T CELLS DURING ACUTE DENGUE VIRUS INFECTION

Regulatory T cells (Tregs) play an essential role in homeostasis by controlling unwanted immune response and maintaining peripheral tolerance. During acute dengue infection, increased frequencies of Tregs have been reportedly beneficial for dengue outcome. However, the roles of Tregs in dengue pathogenesis, their relationship to the disease severity and the reason for their insufficient control of severe dengue still have not been fully understood. We aim to investigate frequency and function of Tregs in acute dengue infection. Blood samples were collected within 96 hours after fever onset from hospitalized children (≥ 2 years old) with dengue-like syndrome who admitted in hospitals in Cambodia. Dengue-positive patients were classified based on the WHO 1997 criteria upon hospital discharge into dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Isolated peripheral blood mononuclear cells were used for multi-color flow cytometry immune-phenotyping and in vitro suppression assay. Our findings showed that the frequency of Tregs increased in mild dengue, but not in severe dengue. Particularly in severe dengue patients, Tregs have increased frequency of Th1-like Tregs and decreased expression of the inhibition marker (CD31). Additionally, Tregs are more proliferative in severe dengue cases. In comparison to healthy controls, Tregs lost their suppressive function in patients with severe dengue. These results reveal the association of Tregs to the severity of the disease.

SCIENTIFIC POSTER

Ms Vei Ting Nyam

INSECTICIDE RESISTANCE MANAGEMENT OF AEDES MOSQUITOES IN SINGAPORE

Insecticide resistance in Aedes vector mosquitoes is a global threat to public health. Insecticide resistance management (IRM) is critical to ensure effective and efficient use of insecticides. The key elements of IRM include judicious use of insecticides, systematic rotation different classes of insecticide classes and adoption of appropriate innovative vector control tools. A sound IRM programme is crucial to limit and prevent the development of resistance especially to new classes of insecticides.

In Singapore, the use of insecticides is an integral component of the vector control programme, particularly in dengue outbreak management. To manage insecticide resistance and effective use of insecticides, regular review of the susceptibility status of local Aedes mosquitoes to insecticides and field assessment are important. Field efficacy assessments of formulated products using field mosquitoes are routinely conducted to ensure effective control and to guide operational use for local context. Being part of the Worldwide Insecticide Resistance Network also provides opportunity for knowledge exchange that would be essential in guiding decision-making on insecticide use and to manage insecticide resistance on the local and global scale.

SCIENTIFIC POSTER

Dr Venkata Raghuvamsi Palur

AN INTEGRATIVE APPROACH TO ENGINEERING DENGUE VIRUS-LIKE PARTICLES

Dengue virus (DENV) infects millions of people worldwide. Due to the serotype variations and antibody-mediated enhancement (ADE) of DENV infection, development of effective and safe vaccines has been challenging. This necessitates new strategies for novel vaccine development. Virus-like particles (VLPs) represent non-infectious and potentially highly immunogenic vaccine candidates. The DENV VLP is composed of sixty envelope (E) and membrane (M) proteins embedded in a lipid envelope and is known to elicit neutralizing antibodies similar to those of infectious virions. However, in the absence of a genomic core, such VLPs are highly unstable, heterogeneous in size, and exhibit poor secretion. This motivates the characterization of the biophysical and structural properties of VLPs to facilitate engineering of particles with improved stability and homogeneity. In this work, the structure, and dynamics of VLPs and conformational transitions were investigated using an integrative approach by combining cryo-electron microscopy, lipidomics, multiscale modelling, and molecular simulation techniques. Coarse-grained simulations of mature and immature VLPs revealed critical features that contribute to VLP stability and captured the conformational pathway during maturation in unprecedented detail. This knowledge will facilitate the design of improved VLPs, towards stable and immunogenic next-generation vaccines.

SCIENTIFIC POSTER

Dr Wei-Liang Liu

UTILIZATION OF UNMANNED GROUND VEHICLE SYSTEMS IN URBANIZATION: A STUDY FOR MOSQUITO AND VECTOR SURVEILLANCE IN KAOHSIUNG

Dengue fever is a vector-borne disease that has become a serious global public health problem over the past decade. An essential aspect of controlling and preventing mosquito-borne diseases is reduction of mosquito density. Through the process of urbanization, sewers (ditches) have become easy breeding sources of vector mosquitoes. In this study, we, for the first time, used unmanned ground vehicle systems (UGVs) to enter ditches in urban areas to observe vector mosquito ecology. We found traces of vector mosquitoes in ~20.7% of inspected ditches, suggesting that these constitute viable breeding sources of vector mosquitoes in urban areas. We also analyzed the average gravitrap catch of five administrative districts in Kaohsiung city from May to August 2018. The gravitrap indices of Nanzi and Fengshan districts were above the expected average (3.26), indicating that the vector mosquitoes density in these areas is high. Using the UGVs to detect positive ditches within the five districts followed by insecticide application generally yielded good control results. Further improving the high-resolution digital camera and spraying system of the UGVs may be able to effectively and instantly monitor vector mosquitoes and implement spraying controls. This approach may be suitable to solve the complex and difficult task of detecting mosquito breeding sources in urban ditches.

