Initially Dr. Prasert Auewarakul’s research was in the field of HIV. He studied distribution of viral DNA in subpopulations of CD4+ lymphocytes with different profiles of co-receptor expression. While most HIV DNA in early phase of infection is found in the subpopulation of CD4+ lymphocyte that expresses the chemokine receptor CCR5 (a co-receptor required for the viral entry into target cells), he described an expansion of target cell population to CCR5-negative cells in later stages of infection. He also showed that this was not necessarily caused by a change in viral phenotype as would be generally believed, but reflected abnormal cellular activation, which is an important part of the HIV pathogenesis. The expansion of target cell population is responsible for the accelerated viral replication, in later stages of disease progression. In addition, he studied control mechanisms of the viral gene expression and replication, and discovered a new regulatory element named Cis-Enhancer Sequence, which is a binding site for heterogeneous ribonucleoprotein. These findings further added to our understanding of the control mechanism of viral replication.

An important research is the study of uncoating process. This is the earliest process after virus enters a target cell, in which the viral genome is released from the viral capsid. Uncoating is the least studied step in the viral replication cycle because of the lack of appropriate methodology. He invented an in vitro experimental model to characterize this process. He also discovered that the uncoating process required cellular factors only present in activated cells. This explains the resistance of resting cells to HIV infection. These data will hopefully lead to identification of the cellular uncoating factor in the future.

Another discovery in HIV is the activation of HIV expression by a cellular RNA editing enzyme called Adenosine Deaminase Acting on double-stranded RNA (ADAR). This demonstrates another mechanism, by which HIV takes advantage of existing cellular machinery.

After the outbreak of avian influenza H5N1 in 2004, the research activities shifted to influenza. It was initially a response to the urgent situation of the outbreak. He participated in the team that diagnosed the first patient in Thailand and reported the first case of human-to-human transmission. Subsequently, the main research question focused on viral pathogenesis in human. Important discoveries include the identification of type II alveolar epithelial cells as the main viral target cell. This contributes to the severity of H5N1 infection in human. While seasonal influenza replicates in human upper airway and causes upper respiratory tract symptoms, H5N1 avian influenza replicates deep in the lung and cause pneumonia, which may lead to respiratory failure and death. In addition, he studied viral adaptation to human host. If the virus adapts itself to an efficient transmission among humans, a deadly pandemic will occur. One of the adaptation mechanisms is the changes in receptor usage. He identified a mutation that can cause this adaptive change in the viral receptor usage. The data provide a genetic marker for a more efficient survey of a potentially pandemic virus. In addition to the study of viral mutants, he also studied viral sequences from human tissues at a quasispecies level. With bioinformatics analyses, positive selection sites in the viral genome could be identified. This helps to understand the mechanism of viral adaptation to human host.

Because the incomplete adaptation to human host H5N1 avian influenza virus infects human inefficiently and some host factors are believed to be involved. It was observed that many heavily exposed individuals did not get infected while some patients did not have clear history of exposure. This makes most researchers believe that some individuals are more susceptible to the infection because of certain specific host factors. In order to explore this hypothesis, level of sialic acid in human upper airway was studied. It was found that the level of enzyme responsible for the synthesis of sialic acid in human upper airway was highly variable. Furthermore, the level of sialic acid of both the types that are receptor for human and avian
Influenza viruses is increased in nasal polyp, an allergic nasal condition. The increased sialic acid correlated with higher susceptibility to influenza infection in vitro. This indicates that allergic and inflammatory conditions can affect sialic acid expression and susceptibility to influenza infection. And, for avian influenza, this may help to explain why some individuals are more susceptible to the infection.

In addition, he conducted epidemiological studies in order to understand the perpetuation of virus in the repeated outbreak area. By studying heterogeneity of viral sequences, molecular epidemiological analyses indicated that viral reservoir in the area is small, probably small enough to make eradication possible, and that there was constantly exchanges of viral genetic material by reassortment.

Because of the influenza 2009 pandemic, most of the research activities are now addressing pathogenesis of the pandemic influenza, especially in some patients with severe pneumonia. An ongoing research project has discovered that the pandemic influenza is resistant to an innate antiviral mechanism in the lung. This may lead to a better therapeutic strategy.

In addition, he is also involved in epidemiological studies of the influenza pandemic using novel techniques, such as community survey using questionnaire and mathematical modeling, in order to get a better understanding of the nature of influenza outbreaks and to develop tools for future use in outbreak characterization, prediction and control.

In addition to the research activity, Prof. Prasert Auewarakul has also played important roles in promotion of research as an executive. He served as Deputy Dean for Research at the Faculty of Medicine Siriraj Hospital in 2005-2007, and now as the director of the Institute of Molecular Biosciences at Mahidol University. He also plays important roles in various academic societies, he served as the president of the Virology Association (Thailand) during 2008-2009. And, he cofounded the Biosafety and Biosecurity Network of Thailand, and has been the chairman of network since its establishment in 2008.

