

**EU – South East Asia Expert Meeting on Vector
Borne Diseases:**

“Identifying opportunities for Collaboration”

PROGRAM & ABSTRACTS

**JULY 27 -28, 2009
SINGAPORE**

Foreword Note

The primary objective of the workshop is to bring together scientific experts to identify opportunities for collaboration and form consortia to bid into the upcoming EU FP7 calls on vector borne diseases.

The workshop will take an integrated approach to research and will focus on a spectrum of vector borne diseases, including Dengue, Malaria, Chikungunya and Encephalitis, as well as other relevant newly emerging infections. It will develop a co-ordinated and joint approach between researchers specialising in different disciplines including virology, transmission, epidemiology, diagnostic approaches and/or treatment and prevention strategies, including public health-relevant questions, as well as infections' natural cycles, including basic biology of vectors and diseases reservoirs and how to control them. This will ultimately contribute to a comprehensive approach to counter the threats from these infections.

Significant synergy is expected from uniting EU and ASEAN researchers from different fields around the common goal of generating new knowledge on these diseases, and delivering improved ways to monitor its spread, diagnose, prevent, control and treat it. We want to thank all the speakers for taking time out to participate in this event at such short notice and we are grateful for their contributions. We hope that you will find this meeting useful and enriching.

Last but not least, we would like to express our gratitude and sincere thanks to SlgN Chairman Prof Philippe Kourilsky and SlgN Scientific Director Prof Paola Castagnoli for supporting this event. We also gratefully acknowledge the contributions of the administrative team, Peggy Leong, Cheryl Lee and Rachael Ling from SlgN, and Yunshi Wang from A*STAR for their tireless support.

Sincerely,

The Organising Committee:

Christopher Tan (British High Commission Singapore)

Jessica Wright (British High Commission Singapore)

Laurent Rénia (SlgN)

Lisa F.P. Ng (SlgN)

20 July 2009

General Information

Symposium Title

EU – South East Asia Expert Meeting on Vector Borne Diseases:
Identifying opportunities for Collaboration

Dates

July 27 (Monday) – July 28 (Tuesday), 2009

Venue

Breakthrough Theatrette, Matrix Building, Level 4
Address : 30 Biopolis Street, Singapore 138671

Organizers

Singapore Immunology Network (SIgN), Singapore:

Laurent Renia (renia_laurent@immunol.a-star.edu.sg)

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Symposium Session

EU – South East Asia Expert Meeting on Vector Borne Diseases: Identifying opportunities for Collaboration

Symposium Programme

Monday, 27th July 2009

Time	Details
8.00 – 8.30am	Registration
8.30 – 8.35am	Welcome Laurent RÉNIA <i>Singapore Immunology Network, A*STAR</i>
8.35 – 8.45am	Opening Address (I) LIM Chuan Poh <i>Chairman, A*STAR, Singapore</i>
8.45 – 8.55am	Opening Address (II) Amanda BROOKS <i>Deputy High Commissioner, British High Commission, Singapore</i>
9.00 – 9.40am	O01 - Keynote Lecture 1: Emerging diseases and neglected endemic infections – management and control Sir Roy ANDERSON <i>Imperial College, London, United Kingdom</i>
Session: Consortium Projects Chairperson: Rod HOFF, Regional Emerging Diseases Intervention (REDI) Centre, Singapore	
9.40 – 10.00am	O02 - FP7 funding opportunities in health research Claudia EGGERT <i>FP7 National Contact Point, Health, PT-DLR, Germany</i>
10.00 – 10.30am	O03 - Vector-borne diseases as global health and economic problems: prospects for the future Duane GUBLER, EDEN advisor <i>Program Director, DUKE-NUS, Singapore</i>
10.30 – 10.50am	Morning Tea
10.50 – 11.10am	O04 - Dengue and Chikungunya: a major shift in approach to contain these diseases is desperately needed Sazaly ABUBAKAR <i>Professor, University of Malaya, Malaysia</i>
11.10 – 11.40am	O05 - A network approach to vector-borne diseases: the impact of DENFRAME and the International Network of Pasteur Institutes Roberto BRUZZONE <i>CEO, HKU-Pasteur Research Centre, Hong Kong SAR</i>
11.40 – 12.00pm	O06 - Experiences in conducting biomedical research on dengue hemorrhagic fever in Thailand Prida MALASIT <i>Professor, Mahidol University, Bangkok, Thailand</i>

Time	Details
12.00 – 12.30pm	O07 - An ecological perspective for determining risk of vector-borne disease to the UK Lisa JAMESON <i>Scientist, Health Protection Agency, United Kingdom</i>
12.30 – 2.00pm	Lunch
Session: Re-emerging Infectious Diseases Chairperson: Raymond LIN, National Public Health Laboratory, Ministry of Health, Singapore	
2.00 – 2.30pm	O08 - West Nile Fever Virus - update on the biology and epidemiology Anne BUSCHMANN <i>Deputy Director, Institute for Novel and Emerging Infectious Diseases, Friedrich-Loeffler Institute, Germany</i>
2.30 – 2.50pm	O09 - Use of the single cocktail polymerase chain reaction to identify members of Anopheles minimus group belonging to the Myzomyia Series in Vietnam NGO Giang Lien <i>Associate Professor, Hanoi University of Science, Hanoi, Vietnam</i>
2.50 – 3.10pm	O10 - Biochemical, biological, and antigenic properties of Japanese encephalitis virus Vincent DEUBEL <i>Director - General Institut Pasteur of Shanghai, Chinese Academy of Sciences, PR China</i>
3.10 – 3.30pm	O11 - Flavivirus capsid protein: beyond viral assembly Mary NG Mah-Lee <i>Professor, Department of Microbiology, National University of Singapore</i>
3.30 – 3.50pm	O12 - Alphaviruses, latent infection and chronic pathologies Philippe GASQUE <i>Program Director, Université de La Reunion, Reunion Island</i>
3.50 – 4.10pm	Afternoon Tea
4.10 – 4.30pm	O13 - Dengue virus-infected dendritic cells trigger vascular leakage via metalloproteinase activities Francisco VEAS <i>Research Director, Faculty of Pharmacy, University of Montpellier, France</i>
4.30 – 4.50pm	O14 - Arbovirus encephalitis from the mosquito to the brain John FAZAKERLEY <i>Professor, University of Edinburgh, United Kingdom</i>
4.50 – 5.20pm	O15 - Simple tools for vector control & future threats Steve LINDSAY <i>Professor, London School for Tropical Medicine and Hygiene, London, United Kingdom</i>
5.20 – 5.30pm	Wrap Up Discussions Raymond LIN, National Public Health Laboratory, Singapore

EU – South East Asia Expert Meeting on Vector Borne Diseases: Identifying opportunities for Collaboration

Symposium Programme

Tuesday, 28th July 2009

Time	Details
8.30 – 8.45am	Registration
8.45 – 8.50am	Welcome Lisa F.P. NG <i>Singapore Immunology Network, A*STAR</i>
8.50 – 9.30am	O16 - Keynote Lecture 2: Threats and opportunities from vector-borne diseases for Southeast Asia Yongyuth YUTHAVONG <i>Professor, National Center for Genetic Engineering and Biotechnology (BIOTEC), Bangkok, Thailand</i>
<u>Session: Vector Biology and Control Strategies</u> Chairperson: Laurent RÉNIA, SgN, Singapore	
9.30 – 10.00am	O17 - Global warming and malaria re-emergence in Portugal – EDEN European consortium Virgílio Estólio do ROSÁRIO <i>Director, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Portugal</i>
10.00 – 10.20am	O18 - Community participation and vector control Sustriayu NALIM <i>Consultant, Vector Control Research Unit, Salatiga, Indonesia</i>
10.20 – 10.40am	Morning Tea
10.40 – 11.10am	O19 - Complexity of the vector system in South-East Asia: How to implement effective vector control? Sylvie MANGUIN <i>Research Director, Institute of Research for Development (IRD), Montpellier, France</i>
11.10 – 11.40am	O20 - Dengue and Chikungunya in Singapore Lee-Ching NG <i>Head, Environmental Health Institute, National Environment Agency, Singapore</i>
11.40 – 12.00pm	O21 - Short-term cross-protection to dengue serotypes at the expense of long-term protection? Katja FINK <i>Principal Investigator, Singapore Immunology Network, Singapore</i>
12.00 – 12.20pm	O22 - The early host response in Dengue Martin HIBBERD <i>Associate Director, Genome Institute of Singapore, Singapore</i>