SCIENTIFIC POSTER

Prof Wei-Ting Liu

ACTIVATION OF AUTOPHAGY VIA THE AMPK-MEDIATED TORC1-DEPENDENT SIGNALING PATHWAY IN AEDES AEGYPTI MOSQUITOES FOLLOWING INFECTION WITH DENGUE 2 VIRUS: ESSENTIAL ROLES OF AE. AEGYPTI FIP200 AND AE. AEGYPTI ATG 9 IN VIRAL REPLICATION

Previous studies have suggested that infection with dengue 2 virus (DEN2) induces autophagy, enhancing viral replication in mammalian cells and Aedes aegypti mosquitoes. However, the specific mechanisms in Ae. aegypti remain unclear. This study investigates DEN2-induced autophagy pathways, including the impact of dsRNA silencing and chemicals on viral replication. Our research shows that DEN2 triggers autophagy via the AMPK-mediated TORC1 pathway, boosting viral replication in Ae. aegypti. Following DEN2 infection, Ae. aegypti FIP200 (AaFIP200) expression rises significantly. Silencing AaFIP200 reduces DEN2 replication, and similarly, knockdown of Ae. aegypti Atg9 (AaAtg9) decreases viral replication. In conclusion, autophagy is activated through the AMPK-mediated TORC1 pathway in response to DEN2 infection. AaFIP200 and AaAtg9 play vital roles in promoting DEN2 replication in Ae. aegypti. These findings deepen our understanding of the interplay between viral pathogens and mosquito vectors, with potential implications for dengue virus control strategies.

SCIENTIFIC POSTER

Mr Wuchun Tu

THE POTENTIAL VECTOR OF BOVINE EPHEMERAL FEVER VIRUS

This study provides new insights into bovine ephemeral fever (BEF), a viral disease causing significant losses in cattle farming. While BEF has long been associated with Culicoides transmission, this research presents the first experimental evidence of Culex tritaeniorhynchus transmitting the bovine ephemeral fever virus (BEFV). Assessing the competence of different mosquito species as potential BEFV vectors is crucial for disease management. In this study, the vector competence of five mosquito species for BEFV transmission was evaluated. The totally 4,435 mosquitoes were collected from five cattle farms in Taiwan between 2017 and 2018. Culex tritaeniorhynchus dominated (93.89%), followed by Anopheles sinensis (3.31%), Culex quinquefasciatus (1.56%), Culex pipiens molestus (0.79%), and Armigeres subalbatus (0.45%). RT-PCR analysis primarily detected BEFV infection in field-collected Cx. tritaeniorhynchus. Subsequent experiments revealed Cx. tritaeniorhynchus's high susceptibility to BEFV infection, particularly via oral transmission. The research also noted increased susceptibility to BEFV infection at higher temperatures. These findings suggest a significant role for Cx. tritaeniorhynchus in BEFV transmission on Taiwanese cattle farms.

SCIENTIFIC POSTER

Dr Xinjun Hou

ESTABLISHMENT OF WOLBACHIA-INFECTED AEDES AEGYPTI (SINGAPORE) STRAINS

Aedes aegypti mosquito is an important vector to transmit arbovirus diseases especially dengue in Singapore. To suppress dengue transmission, a Wolbachia-based incompatible insect technique (IIT) has been developed for population suppression strategy, attributed to Wolbachia strain wAlbB derived from Ae. albopictus mosquito. Releasing wAlbB-infected males to specific area succeeded in suppressing mosquito population in field trials. Currently, few studies have described vector competence of wAlbA, another Wolbachia strain from Ae. albopictus, and wAlbB to various arboviruses, making it unclear for the potential application of population replacement strategy with these strains. Here we established wAlbA, wAlbB and wAlbAwAlbB superinfected Ae. aegypti from Singapore local Ae. albopictus. Stable vertical transmission was acquired after self-cross for several generations. All three strains showed bidirectional cytoplasmic incompatibility among each other, suggesting possible use of population suppression program. Furthermore, vector competence to arboviruses is to examine to understand potential anti-viral activities, making possible application of population replacement strategy.

SCIENTIFIC POSTER

Ms Ya Chen Chang

EFFECT OF C-TYPE LECTIN 16 ON DENGUE VIRUS INFECTION IN AEDES AEGYPTI SALIVARY GLANDS

C-type lectins (CTLs) are a family of carbohydrate-binding proteins and an important component of mosquito saliva. Although CTLs play key roles in immune activation and viral pathogenesis, little is known about their role in regulating dengue virus (DENV) infection and transmission. In this study, we established a homozygous CTL16 knockout Aedes aegypti mutant line using CRISPR/Cas9 to study the interaction between CTL16 and viruses in mosquito vectors. Furthermore, mouse experiments were conducted to confirm the transmission of dengue virus by CTL16-/- A. aegypti mutants. We found that CTL16 was mainly expressed in the medial lobe of the salivary glands in female A. aegypti. CTL16 knockout increased DENV replication and accumulation in the salivary glands of female A. aegypti, suggesting that CTL16 plays an important role in DENV transmission. We also found reduced expression of IMD and JAK/STAT pathway components correlated with increased DENV viral titer, infection rate, and transmission efficiency in the mutant strain. The findings of this study provide insights not only for guiding future investigations on the influence of CTLs on immune responses in mosquitoes but also for developing novel mutants that can be used as vector control tools.