Prof. Sukhathida Ubol

Research interests

- Molecular pathogenesis of viral infection using dengue virus, avian H5N1 virus and Chikungunya virus as models
- Viral prevention focusing on development of viral nanovaccine

Current Research

Currently, our group is able to elucidate the molecular mechanism of intrinsic antibody-dependent enhancement of infection in dengue virus model. The obtained information serves as a stone step for our group to move forward to vaccine development.

Current Funding

1. Determinants for chikungunya virus induced arthritis: funded by NSTDA
2. Understanding the mechanism of dengue virus attenuation: funded by EID program, BIOTEC

Representative publications (1999 - present)

Halstead SB, Mahalingam S, Marovich M, Ubol S and Moser D. Intrinsic antibody-dependent enhancement of microbial

Ubol S and Halstead SB. How innate immune mechanisms contribute to antibody-enhanced viral infections. CVI (in press)

Modhiran N, Kalayanarooj S and Ubol S. Subversion of innate defenses by the interplay between DENV and pre-existing enhancing antibodies: TLRs signaling collapse. PLoS Negl Trop Dis (in press)


Reference: [http://www.sc.mahidol.ac.th/scmi/sukathida.htm](http://www.sc.mahidol.ac.th/scmi/sukathida.htm)

**Associate Professor Dr. Panisadee Avirutnan**

- **Specialty:** Immunology-Complement Biology, Dengue Virus, Viral Immune Evasion
- **Position:** Head, Division of Dengue Hemorrhagic Fever Research
- **Qualification & Education:**
– B.Sc. in Medical Science (Mahidol University)

– M.D. (Mahidol University)

– Ph.D. in Microbiology (Mahidol University)

– Postdoctoral fellow in Immunology and Pathology (Washington University School of Medicine, St. Louis, USA)

**Areas of Interest:** Dengue Pathogenesis, Complement Evasion by Viruses

**Positions and Employment**

2001-2002 Internship, Makarak Provincial Hospital, Kanchanaburi, Thailand

2002-2005 Lecturer, Department of Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

2006- Assistant Professor, Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

2006-2011 Postdoctoral Research Associate, Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA

2010- Head of Dengue Hemorrhagic Fever Research Unit, Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

**Other Experience and Professional Memberships**

2001- Member, Medical Council of Thailand

2001- Member, Allergy and Immunology Society of Thailand

2001- Program Committee of Immunology Curriculum, Department of Immunology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

2001- Member, Siriraj Medical Alumni Association

2002- Member, Virology Association (Thailand)

2003- Member, Infectious Disease Association of Thailand
2012- Member, Mahidol University Alumni Association

Honors

2007 Excellent Research Work Award, National Research Council of Thailand: “Researches indengue hemorrhagic fever and dengue virus”

2007 Mahidol University Award for Research: “Vascular leakage in severe dengue infections: a potential role for the nonstructural protein NS1 and complement”

2008 Outstanding Employee Award, Faculty of Medicine Siriraj Hospital, Mahidol University

2011 Certificate of Commendation, Medical Association of Thailand

Selected Peer-reviewed Publications


**Patents**


- The use of NS1 protein together with terminal complement complex SC5b-9 for the detection of dengue fever and prediction of dengue hemorrhagic fever. June 2006. No. 10 2006 000 305.5 Germany

- Determination of risk of developing dengue hemorrhagic fever/dengue shock syndrome, methods and compositions therefore. June 2006. No. 11/764, 019 USA
Ongoing Research Support

• Thailand Research Fund (TRF); Avirutnan (PI); June 2013-May 2016. Roles of the complement system in the infectivity/neutralization, viral trafficking and activation of human peripheral blood cells during dengue virus infection in patients with different clinical severity. Role: PI

• Cluster and Program Management Office, National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand; Avirutnan (PI); June 2013-May 2014. Searching for correlate of protection against Dengue hemorrhagic fever: Impact of complement on neutralization and enhancement of anti-dengue antibodies. Role: PI

• Cluster and Program Management Office, National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand; Noisakran (PI); June 2013-May 2014. Searching for Correlate of Protection against Dengue Hemorrhagic Fever: Anti-Dengue Virus NS1 Antibody Assay. Role: Co-PI

• Siriraj Grant for Research Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand; Avirutnan (PI); February 2013-August 2014. Study of biochemical and functional properties of secreted mosquito cell-derived dengue nonstructural protein NS1 and its role in dengue pathogenesis. Role: PI

• Mahidol University, Thailand; Avirutnan (PI); 2010-1013. Roles of microparticles in dengue pathogenesis. Role: PI