Time	Details
12.20 – 12.40pm	<p>O23 - Impact of Human genetics on susceptibility to and transmission of vector-borne diseases in South-East Asia Richard PAUL <i>Staff Scientist, Institut Pasteur, Paris, France</i></p>
12.40 – 1.30pm	Lunch
<p>FP7 Session: PANEL: Claudia Eggert, Virgílio Estólio do Rosário, Anne Buschmann, Tin-Wee Tan, Roberto Bruzzone, Sazaly AbuBakar and Laurent Rénia (leader of committee)</p>	
1.30 – 3.00pm	<p><i>The panelists to gather and compare the topics presented and stimulate discussions on those who are keen to foster collaborations.</i></p>
3.00pm	Meeting Close

ORAL SESSION

ABSTRACTS



Sir Roy ANDERSON
Rector of Imperial College London, UK
Chairman of the science advisory board of
WHO's Neglected Tropical Diseases programme
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Emerging diseases and neglected endemic infections – management and control

Sir Roy Anderson FRS, FMedSci became Rector of Imperial College London on 1 July 2008, following a 40-year association with the College. He continues to be Professor of Infectious Disease Epidemiology in the Division of Epidemiology, Public Health and Primary Care. He gained a first in zoology in 1968 and a PhD in parasitology, both at Imperial College London. After completing his PhD in 1971 he became an IBM biomathematics research fellow at the University of Oxford, before moving to King's College London to become a lecturer in parasitology in 1973. He returned to Imperial in 1977 as a lecturer and was made professor in 1982 and Head of the Department of Biology in 1984, a position he held until 1993 when he became Head of the Department of Zoology and Linacre Chair of Zoology at the University of Oxford. In 2000 he returned to Imperial to set up and lead the Department of Infectious Disease Epidemiology, focused on the epidemiology, population biology, evolution and control of infectious diseases such as AIDS and HIV, SARS, bird flu and pandemic influenza, BSE and vCJD and the epidemic viral infections of livestock including foot and mouth. Between 2004 and 2007 Sir Roy was on secondment from Imperial College to act as Chief Scientific Adviser to the Ministry of Defence. Sir Roy has also served as Director of the Wellcome Centre for Parasite Infections from 1989 to 1993 (at Imperial) and as Director of the Wellcome Centre for the Epidemiology of Infectious Disease from 1993 to 2000 (at Oxford).

He is the author of over 450 scientific articles and has sat on numerous government and international agency committees advising on public health and disease control including the World Health Organisation and UNAIDS. From 1991-2000 he was a Governor of the Wellcome Trust. He currently chairs the science advisory board of WHO's Neglected Tropical Diseases programme, is a member of the Bill and Melinda Gates Grand Challenges advisory board, and chairs the Schistosomiasis Control Initiative advisory board (SCI) funded by the Gates Foundation. He is a non-executive director of GlaxoSmithKline. Sir Roy was elected Fellow of the Royal Society in 1986, a Founding Fellow of the Academy of Medical Sciences in 1998, a Foreign Associate Member of the Institute of Medicine at the US National Academy of Sciences in 1999 and he was knighted in the 2006 Queen's Birthday Honours.

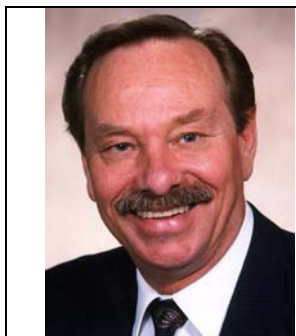
O02



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FP7 funding opportunities in health research

FP7 is the short name for the 7th Framework Programme for Research and Technological Development. This is the EU's main instrument for funding research in Europe and it will run from 2007-2013 with a total budget of approx. 53 billion Euro .An overview of the funding opportunities of FP7 will be presented with a special focus on international cooperation and the area “infectious diseases” within the upcoming Call for Proposals in the HEALTH theme of FP7. The Health theme is a major theme of the Cooperation programme and the EU has earmarked a total of 6.1 billion Euro for funding this theme over the duration of FP7.



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Vector-Borne Infectious Diseases as Global Health and Economic Problems: Prospects for the Future

The middle part of the 20th century was a defining period in the history of mankind. Infectious diseases, which had been the leading cause of illness and death were effectively controlled in most regions of the world through good public health programmes and the effective use of new drugs, vaccines and insecticides. This success ushered in an era of complacency that lasted for 30 years, and resulted in policy changes and a re-direction of resources that ultimately lead to the deterioration of the public health infrastructure required for prevention and control of infectious diseases in general and vector-borne diseases in particular. Beginning in the 1970s, and accelerating in the 1980s and 1990s, a global re-emergence of epidemic infectious diseases occurred. As we enter the 21st century, infectious diseases are once again the leading cause of illness and death in the world. Moreover, epidemic infectious diseases, especially those transmitted by mosquitoes, pose a major threat to global economic security as pathogens and vectors move rapidly within and among regions via modern transportation and globalization. Selected vector-borne diseases will be used as case studies to illustrate these threats. The current epidemiologic trends, lessons learned, and the prospects for the future will be discussed.



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Dengue and Chikungunya: a major shift in approach to contain these diseases is desperately needed

Dengue is a mosquito-borne disease first described in Malaysia in 1902. Until the early eighties, dengue outbreaks occur mainly in major cities notably Kuala Lumpur and its vicinity. Dengue has since become endemic in almost all states of Malaysia. The number of dengue cases has increased at an almost exponential rate over the last few years. By mid 2009, the number of suspected dengue fever cases has already surpassed by a few thousand cases that of the same period last year with higher number of deaths. While still grappling with the reasons for the dramatic increase in dengue cases notably over the last two years, another mosquito borne disease, chikungunya, has swept across the entire Peninsular Malaysian with reports of outbreaks occurring in almost all states. The first chikungunya outbreak in Malaysia was described in Port Klang near Kuala Lumpur in 1998. Two subsequent outbreaks occurred in Bagan Panchor and in a suburban community outside of Ipoh in 2006. The three outbreaks were limited to their outbreak foci. An outbreak in Singapore from January to February 2008 was immediately followed by an outbreak in the neighboring Malaysian state of Johor. By the end of 2008 almost all states in Malaysia have reported cases of chikungunya and by mid 2009 massive outbreak of chikungunya has been reported in the Southern parts of Thailand. In contrast to dengue, chikungunya outbreaks occurred mainly in rural areas and to date major outbreak has yet to occur in the major urban centers such as Kuala Lumpur and Shah Alam, where dengue is already entrenched. Despite the differences, it is noted that the swift movement of chikungunya across Malaysia coincided with the dramatic increase in dengue cases. There appears to be common factors that somehow favor the rapid spread of both diseases within the last two years. Incidentally, dengue virus and chikungunya virus are both transmitted by mosquitoes of the genus *Aedes*. Whether there is a preference for *A. albopictus* versus *A. aegypti* for the effective transmission of either the diseases is still not well studied. Since similar control measures applied for dengue, were also employed in attempts to control chikungunya, the unfavorable outcomes of the control measures for both diseases strongly suggest the need to relook at these measures. The role of asymptomatic or mildly infected viremic human host and its contribution in the maintenance of the virus in the population needs to be investigated.