SCIENTIFIC POSTER

Dr Yaw Bia Tan

MOLECULAR ARCHITECTURE OF ALPHAVIRUS REPLICATION MACHINERY ADVANCES ANTIVIRAL DRUG DEVELOPMENT

Mosquito-borne infectious diseases caused by alphavirus and flavivirus occur at alarming rate globally with rapid urbanization and climate changes. Without approved antiviral therapy, the reemerging chikungunya virus (CHIKV) from the alphavirus genus affects millions of people worldwide. Despite non-lethal, chronic CHIKV infections present long-term polyarthritis that may last for years post-infection. Upper portion of CHIKV RNA genome encodes four nonstructural proteins (nsP1-4) which is autoprocessed into a viral replication machinery which initiates the formation of host-membrane-derived replication spherule as active viral RNA replication site. The biogenesis and molecular detail of the multi-component replication spherule which comprises of both viral and host materials are largely unknown. Combining cryo-electron microscopy (cryo-EM) and tomography, elucidated molecular architectures of CHIKV RCs within CHIKV-infected human cell revealed a megadalton-scale replication machinery core consisting of an RNA-capping nsP1 dodecameric ring with its central pore occupied by a copy of nsP4 polymerase in complex with nsP2 helicase-protease. Further, I developed a cryo-EM based drug discovery platform to develop potential antiviral therapy for both alphavirus and flavivirus. Overall, this work advances the molecular understanding of the viral RNA replication process which has broad application to RNA virus research and prepares for better antiviral therapeutic design.

SCIENTIFIC POSTER

Prof Kabirul Bashar

ADAPTATION OF AEDES AEGYPTI MOSQUITO LARVAE IN SEWAGE, SEA, BRACKISH & DRAIN WATER: A NEW CHALLENGE FOR DENGUE CONTROL

Aedes aegypti is the principal tropical mosquito vector of arboviruses causing yellow fever, dengue, chikungunya, zika & rift valley fever. The larvae of this species was considered to live in clean freshwater containers in close proximity to humans; however, over the last few years, there have been some reports of this species exploiting more cryptic, and previously ignored habitats such as sewage, and subterranean septic tanks. The present study was designed to evaluate the possible oviposition and adaptation of larvae in sea, brackish, sewage, and drain water. The water samples were collected from the different districts of Bangladesh and the experiment was conducted in the (temp 30±3oC, RH 80%) laboratory (Insect Rearing and Experimental Station) at Jahangirnagar University. In both choice (227±2.72) and no-choice (286.67±27.98) experiments, the highest number of eggs were laid by Aedes aegypti in sewage water but the survivability was found lowest (91.67%) there. Insignificant ($p>0.05$) oviposition preferences were recorded between control (rainwater), and other types (sea, and drain) of water. Nearly 96% of larvae survived and emerge as adults after 20 days in all tested (rain, brackish, sea and drain) water. The result of the study concluded that, Ae. aegypti can adapt and survive in new sites and lay eggs in sea, brackish, sewage, and drain water. These findings have serious importance for dengue vector surveillance and control programs, which conventionally focus on limiting mosquito breeding in freshwater habitats during wet seasons. Besides, the development of Ae. aegypti larvae in various types of water can have grave consequences in terms of disease transmission. Therefore, the elimination of the breeding place program in different countries needs to be amended keeping in mind that Aedes aegypti can be breed and oviposit in sewage, brackish, sea & domestic waste, or clean water.

SCIENTIFIC POSTER

Dr Samuel Tong Jia Ming

VCP LYSINE 315 TRI-METHYLATION IS IMPORTANT FOR VCP ALPHAVIRUS PROVIRAL ACTIVITY

The Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that causes a tropical febrile illness, often manifesting with debilitating joint-point in the extremities which affects millions annually. Recent outbreaks have shown a rapid re-emergence and increased spread of CHIKV infections with no effective anti-viral or vaccine currently available. We recently identified valosin-containing protein (VCP) as an important proviral replication factor for CHIKV infections. However, being a ubiquitous and essential component for cell survival, directly targeting VCP is not an ideal therapeutic solution. In this study, we investigate the role of the VCP activating protein, VCP lysine methyltransferase (VCPKMT), and its role on alphavirus replication. Using knockdown and complementation assays, we determined that VCPKMT is important for the replication of both CHIKV and the closely related alphavirus, O'nyong nyong virus (ONNV). VCPKMT-/- mice showed reduced viremia and inflammation for both alphaviruses, demonstrating the proviral role of VCPKMT in vivo. These results highlight VCPKMT to be a promising antiviral therapeutic target.

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