Completed Research Support

• National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand; Puttikhunt (PI) 2007- 2008. Development of an enzyme-linked immunosorbent assay for identification of serotype-specific dengue NS1 antigen in dengue patient sera. The goal of this project was to develop serotype-specific dengue NS1 ELISA as a diagnostic tool to define serotype of dengue virus in clinical specimens. Role: Co-PI

• Thailand Research Fund (TRF) & National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand; Avirutnan (PI); 2004-2008. Dengue nonstructural protein-1 (NS1) and its contribution to the immunopathogenesis of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). Role: PI

• Siriraj Grant for Research Development and Medical Education, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand; Avirutnan (PI); 12/01/03-06/31/05. Development of new focus reduction neutralization test (FRNT) for the determination of neutralizing antibody to dengue and Japanese encephalitis virus. The goal of this project was to develop a high-throughput focus reduction neutralization test (FRNT) to determine neutralizing antibody titers against dengue and Japanese encephalitis viruses. Role: PI

Dr. Sansanee Noisakran

Current position: Senior Researcher at National Center for Genetic Engineering and Biotechnology, National Science and
Technology Development Agency Thailand

Education

1990-1994 Undergraduate, B.Sc. (Medical Technology) (Hon), Mahidol University, Bangkok, Thailand

1995-1997 Graduate, M.Sc. (Virology/Immunology), Louisiana State University Medical Center (LSUMC), New Orleans, LA, USA

1997-2000 Graduate, Ph.D. (Virology/Immunology), Louisiana State University Health Sciences Center (LSUHSC), New Orleans, LA, USA

Research training

1997-1999 Graduate student, Department of Microbiology, Immunology, and Parasitology, LSUHSC, New Orleans, LA, USA

Mentor: Daniel J.J. Carr, Ph.D., Professor

1999-2000 Graduate student, Department of Ophthalmology, Dean A. McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

Mentor: Daniel J.J. Carr, Ph.D., Professor

2000-2001 Postdoctoral fellow, Department of Microbiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Research Topic: Manipulation of full-length infectious dengue cDNA clone (DENV-2, strain 16681) Site-directed mutagenesis and characterization of dengue virus mutants in vitro Establishment of an in vitro stable transfection system for expression of dengue viral proteins

Supervisor: Nopporn Sittisombut, M.D., Ph.D., Associate Professor

2005 Postdoctoral fellow, Department of Immunoregulation, Research Institute for Microbial Diseases (BIKEN), Osaka University, Osaka, Japan.

Research Topic: Biochemical analysis of glycosylphosphatidylinositol linkage of dengue virus NS1 protein

Supervisor: Taroh Kinoshita, Ph.D., Professor

2008-2010 Research Associate, Department of Pathology and Laboratory Medicine and Emory Vaccine Center, Emory University, Atlanta, GA, USA.

Research Topic: Investigation of dengue virus infection in a non-human primate model

Supervisor: Guey Chuen Perng, Ph.D., Associate Professor
Appointments

1996-1999 Laboratory Instructor, Medical Microbiology, LSUMC, New Orleans, LA
Lecturer, Nursing Microbiology, LSUMC, New Orleans, LA

2008-2010 Research Associate, Department of Pathology and Laboratory Medicine and Emory Vaccine Center, School of Medicine, Emory University

2000-present Researcher, Medical Biotechnology Unit, National Center for Genetic Engineering and Biotechnology, Thailand

2005-present Special lecturer, Department of Immunology, Faculty of Medicine Siriraj Hospital, Mahidol University

Awards

1990-1994 First class honors (Silver Medal), Faculty of Medical Technology, Mahidol University, Bangkok, Thailand

1994-1995 Full scholarship for a master's degree program in Thailand from National Sciences and Technology Development Agency (NSTDA), Thailand

1995-2000 Full scholarship for an international graduate program (M.Sc. and Ph.D.) from National Center for Genetic Engineering and Biotechnology, Thailand

1997 Neuroscience travel award, LSUMC, New Orleans, LA, USA 1998 Travel award for the Fifth International Congress, International Society of Neuroimmunology, Montreal, Canada

1998 Second place for poster presentation, LSUMC, New Orleans, LA, USA

1999 Second place for platform presentation, LSUMC, New Orleans, LA, USA

2000 Chancellor's award, LSUHSC, New Orleans, LA, USA

2005 Travel scholarship from the Regional Emerging Diseases Intervention (REDI) Centre for the 2nd Asian Regional Dengue Research Network Meeting, Singapore

2007 Travel scholarship for the 3rd Asian Regional Dengue Research Network Meeting, Taipei, Taiwan

2009 Robert E. Shope International Fellowship in Infectious Diseases from American Society of Tropical Medicine and Hygiene