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A network approach to vector-borne diseases: The impact of DENFRAME and the International Network of Pasteur Institutes

The main aim of DENFRAME was to make fundamental contributions to the management of dengue disease in the human populations of Latin America and Asia. We have been involved in the development of new tools that can be used either to study viral egress or as a source of native antigens for diagnosis and/or vaccine purposes. We have developed of an efficient method to produce dengue virus like particles (VLP) of four serotypes that undergo similar maturation process than dengue viruses. We have used a stably transfected cell line, which allows the continuous production of DV1 subviral particles, to develop a safe and semi-quantitative system that can be used in an siRNA screening to identify cellular genes that are involved in DV egress process. This approach has been used to identify a family of cellular factors involved in production of viral particles. Moreover, VLPs are now being used in preliminary sero-epidemiological tests in collaboration with two labs of the International Pasteur network (French National Reference Center on Arboviroses of Institut Pasteur-Paris and at Institut Pasteur-New Caledonia). We have also completed the screening of an original library in collaboration with the team of Jian Ping Zuo from the Shanghai Institute of Materia Medica (PR China) to identify inhibitors of dengue replication. This was possible by adapting a dengue replicon system developed by Michael Jacobs (UCL, London) to a cell-based assay for large-scale library screening in 96-wells plate format. Among the 20 hits considered as potential inhibitors of dengue replication, 4 demonstrated significant activities against the wild-type dengue subtype 2 in an *in vitro* assay.

In a related effort, the International Network of Pasteur Institutes has launched a surveillance program that involves centers in Vietnam, Lao PDR, Cambodia and PR China, with two main goals. The first is to provide an algorithm to improve the diagnosis and clinical management of meningoencephalitis and to initiate a surveillance system to improve early detection and response to any outbreak of CNS infection. The second objective is to study the etiology of meningoencephalitis and provide an inventory of neurotropic pathogens circulating in South East Asia. Together, this program should lead to the development of a network of expertise in the Asian region for clinical recognition and diagnosis of CNS. This program is supported by the *French Development Agency*.




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Experiences in conducting biomedical research on Dengue Hemorrhagic Fever in Thailand

Dengue haemorrhagic fever DHF is one of the major public health problems causing mortality and morbidity in children of school age in Thailand and the whole of Southeast Asia. The disease, once endemic in the region, has no trend of decreasing but instead is spreading globally to South Asia and the American continent. About 100,000 patients were seen in Thailand each year. Epidemiological studies have indicated that most of the DHF occurs in hosts who respond secondarily to different heterotypic virus; suggesting that host immune response play an important roles in the pathogenesis processes. This latter fact complicates the design and development of dengue vaccines which are badly needed.

Realizing the magnitude of the problem and the opportunity of having to provide clinical and public health services to patients, we sought out during the last decade to form a network of clinicians and scientists designed to develop and carry out clinical and basic research projects on DHF; aiming at unraveling the immuno-pathogenesis of DHF and translate them to practical uses. The network consists of two laboratories, two clinical sites in Thailand, collaborating with international institutions and colleagues who mutually share the same interests, facilities, research funds. The long term investment of national granting agencies throughout the last two decades, supporting the infrastructure of the laboratories, graduate and post-graduated programs, and goal oriented management, have been the key factors in bringing the network to perform efficiently with our international colleagues. The network has generated new data useful for the understanding of the pathogenesis of the disease and opened new possibilities of linking more basic and translational researches that would lead to new and efficient diagnosis technology and treatments. The detail of the scientific investigations and managerial experiences will be presented. It is anticipated that more collaborations could be made possible to realize the real impacts on providing better diagnosis, treatment and prevention of DHF.

O07

	<p>Lisa JAMESON Scientist Medical Entomology & Zoonoses Ecology Group Microbial Risk Assessment Emergency Response Division Health Protection Agency Porton Down, Salisbury, Wiltshire, UK Email: Lisa.Jameson@hpa.org.uk</p>
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An ecological perspective for determining risk of vector-borne disease to the UK

The Medical Entomology and Zoonoses Ecology (MEZE) Group within Microbial Risk Assessment (MRA) department, Health Protection Agency (HPA) assesses the risk posed by various zoonotic and vector-related issues specific to UK public health. A large proportion of emerging human pathogens have a zoonotic source and many of these have wildlife origins or are transmitted via arthropod vectors. Such pathogens occur in enzootic cycles within nature, with humans often acting as incidental hosts. From a public health perspective our ability to better predict human outbreaks of these diseases and prepare intervention and mitigation strategies relies upon understanding the natural cycle of pathogen transmission. Without such an understanding the ability for public health bodies to prepare, react and mitigate for these pathogens is severely hindered. This requires appraisal of for example, invertebrate and vertebrate ecology and biology, climatology, land use and habitat change. This presentation aims to introduce the activities of the MEZE group and will review the importance of ecology in assessing the public health risk from vector-borne diseases incorporating ongoing research activities to better understand UK vector populations now and in the future, the impact of weather and climate on vectors hosts and pathogens and the impact of humans and our policies. Also to be discussed is the ongoing collaborative work between the HPA, the National Institute of Public Health of Kosova and the University Clinical Centre of Kosova & Faculty of Medicine with special reference to Crimean-Congo haemorrhagic fever.



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West Nile Fever Virus - update on the biology and epidemiology

Anne Buschmann, Ute Ziegler, Diana Seidowski, Markus Keller, Katja Schmidt, Martin H. Groschup

West Nile Fever Virus (WNV) belongs to the Japan-Encephalitis-serocomplex of the Family of Flaviviridae, genus Flavivirus. This Arbovirus is transmitted by *Culex* spp. and, to a lesser extent, by *Aedes* spp.. Natural disease has mainly been reported in humans and horses, however a variety of other mammalian species are also susceptible to an infection. While over 80% of the infections remain asymptomatic, the clinical picture is dominated by febrile and neurological symptoms. Neurological signs are more severe in horses than in humans and the fatality rate is also higher in this species. WNV presents in four lineages of which lineage I and lineage II are the most distributed. In the past, lineage I was restricted to Northern Africa, Asia, Australia, North and South America and Europe, while lineage II was reported from Sub-Saharan Africa and Madagascar. However, WNV cases caused by lineage II subtypes have most recently been reported from Hungary and Austria. The epidemiology of these outbreaks still needs to be elucidated, but it clearly demonstrates the necessity for an epidemiosurveillance in countries that may be at risk for the development of an endemic WNV situation. The impact of a rapid manifestation and expansion of this agent has become apparent in the recent WNV epidemic in North America. A serological and virological surveillance of wild birds and of horses in Germany has been initiated. Preliminary results of this project will be presented.



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Use of the single cocktail polymerase chain reaction to identify members of *Anopheles minimus* group belonging to the *Myzomyia Series* in Vietnam

Ngo Giang Lien, Pham Duc Ngoc Faculty of Biology, Hanoi University of Science
Ngo Thi Huong, Truong Van Co IMPE, Quy Nhon, Vietnam

Malaria continues to be a major cause of ill-health and death in the tropics. In Vietnam malaria occurs widely with varying levels of endemicity in hilly and mountainous districts. Since the late 1980s there has been an increase in both morbidity and mortality from malaria reaching a peak in 1992 with over 1 million cases and some 4.646 + deaths.

The reasons for this increase are complex and include social, environmental and technical problems. In particular, it is due to a lack of capacity to apply advance techniques to resolve problems in the taxonomy and identification vector species. We use traditional methods for vector identification such as morphology, karyotype analysis, and isozyme electrophoresis. In order to get mosquito samples for karyotype analysis, researchers allowed themselves to be bitten by infected mosquitoes before capturing the full blood females with aspirators to study their genetic makeup. However, this model bears some shortcomings itself as it requires a large sample collection, and samples need to be taken at a fixed stage (4th stage of larvae), therefore requiring more time and efforts. Even for expert taxonomists, the adults of the *Anopheles* species remain difficult to be identified morphologically, and may lead to misidentification of species that are not formally within the *minimus* group belonging to the *Myzomyia Series*. Misidentification of these members using morphological characters could be avoided by the rDNA-ITS2 based diagnosis. Four species-specific oligos have been used as a single cocktail for a diagnostic polymerase chain reaction assay discriminating four closed species.

The cocktail PCR has already provided a new diagnostic tool for the study of closely related insect species. Bearing rapid and sensitive characteristics, this technique has more advantages and can overcome the shortcomings of previous methods. Elucidating and characterizing the individual species within each complex will provide insights into the complexity of the vector systems in South-East-Asia and assessment of the impact of vector control measures.

Another consequence not anticipated at the start of this technology, was the extent to which the applied analytical techniques are relevant to those working on other diseases agents such as: SARS and avian influenza, Hepatitis B and C, measles and morbillivirus



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Biochemical, biological, and antigenic properties of Japanese encephalitis virus NS1 protein

Yize Li, Dorian Counor, Vincent Deubel

Japanese encephalitis virus (JEV) is a member of the genus *Flavivirus*, family *Flaviviridae*. Flavivirus NS1 glycoproteins are essential proteins which exhibit a high degree of sequence homology. The NS1 protein is secreted from cells as a soluble hexamer and can induce protective immune response in mice against lethal encephalitis. However, its role in neuroinvasion of JEV remains unknown.

Our aim is to identify the role of NS1 protein in JEV neuropathogenesis. In this study, we have produced recombinant JEV NS1 protein in *Drosophila* S2 cells and have characterized its biochemical, biological and antigenic properties. The signal sequence and full-length of NS1 protein of JEV Nakayama strain was produced to high level in supernatant of *Drosophila* S2 stable cell line, and purified. We observed one form of ~300kD of NS1 by size exclusion column, corresponding to the hexameric form of NS1. We demonstrated high mannose and hybrid glycosylation forms of NS1 N-glycans. Epitope mapping was carried out using overlapping decapeptides and a panel of well characterized monoclonal antibodies (MAbs). Purified NS1 protein was used to vaccinate C3H mice and showed partial protection against a challenge of JEV. However, none of the MAbs transferred into challenged mice induced any passive protection. MAbs showing high affinity and specificity were used to develop an NS1 antigen capture-ELISA. The assay showed low production of the protein *in vitro* and in biological samples compared to that previously observed in dengue-infected specimens.

Interaction of NS1 with endothelial cells was observed *in vitro* and *in vivo*.

Altogether, these data contribute to better characterize NS1 protein and to study its role in neuropathogenesis.

Acknowledgments: Peng Lu (IPS-CAS, Shanghai), Michel Huerre, Patrick Ave, Philippe Despres, Marc Grandadam, Felix Rey, Marie Flamand and Myriam Ermonval (IP Paris), Eve-Isabelle Pecheur and Jean-Pierre Lavergne (IBCP, Lyon), Philippe Buchy (IP Cambodia), Huynh Thi Kim Loan and Vu Thi Que Huong (IP HCMC), Guotong Liang (China CDC, Beijing)



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Flavivirus Capsid Protein: Beyond Viral Assembly

Flavivirus capsid (C) protein is a small viral structural protein. Because of its positively charged nature, traditionally it is assumed that its apparent function is packaging of viral RNA into the nucleocapsid core. Our study demonstrated that C protein-RNA association is regulated by the phosphorylation/dephosphorylation of C protein. Surprisingly, *in vitro* experiments indicated that the C protein does not seem to distinguish its interaction between positive or negative strand RNA. Although *in vivo* it is assumed that C protein will preferentially packaged positive strand RNA to ensure assembly of infectious virus particles. At this stage we have not been able to reconcile if there are host protein involvement during the packaging process *in vivo* to allow the correct strand to be packaged preferentially.

Extending the study to identify possible host factors that may be involved in C protein function, non-structural functions of C protein were discovered. One of the host proteins identified to interact with C protein is importin- α and this interaction is essential to mediate the nuclear import of C proteins. The nuclear phase of C protein is important to influence cell cycle/apoptosis to favour viral replication. Prevention of C protein translocation to the nucleus resulted in no infectious virus production. Another host protein that associated with C protein specifically is the human exocyst component. Elucidation of biological significance of C protein-exocyst component association revealed that this binding is essential to facilitate efficient viral RNA transcription and translation through the sequestration of elongation factor 1 α . Our study confirmed that C protein is involved in several steps important in flavivirus replication cycle which ultimately could affect the proper assembly of the viral nucleocapsids.

Most of antiviral research targets flaviviral envelope or the enzymatic activity of non-structural proteins such as NS3/NS5. Our study pinpointed C protein as a potential novel antiviral target because of its multi-functional roles in its engagement with host proteins at various points of the replication cycle including its primary role of nucleocapsid formation to form the infectious virus.



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Deciphering host defence mechanisms in infectious diseases and chronic inflammation. Focusing on acute and severe chikungunya arthritogenic pathology and long term consequences.

Over many years my laboratory has worked on innate immune responses in health and diseases of the CNS. Defining the role of innate immune complement molecules has been a major focus of our research and particularly addressing its 'double edge sword' activity in the CNS to promote either neuroprotection or neurodegeneration. More recently, we have extended our investigation to other innate immune receptors such as Toll like receptors (TLR), Retinoic acid-inducible gene (RIG) and lectin/scavenger receptors (CR3, CD93) which belong to large family of 'pattern recognition receptors, PRRs'. Several of these PRRs are involved in sensing intracellular pathogens such as viruses, but it is increasingly evident that their primary and perhaps more ancestral function is to protect against the accumulation of toxic compounds (e.g, HMGB1, nucleic acids, Prion, amyloid fibrils) released by necrotic and apoptotic cells in sterile non-infectious settings. Currently, the main focus of our study is to further delineate the fundamental innate immune defence mechanisms to protect from viruses such as chikungunya virus (CHIKV, ssRNA alphavirus) which has affected several millions of people in the Indian Ocean and particularly in La Réunion (1/3 of the population, ie 270000 inhabitants). CHIKV produces a transient illness in humans characterized by myalgia and arthralgia, but in some elderly patients, we found severe forms notably leading to chronic incapacitating arthritis. The pathogenesis of aphaviruses and the fundamental mechanisms by which they cause chronic diseases are poorly understood. I will present a comprehensive and prospective cohort study of hospitalized patients and through the development of experimental models of synovial/immune cells to decipher the host-pathogen interactions. Of note and remarkably, we found that CHIKV persists in tissues despite the presence of neutralizing antibodies and infiltrating NK and T cells. Our data suggests that host immunological and tissue-specific factors albeit critically involved in the acute elimination of CHIKV may also promote its persistence in synovial tissues and driving chronic arthralgia reminiscent of but distinguishable from rheumatoid arthritis. Experiments are highly warranted to address the specific role of CHIKV in controlling host's defense mechanisms and to identify novel therapies which could be better targeted to tissue sanctuaries to eliminate persistent CHIKV infection and control chronic inflammation.