2012 L’Oréal (Thailand) For Woman in Science 2012 fellowship

Research Grants

2001-2003 Principle Investigator Title: Utilization of human cell lines stably expressing various forms of dengue NS1 protein to
study contributions of NS1 in dengue virus infection Funded by: Thailand Tropical Diseases Research Programme (T2)

2003-2005 Co-investigator Title: Study of interactions between dengue viral non-structural protein 1 and human host cellular proteins Funded by: Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

2004-2006 Principle Investigator Title: Generation and characterization of dengue virus NS1 N-linked glycosylation site mutants Funded by: National Center for Genetic Engineering and Biotechnology, Thailand

2004-2006 Co-investigator Title: Interaction cloning of NS1-BP (NS1 binding protein), a human protein that binds to non-structural NS1 protein of dengue virus Funded by: Thailand Research Fund

2006-2009 Co-investigator Title: Biochemical analysis of glycosylphosphatidylinositol linkage of NS1 in dengue virus infection Funded by: Thailand Research Fund

2007-2008 Co-investigator Title: Antiviral efficacy of plant extracts against dengue virus infection Funded by: A private company in the U.K.

2011-2014 Principle Investigator Title: Human Host Cellular Protein System Interacting with the Dengue Virus NS1 Protein Funded by: Thailand Research Fund and National Center for Genetic Engineering and Biotechnology

2012-2015 Co-investigator Title: Molecular Targeted Therapy to Alleviate Dengue Virus-Induced Liver Injury Funded by: Mahidol University


2014-2015 Principle Investigator Title: Establishment of dengue viral translation assay for potential application in anti-viral drug screening against dengue virus infection Funded by: Asia Research Center under collaboration between Chulalongkorn University and the Korea Foundation for Advanced Studies

2014-2017 Co-investigator Title: Project title: Targeting Intracellular Membrane Trafficking to Combat Dengue Virus Funded by: Thailand Research Fund

2014-2017 Co-investigator Title: Project title: Systematic identification of Inhibitors against Dengue Virus from US FDA-Approved Drug Library Funded by: Mahidol University

Dr. Thaneeya Roytrakul

EDUCATION

specific T lymphocytes in Thai population.

Supervisors: Professor G.R. Screaton and Professor Andrew McMichael

Thai government scholarship fund

1995-1997 Biochemistry, faculty of Science, Mahidol University, Bangkok, Thailand MSc Biochemistry: RFLP analysis of rifampicin resistant M. tuberculosis in Thailand.


WORK EXPERIENCES

11/06 – 02/07 Department of Immunology, Imperial College London, UK

Postdoctoral researcher

Project: Study of T cell responses in Dengue virus infection.

1998-2000 Medical Biotechnology Unit

National Center for Genetic Engineering and Biotechnology (BIOTEC),

National Science and Technology Development Agency (NSTDA) Thailand

Research assistant in the project involving techniques in cell culture (virus, hybridoma, endothelial cells), hybridization (in situ and dot blot), monoclonal antibody production (small and medium scale), and ELISA.

1996-1997 Teacher assistant in Biochemistry courses for students in faculty of Sciences and faculty of Clinical medicine at Mahidol University. Experiment demonstration, collection and checking the paper exam.

RESEARCH INTERESTS

- T cell responses in virus infection

- Pathogenesis of Dengue Hemorrhagic Fever (DHF)

HONORS AND AWARDS

2001-2004 Thai government scholarship
Grants

2010-2013 Co-investigator of grant from National Research University (to Dr. Juthathip Mongkolsapaya) on “Immunological study of dengue infected subjects” supported by National Research Council of Thailand

2011-2012 Principle investigator of grant from National Science and Technology Development Agency on “Detection of anti-dengue virus envelope domain III antibodies” supported by Cluster and Programme Management, NSTDA

2012-2013 Principle investigator of grant from National Science and Technology Development Agency on “Searching for correlate of protection against Dengue hemorrhagic fever: Detection of Dengue virus envelope domain III specific antibody” supported by Cluster and Programme Management, NSTDA

2014-2015 Principle investigator of grant from National Science and Technology Development Agency on “Searching for correlate of protection against Dengue hemorrhagic fever: Development of Dengue virus specific antibody-dependent-cell cytotoxicity (ADCC) antibody assay” supported by Cluster and Programme Management, NSTDA

PUBLICATIONS


PRESENTATIONS

May 2009 Attended the 5th Congress of Asian Society for Paediatric Research organised by Chinese Paediatric Society, Chinese Medical Association at Hangzhou, China (poster presentation)

August 2007 Attended the 3rd Asian Regional Dengue Research Network meeting organised by Paediatric Dengue Vaccine Initiative (PDVI) at Taipei, Republic of China (poster presentation).

December 2003 Attended the Immunology conference organised by the British Society of Immunology (BSI) at Harrogate, UK. (poster presentation).