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Dengue virus-infected dendritic cells trigger vascular leakage via metalloproteinase activities

Dengue viruses are considered as the most efficient re-emerging and expanding pathogens of global importance. The hallmark of Dengue infection is the Dengue hemorrhagic fever (DHF). This physiopathology could produce fatal outcomes in patients evolving to the Dengue shock syndrome (DSS). Neither treatment, nor vaccine is available. Understanding of molecular mechanisms of haemorrhage is pivotal to develop new therapeutic approaches targeting molecules involved. In order to study the molecular mechanisms involved in vascular leakage, we carried out *in vitro* and *in vivo* studies. Primary dendritic cells, the main target cells for Dengue and other hemorrhagic viruses, were infected with Dengue virus and supernatants were collected. These supernatants were used to assess both their role in the vascular permeability enhancement (VPE) in *ex vivo* and *in vivo* experiments, as well as to measure factors associated in these mechanisms. Using primary human umbilical vascular cells (HUVEC) we have found molecules already described to be involved in the vascular leakage mechanisms such as TNF-alpha and clearly determined that gelatinolytic metalloproteases (gMMP) molecules associated to VPE and are overexpressed in the supernatant of infected-DC cells. Moreover, these supernatants are able to induce an increase of VPE evidenced in an *ex vivo* systems and a vascular leakage in an *in vivo* mouse vascular leakage model. These effects were inhibited by monoclonal anti- gMMP monoclonal antibodies and also by chemical compounds specific gMMP-inhibitors. We have elucidated the major molecular mechanisms of vascular leakage induced by viral infection opening for the first time therapeutic approaches to improve the prognostic of DHF patients. Clinical trials are designed to undertake the clinical proof of concept by targeting gMMP with specific inhibitors. We have initiated the formation of a consortium that can be enlarged to work on different viruses involved in the enhancement of vascular permeability with the objective to be funded by the European Commission.



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Arbovirus encephalitis from the mosquito to the brain

Infection of vertebrates with many mosquito- and tick-borne arboviruses can give rise to encephalitis, examples include the equine encephalitis alphaviruses, West Nile, St Louis, Japanese encephalitis and tick-borne encephalitis flaviviruses and La Crosse bunyavirus. In their arthropod vectors, these viruses are generally controlled by cellular defences, probably most importantly RNAi. A low level persistent infection is established in the arthropod which does little or no damage; this is in contrast to arthropod-only virus infections which often replicate to high titre and destroy the arthropod. In the vertebrate, arboviruses generally produce a transient viraemia. Depending upon virus strain and vertebrate species, this can be a very high titre viraemia. It is likely that this is required, in at least some species, to complete the virus life cycle. In mammals, clinical disease is generally febrile and ranges from mild to fatal. With many encephalitic arboviruses, relative to subclinical or mild infection, encephalitis is rare. Pathologically, encephalitis is characterised by gliosis and a strong inflammatory response with hall-mark mononuclear cell perivascular cuffing. Studies of alphavirus encephalitis in experimental model systems indicate that interferon responses are particularly important in the protection of meningeal and ependymal cells, antibody responses are generally protective and required to control spread of the infection and T-cells are required to eliminate the infection but may also be pathogenic. The molecular and cellular basis of the interaction of these viruses with the specialised cells of the CNS is incompletely understood but persistent non-destructive infections can occur.

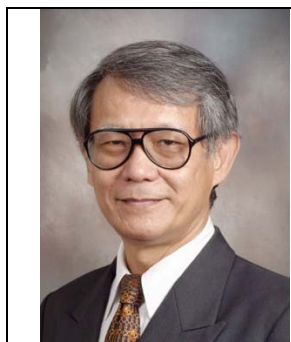
O15



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Simple tools for vector control & future threats

For the first time in a generation malaria is declining in many parts of Africa. This remarkable achievement has been brought about by having effective antimalarials, together with the large-scale distribution of long-lasting insecticide treated nets. Transmission has been reduced to such an extent that policy makers are now considering elimination as a viable option. This ambitious target can only be achieved by combinations of tools. This talk reviews some of the recent tools that could be incorporated into Integrated Vector Management strategies and looks at future threats to this approach; serving as a case study on the control and elimination of a vector-borne disease.



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Threats and Opportunities from Vector-Borne Diseases for Southeast Asia

Vector-borne diseases, including malaria, Dengue haemorrhagic fever, and many other diseases from protozoal, helminthic or viral pathogens, have been major problems for the developing world all through history. The problems are not only biomedical in nature, but also involve socio-economic and environmental factors. Southeast Asia has its share of problems of vector-borne diseases, but as advanced developing region can turn many threats into opportunities, for examples, in R&D for new drugs, diagnostics and vaccines. Examples of success in indigenous drug development in developing countries are given, as also achievements in other areas of capability strengthening for R&D. International co-operation is needed for meeting the threats and for success in the opportunities. SEA-EU collaboration is a potential factor for this success, but this requires hard work in obtaining the resources and in networking among the R&D centres in both regions.

Prof Yongyuth Yuthavong is a scientist with interest in the broad issues of public policies, especially concerning application of science and technology for development and human development in general. He was awarded a Thai Government scholarship to study in the UK, where he obtained a bachelor degree in chemistry with first class honours from University of London (1966), and a doctoral degree in organic chemistry from University of Oxford (1969). He spent a long research and teaching career at Mahidol University, where he was appointed Professor of Biochemistry (1983). He was the first President of the National Science and Technology Development Agency (NSTDA, 1992-8) of Thailand. He heads a research group in BIOTEC, working on development of new anti-malarials. In 2004, he received the Nikkei Asia Prize for Science, Technology and Innovation from the Nihon Keizai Shimbun, Japan, for his work on anti-malarial drug targets, and the "Person of the Year" Award from Thailand's National Identity Board. Prior to that, he received the "Outstanding Scientist of Thailand" Award from the Foundation for Promotion of Science and Technology (1984). In 2006, the Nation newspaper named him one of 35 most influential Thais over the past 35 years. He served as Minister of Science and Technology (2006-8), after which he returned to the research career.



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Global warming and Malaria re-emergence in Portugal – an example for an European consortium

Team: Carla A. Sousa, César Capinha, Eduardo Jonas, João Pinto, Jorge Rocha, José Luis Vicente, Paulo Almeida, Rosa Teodósio.

Networking is an essential tool for better understanding of data, dissemination of results and standardization of different techniques, at a time of globalization.

Several networks have been implemented, as , for example, EDEN (Emerging Diseases in a Changing European Environment) , which aims at the risk analyses of introduction or spread of several diseases (malaria, leishmaniasis, West Nile and other arboviroses, rodent and tick born diseases) in Europe. As expected, some of these networks can expand geographically or thematically.

EDEN is composed of 48 institutions from 24 countries, divided by leaders of thematic areas, all responsible for 5 scientific main subjects: a) environment and climate; b) vector studies; c) pathogens; d) human population; e) models. Training of new scientist is a major component of the programme (PhD network).


Global warming and emerging diseases is the EDEN major topic of study. Though malaria has been eradicated in Europe, migration and potential introduction of parasites and alien mosquitoes are a regular risk, enhanced by new conditions for the establishment of its biological cycle.

In Portugal the study was carried out in an area of former malaria transmission where vector densities have not been substantially altered. Data will be presented on laboratory and field work, and focused on the networking discussions on interchange of material and data analysis.

Though temperature increase has been determined, malaria, at the moment, seems to be a minor risk for Portugal as an emerging disease, but regular surveillance and contact between scientists and the Health authorities requires a new format of work.

As in other networks it is relevant to evaluate how to proceed with studies when funds from financial agencies terminate.

O18

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Community participation and vector control

Vector control has been widely used in Indonesia, however, even at present we face continual difficulties in vector control. We will discuss past experiences in vector control where the community is involved and the reasons behind. Typical Dengue vector control uses the weekly picket by the women groups (Dasawisma), while Malaria vector control involves the use of bednets which is organized by the women's group. In both experiences we are not able to just conclude that vector control was successful until we have an effective system to monitor the community.

O19



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Complexity of the vector system in South-East Asia: How to implement effective vector control?

The biodiversity of mosquito species involved in pathogen transmission throughout South-East Asia is particularly rich as compared to the other continents. Species belonging to the genera *Anopheles* and *Aedes*, respectively involved in the transmission of parasites (*Plasmodium* spp., *Wuchereria bancrofti*, *Brugia* spp.) and viruses (Dengue, Chikungunya) can occur in the same localities. In addition, the vector system is composite as each malaria vector in Asia belongs to a species complex in which sibling species are morphologically indistinguishable and may present different trophic behaviors and vectorial capacities ranging from non-vectors to major vector species.

Therefore, it is crucial to study appropriately the vector populations prior to apply any vector control program. Precise identification and bionomic studies allow targeting the correct vector species in control programs, and help to define the appropriate way to control them in relation to their specific behavior. Robust diagnostic tools have now been developed for improving knowledge on vectors and important information can be obtained on various aspects, such as species identification, vectorial capacity, behaviour, resistance/susceptibility level to insecticides, and seasonality along with environmental factors affecting the geographic distribution.

However, there is still a considerable lack of knowledge on the vectors. Do we know all the vectors, even secondary ones that may sporadically transmit and then maintain transmission? Can we prevent from an outbreak using a very early pathogen detection method? Can we assess the capacity of pathogen transmission by vectors harbouring a diverse microbiota? Can we develop simpler and cheaper diagnostic tools for vector characterization?

These are some of the questions we need to answer as part of a collaborative initiative for improving the control of vector borne diseases.



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Dengue and Chikungunya in Singapore

Dengue and chikungunya, transmitted by the Aedes mosquitoes, have caught world-wide attention due to increase in the frequency of major epidemics in recent years. Though transmitted by the same vectors, they are caused by different viruses (DENV and CHIKV) that belong to the genus Flavivirus and Alphavirus respectively.

There has been a worldwide resurgence of dengue in the last few decades. Today, it is estimated that it affects at least 50-100 million people every year. With more than 100 countries, between the 10°C isothermal lines, being endemic, 2.5 billion people are at risk of infection. Facilitated by rapid urbanization and increased travel, the disease continues to make its geographical spread, and the number of cases continues to rise across the world.

Chikungunya outbreaks have been reported in Asia and Africa. Major epidemics appear and disappear cyclically, usually with an inter-epidemic period of 7-20 years. However, its recent unprecedented explosive outbreaks since 2005, revealed an altered epidemiology. Millions of cases have been reported as the disease swept across the islands in the Indian Ocean, followed by countries in South Asia and South East Asia. More surprising is the outbreak experienced by temperate Italy.

Singapore, a green tropical city state, has been challenged by the two diseases. She has seen a resurgence of dengue cases since the late 1980's, after two decades of successful control that relies largely on an integrated vector control programme. In 2008, Singapore also saw an emergence of Chikungunya. This talk will discuss the epidemiology of the two diseases, through presenting the latest findings, particularly those of entomology and virology. The presentation will also provide an update on the control strategies employed by the National Environment Agency, in the face of new challenges.



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Short-term cross-protection to dengue serotypes at the expense of long-term protection?

High fever, joint and muscle pain are amongst the symptoms of dengue disease that are caused by the strong immune reaction after infection. Immune activation and cytokine production have been correlated with disease severity in various studies. However, the mechanistic links between immune activation and disease and the impact of early immune activation on the outcome of immunological memory and protection for subsequent infections are not well understood.

In a prospective dengue study in Singapore (Early Dengue infection study EDEN) we analyzed acute and convalescent blood samples from dengue patients and fever control patients. Flow cytometry analysis of blood cells revealed significantly higher cell activation in dengue patients compared to non-dengue fever patients. Activation of monocytes, which are effector cells of the unspecific response, was accompanied by prolonged T cell activation and B cell proliferation and differentiation, both representing the specific response. In this inflammatory environment, B cells were triggered to produce high amounts of antibodies that were mostly cross-binding and cross-neutralizing. The abundant formation of antibody-producing B cells was short-lived and is seemingly efficient for short-term protection, but might not be optimal for the generation of affinity-matured antibodies which would be most efficient for specific virus neutralization. The aim of these studies is to contribute to the understanding of population immunity and the spread of dengue epidemics, and to benefit the generation of efficient vaccines.

O22



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The Early host response in Dengue

Dengue symptomatology includes high fever, vascular leakage and hemorrhage. The pathogenesis is believed to be related to immune activation and in particular to cytokine production. The innate immune response is largely mediated by polymorph nuclear cells including granulocytes, dendritic cells and monocytes/macrophages. The latter are of particular interest in dengue infection as they are targets for viral replication. To address innate immunity-related early gene expression after infection, we performed microarray analysis on sorted CD14+ cells infected in vitro. Comparing these data the gene-expression profiles from sequential samples from dengue infected patients revealed a striking similarity, suggesting that monocytes are predominantly activated during dengue infection and highly express several chemokines and interferon-induced proteins. Our data underscore the importance of monocyte-mediated innate immune activation and cell migration on dengue pathology.



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Impact of Human genetics on susceptibility to and transmission of vector-borne diseases in South-East Asia

Richard Paul and Anavaj Sakuntabhai

The study of the role of host genetics in infectious diseases aims at identifying genes influencing host resistance and susceptibility, and increasing our understanding of their function and role in the microbial pathogenesis. The medical implications of improved knowledge of the genetic basis to host resistance to infectious disease studies are numerous and important, permitting both molecular diagnosis and immunomodulatory treatment to be based on a rational understanding of the pathogenic process. Hitherto research effort has concentrated on clinical disease and yet, as far as unravelling the biological basis leading to pathology is concerned, asymptomatic infection outcomes are equally important. Mosquito-borne pathogens cause some of the most important tropical and sub-tropical diseases, some of which show a potential for spreading into more temperate zones. In addition to long recognized pathogens such as malaria parasites, *Plasmodium* spp., we now acknowledge the emergence of additional pathogens, most notably the arboviral diseases including West Nile, Chikungunya, Japanese Encephalitis and in particular Dengue. The aim of our laboratory is to genetically dissect the pathophysiological process that determines the outcome of infection by malaria parasites and dengue virus.

For malaria parasites, *Plasmodium falciparum* and *P. vivax*, we analyse a cohort that has been under surveillance for the past ten years, in collaboration with epidemiologists in Thailand. Using family-based methods we explore human genetic variation disease outcome and the reservoir of infection, first by heritability analyses and then by a candidate gene approach targeting genes that have either been previously shown or suspected to impact on malaria parasite infection outcome (e.g.G6PD), or that have been identified through our genome scan linkage studies. For dengue, case-control studies of candidate genes (DC-SIGN and OAS gene family) have revealed specific genetic variants associated with disease outcome. Future work will include identification of individuals susceptible to spread the disease at a community level. Identified significant genetic variants are subject to functional study to demonstrate their effect on expression and/or functioning of the gene product *in vitro* and *in vivo*.

ABSTRACTS
FOR DISCUSSION

D01

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The co endemicity of malaria and helminth infections in Indonesia: from epidemiology to immune responses

In many areas of the tropics, malaria infection coexists with helminth infections. Although the importance of coinfection has been known, there are few studies that systematically address the extent of coinfection geographically, the risk factors associated with coinfection and the immunological consequences of coinfection.

On the Flores Island in Indonesia, *Ascaris lumbricoides*, *Trichuris trichiura* and Hookworm infections are prevalent alongside *Plasmodium falciparum* and *Plasmodium vivax*. In the area of Ende, two villages have been studied cross sectionally and will be studied longitudinally. Using classical as well as molecular diagnostic methods, the prevalence of the intestinal helminth infections as well as malaria has been determined. Using GPS, the distribution of household with subjects infected with any of these parasites has been recorded to allow the analysis of the extent of clustering of co-infections throughout the villages.

The immunological responses of the residents have been determined to both malaria and helminth antigens. The cytokine production of PBMC to specific antigens has revealed that responses to infected red blood cells is skewed towards Th1 as characterized by high IFN γ and some TNF α responses, whereas responses to helminth antigens such as *Ascaris* is clearly dominated by Th2 cytokines, (IL-5 and IL-13 and low IFN- γ production).

The extent to which helminth infections cluster with malaria infections will be shown along with the immunological consequences of coinfection.

D02

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Interest Area: drug resistance in malaria

D03

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Interest Area: Immunology

PROSPECT OF CHICKEN IMMUNOGLOBULIN AS A RABIES VACCINE CANDIDATE By SAYU PUTU YUNI PARYATI Faculty of Medicine Jenderal Achmad Yani University, Cimahi.

ABSTRACT The principle of anti-idiotypic vaccination has been applied successfully for several viral systems. In the case of hepatitis B virus.

D04

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Interest Area: bioinformatics modeling simulations

Recently, we developed a computational scheme for extracting coarse-grained dynamical information by statistically clustering a large number of time series data. We applied the method to financial markets, earthquake monitoring, and molecular dynamics simulations, and have had remarkable success. We believe the method will be very helpful in interpreting large-scale, high-throughput transcriptome experiments. We have also been building models to simulate the ecological dynamics of mosquito vectors, and how interactions between mobile vectors and mobile hosts affect the spread of vector-borne diseases. We have completed our preliminary study of a model of larval competition between mosquito species, and found in the scenario that *Aedes aegypti* competes with a *Culex* species for breeding spots, *Culex* can act as an effective control for *Aedes* only when breeding spots are uniformly distributed. Whenever breeding spots exhibit any degree of spatial clustering, *Aedes* frequently dominates in the long run. This long-run dominance of *Aedes* persists even when periodic fogging is introduced into the simulations. A very dramatic enhancement of infection rate due to spatial concentration of human mobility patterns was also found in our ongoing project on host-vector interactions.

D05

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Interest Area: dengue

Our work over the last few years has focused on understanding the interaction between the dengue virus and host cells, and how this interaction is influenced by dengue serotype. In particular, as considerable clinical evidence has suggested that the liver is a target organ of the dengue virus particularly in severe C.

D06

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Interest Area: Vector biology and control

Can vector control suppress dengue transmission? Strategies for the control of *Ae. aegypti* changed several times in the 20th century. In the early decades, source reduction—the systematic elimination of breeding sites—was highly successful; urban yellow fever, and (presumably) dengue, were eliminated from many countries. Following World War II, “peri-focal” application of DDT was remarkably effective, but hopes for eradication faded with increasing problems of insecticide resistance, political and logistical factors, and concern for the environmental impact of DDT. Emphasis shifted to organophosphorous larvicides and adulticides applied as “Ultra-low Volume (ULV)” aerosols. Failure of these led to the adoption of “integrated” control—defined as “the rational combination of all available control methods in the most effective, economical and safe manner to maintain vector populations at acceptable levels”—with increasing emphasis on community involvement. This approach has also been a failure. Indeed, since the DDT era, no country in the world can boast sustained suppression of dengue transmission. In truth, we have no clear knowledge of what the “acceptable levels” are, nor any accepted method for monitoring them, nor how these vary with herd immunity, vector longevity, and other critical parameters. Moreover, there can be no standard model for these relationships because there is such wide variation in the structure and ecology of urban areas, even at short distances. Above all, in the past 50 years, we have paid remarkably little attention to evaluating and monitoring the impact of control operations on the target species, and we have been singularly un-innovative in our search for new approaches to control. Unless we tackle these questions in a creative spirit, we cannot honestly say whether dengue transmission can be suppressed by suppressing the vector.

D07

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Interest Area: complex systems and networks

We have been studying air-borne disease spreading in Singapore by carefully modeling the local social networks. An individual-based simulation platform has been largely built and is currently being refined. It would be interesting to study the effects of human social activities on the spreading of vector borne diseases. It would also be interesting to study the possible ways for controlling vector borne diseases by viewing the spreading of such diseases as through complex systems interacting with human society. In short, we are motivated to study disease spreading and control with complex system approaches. Singapore as a tropical city provides a perfect platform for conducting such studies.

D08

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Interest Area: Bacterial of disease

Detection of *Enterobacter sakazakii* and other *Enterobacter* sp from Dairy Cow's Milk in Two District area In Indonesia A.E.T.H. WAHYUNI 1), TRI YAHYA BUDIARSO 2) 1) Laboratory of Microbiology, Faculty of Veterinary Medicine Gadjah Mada University, Indonesia 2) Faculty of Biology, Duta Wacana Christian University, Yogyakarta, Indonesia *Enterobacter sakazakii* is considered an opportunistic pathogen that has been implicated in severe forms of necrotizing colitis and meningitis especially in neonates with a mortality rare varying from 40%-80%. The natural habitat *E.sakazakii* is not well understood and have been reported as frequency isolated from different environments including soil, rats, flies, milk powder factories, chocolate factories and households. A total of 100 samples were obtained from dairy cow's milk were studied. The presence of *E.sakazakii* and *Enterobacter* sp was detected using the Guillaume et al, 2005 and Turner et al., 2000 procedure on TSBA medium. *E.sakazakii* was not isolated from both district Sleman and Boyolali. However, *E.cloacae* was found in 33 of 75 isolates (44%) of samples from Sleman. Meanwhile 12.7% *E.cloacae* and 5.4% *E.gergoviae* was found of samples from Boyolali. Key Words: *Enterobacter sakazakii*, *Enterobacter* sp, dairy cow's milk

D09

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Interest Area:Recombinant protein and bioinformatics

Dengue is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, Southeast Asia and the Western Pacific, with Southeast Asia and the Western Pacific being the most seriously affected. The United Nations' 2007–2008 Human Development Report predicted that global warming could cause increase cases of dengue worldwide more than double by 2080 and expand the dengue infection area into U.S. and European territories. The purpose of this research is to study whether dengue antigens could be expressed in recombinant model systems. The final goal of this research is to develop a diagnostic tool such as biosensor to detect a high-risk dengue infection at an early phase of infection. Possibility of using fragmented dengue antigens as vaccine candidates are also being explored. An effort is made to build up a database of Indonesia's dengue strain genomic sequencing data. This database will be a fruitful resource for molecular biology information about dengue virus and its health data system.

D10

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Interest Area: Vector-borne diseases

My name is Vu Thi Que Huong (M.D., Ph.D) who is Head of Department of Microbiology and Immunology in Pasteur institute of Ho Chi Minh city that began my first term of five years on January 15, 2007. I have been involved for more than 20 years in arbovirology at the Pasteur institute of Ho Chi Minh City, with major emphasis on dengue virus. I have still being the head of arbovirus laboratory and the member in my institution review board as well as in steering committee of national program for dengue control in Vietnam. My solid scientific background in genetics and molecular diagnostics of dengue and Japanese encephalitis viruses was acquired during several visits in foreign laboratories, in France, in Canada, and in Japan. I am directing several international research programs on arboviruses. My Ph.D. degree in Medical University of Ho Chi Minh City was obtained in 2002 with a subject on the genetic and phenotypic variability of dengue viruses in Vietnam. Other studies on the genetic variability of Vietnamese strains of Japanese encephalitis and of dengue viruses as well as human genetics related to dengue infection have already been published in international journals. I have a professorship at the medical and science University of HCMC and have the responsibility of several students in my laboratory. My young students, young colleagues with multi-professional skills have supported me to conduct many national and international collaborative researches concerning new diagnostic tools' development and evaluation, virology, molecular epidemiology, pathophysiology, clinical trial and surveillance on flaviviruses (particularly dengue and japanese encephalitis), alphaviruses (new vietnamese alphaviruses and chikungunya), hantaviruses and henipahviruses. Beside very attractive dengue field, I am also involving some studies on pathogens causing human fever/hemorrhagic fever, meningo-encephalitis and acute respiratory syndromes in southern Vietnam.

D11

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Interest Area: geographical information system (GIS), image processing, bioinformatics and scientific visualization.

Recently completed projects include study of environmental factors that affect dengue incidence in Singapore, development of mosquito monitoring and alarm system for dengue infections, application of geographic information system

(GIS) to the study of man-macaque interaction, development of identification system for the larvae of *Aedes aegypti* and *Aedes albopictus* and automated grading of Her2/Neu immunohistochemistry images.

D12

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DHF, a Vector Borne Disease Still a Health Problem in Indonesia

The threat of vector borne diseases are still regarded as a serious matter in Indonesia. As an archipelago country, the climate, geography and the population density are one of high factor of prevalency vector borne diseases especially Dengue Haemorrhagic Fever (DHF). The 2008 National target for Case Fatality Rate (CFR) DHF is < 1% and has only been achieved in 12 provinces among 33 provinces in Indonesia. The highest CFR is found in the provinces of Papua, Bengkulu, Maluku and East Nusa Tenggara (CFR 2-3 %). Various strategies have been done by government such as elimination of masquito's nest, increase community health education, the speed to handle against DHF etc but those have not completely reducing the death rate because of DHF. In East Java Province (CFR 1,3%) which consists of 38 districts, 15 districts show CFR >1%.

Public Health Laboratory Surabaya as Referral Laboratory in East Java Province continues to support government in handling program for infectious diseases and non infectious diseases. The cooperation with all level of Department of Health especially with Provincial Health Offices in East Indonesia and East Java has been implemented intensively.

Rapid and accurate examination results will help the government to take actions as early as possible to avoid the spread of the disease in wider area.

In the future, we need to consider a cooperation which involve many sectors so that the prevalency and mortality rate can be decreased significantly and at the end impact on health sector, productivity, economy and social can be reduced.

D13

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Interest Area: Bioformatics

To apply bioinformatics modelling methodolgies and machine learning methods to spread of vectors; application of remote sensing technologies (analysis of satellite images) and geographic information system (ArcGIS) to for control of vectors. Modification and design of software for field equipments in vector control, e.g. automated/triggered photography and GPS.

D14

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Interest: Entomology and public-health

It can be argued that many vector-borne diseases can already be prevented by control strategies that have existed for at least 50-100 years. However, significant shortcomings remain in understanding vector-borne disease emergence/transmission in regard to more recent societal changes and changes in disease ecology and epidemiology, especially in complex urban areas. More efficient entomological sampling methodologies that can be employed reliably across a variety of temporal and spatial scales, and analyzed geo-spatially, will provide critical capacities to investigate complex epidemiological and ecological interactions, estimate entomological risk, guide control operations, and assess prevention programmes. Our short-term research objectives include the evaluation of sampling programmes for monitoring adult container habit mosquitoes through the validation of two simple mosquito trap technologies (i.e. sticky and oviposition traps) within a geospatial monitoring and control system. It is expected that these capacities will permit the spatio-temporal identification of high risk areas that can be efficiently targeted while also providing a more thorough understanding of the relationship between vector densities, human densities, and important epidemiological and environmental features. These trap methodologies can also be of value in areas of low vector infestations when used in large numbers; however, in order to test their effectiveness for control and prevention a cost-effective surveillance programme that can be employed at epidemiologically relevant scales must be established. The underlying premise of this research is that integrative approaches, to improve the efficiency in which we understand changes in disease ecology and improve vector control, already exist but necessitate the innovative use of currently available tools and knowledge.

D15

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Interest Area: Immunology

The principle of anti-idiotypic vaccination has been applied successfully for several viral systems. In the case of hepatitis B virus system, Kennedy et al. (1985) have produced a rabbit anti-idotypic antibody which can induced virus neutralizing antibody in mice. Anti rabies serum (ARS) called antibody 1 (Ab1) was use.

D16

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Interest Area : Malaria

Preliminary report: Gametocyte carriers are source of transmission in malaria endemic areas. Artemisinin derivatives is capable to eliminate young gametocyte, whereas primaquine kills mature gametocyte of *P. falciparum*. The objective of the study is to evaluate whether primaquine is necessary as additional drug for dihydroartemisinin-piperaquine in order to eradicate gametocyte in malaria treated individuals. An ongoing study is conducted in a primary health center since December 2008 up to now. More than 1000 feverish patients who came to seek treatment were screened for inclusion and exclusion criteria. Subjects are randomized to receive either dihydroartemisinin-piperaquine (Days 0 – 2) alone or DHP plus primaquine single dose (Day 3). Patients are followed up until Day 42, and finger prick blood is collected on Days 0, 2, 3, 7, 14, 21, 35 & 42. Microscopic examination is used to justify gametocytemia condition. Eighty seven subjects were analyzed for this preliminary report and consisted of 43 DHP and 44 DHP plus PQ. Base line characteristic showed no significant differences between these two groups on age, sex, body temperature, percentage of fever, hemoglobin value and asexual parasite density on day of enrollment. Gametocyte prevalence on day 0 was not significantly difference between the two groups (25.6% = 11/43 vs 15.9%=7/44, p value= 0.27, Fisher exact test). After drug administrations, the prevalence decreased gradually and became significant difference only on Day 14 (DHP vs DHP+PQ= 14% vs 2.3%, p= 0.045, Fisher exact test). Gametocyte development was 6.3% (2/32) on Day 2 in DHP treated group, and were 10.8 % (4/37) and 3% (1/33) in the other group on Day 2 and 3, respectively. In DHP treated subjects, gametocyte cleared completely on Day 35, whereas in DHP + PQ group this was achieved on Day 28.

D17

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Interest Area: Genetic Control of Aedes and Dengue

In the absence of vaccines, control of dengue and chikungunya can only be achieved by suppression of mosquito populations. However, current control methods are inadequate to reduce the population of Aedes mosquitoes below the disease transmission threshold. Recent advances in insect genetic engineering have opened new possibilities for the control of mosquitoes. The genetic approach that is closest to practical application is a “population suppression” based on the Sterile Insect Technique (SIT). SIT has been used successfully for the suppression or local elimination of several insect species in agriculture, and mathematical modeling indicates that it would be effective against Aedes mosquitoes. Sterile male mosquitoes are released continually over a wide area to mate with the target pest population; no progeny result from these matings and the target population declines. Sterility has conventionally been induced with gamma-irradiation, which is too damaging for most mosquitoes, or chemicals which are no longer approved. In the RIDL® method mosquito strains are homozygous for one or more dominant lethal genes. We have successfully constructed RIDL strains of *Aedes aegypti* and *Aedes albopictus*, using the tetracycline-repressible ‘tet-off’ gene expression system to repress the lethal effect with dietary tetracycline. The first RIDL strains have been successfully tested in confined semi-field conditions for mating competitiveness with wild-type mosquitoes and a range of life history and behavioural traits. An area-wide control program based on mass-release of mosquitoes would preferably not release biting females. Sex-separation methods are therefore required. Effective mechanical separation methods are available, and we are developing genetic sexing methods which will be more accurate and efficient. Our successful development of such systems in *Aedes aegypti* will be discussed.