## BIOGRAPHICAL SKETCH

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| NAME | POSITION TITLE |
|---|---|
| Wang, Wei-Kung | Professor, Department of Tropical Medicine, Medical Microbiology and Pharmacology |
| eRA COMMONS USER NAME<br>wangwk | |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| National Taiwan University, College of Medicine, Taipei, Taiwan | M.D. | 1986 | Medicine |
| Harvard School of Public Health, Boston, Massachusetts | Sc.D. | 1995 | Virology |

### A. Personal statement

While considerable efforts have been devoted to identifying targets for the antiviral drugs against flaviviruses, including dengue virus (DENV), West Nile virus (WNV), Japanese encephalitis virus (JEV), and yellow fever virus (YFV), no such treatments are currently available. Most of the drug targets explored to date focused on blocking RNA replication. However, growing evidence suggests that the stem region of the envelope (E) protein is involved in entry and assembly steps of flavivirus life cycle. This stem region contains several highly conserved residues in diverse flaviviruses. We hypothesized that the highly conserved residues in the stem region play important roles in these steps. We will explore the stem region of DENV and other medically important flaviviruses as novel targets for antivirals. Dr. Wei-Kung Wang, who received an M.D. from the National Taiwan University and Sc.D. in virology from Harvard School of Public Health, has the requisite training, expertise and leadership for the proposed research. Previously, he demonstrated that the level and rate of decline of DENV load and virus-containing immune complexes correlated with disease severity, and reported for the first time the quasispecies nature of DENV in humans and mosquitoes. His lab has focused on the precursor membrane (prM)/E protein of DENV in the past and discovered the ER retention signal as well as critical elements of the DENV E protein. Recently, his lab reported that C-terminal helical domain of the prM protein is involved in assembly and entry of DENV. These studies, which involved virus-like particles (VLPs) and replicon particles, laid the groundwork and techniques for exploring the functions of stem region.

### B. Positions and Honors

Positions and Employment

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| 1995-1997 | Research Associate, Department of Cancer Biology, Harvard School of Public Health, Boston, Massachusetts |
| 1997-1998 | Research Associate, Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, Massachusetts |
| 1998-2001 | Assistant Professor, Institute of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan |
| 2001-2006 | Associate Professor, Institute of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan |
| 2006-2009 | Professor, Institute of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan |
| 2009- | Adjunct Professor, Institute of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan |
| 2009-2011 | Associate Professor, Department of Tropical Medicine, Medical Microbiology and Pharmacology, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, Hawaii |
| 2011- | Professor, Department of Tropical Medicine, Medical Microbiology and Pharmacology, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, Hawaii |

Other Experience and Professional Memberships

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| 1985-1986 | Intern, National Taiwan University Hospital, Taipei, Taiwan |
| 1987-1990 | Resident, Department of Medicine, Veterans General Hospital, Taipei, Taiwan |
| 1990-1995 | Fogarty Research Fellow and Graduate Student with Professor Max Essex, Department of Cancer Biology, Harvard School of Public Health, Boston, Massachusetts |
| 1990- | Board Certificate, Taiwan Society of Internal Medicine |
| 2002-2005 | Directorate Committee, Taiwan Society of Microbiology |
| 2003- | Infectious Disease Specialist, Infectious Diseases Society of Taiwan |
| 2009- | Member, American Society for Microbiology Hawaii Branch |
| 2010- | Member, American Society for Microbiology |
| 2011- | Member, American Society of Tropical Medicine and Hygiene |
| 2014- | Travel Award Committee, American Society of Tropical Medicine and Hygiene |

Honors

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|---|---|
| 1999 | Research Award, National Science Council, Taiwan |
| 2001 | Medical Virology Club, Travel Grant Award, American Society for Virology |
| 2002 | Travel Award, American Society of Tropical Medicine and Hygiene, 51st Annual Meeting |
| 2004 | Annual Excellent Article Award, Taiwan Society of Microbiology |
| 2004 | Research Award, National Taiwan University |

Patents

U.S. Patent “Viral Entry of Target Cell” Application No.: 09/302,672

U.S. Patent “Detection of dengue virus” Application No.: 10/085,944, Patent No.: US 7,041,255B2

Professional Activities

Grant Review:

Reviewer, Microbiology BSc 1 Committee, American Heart Association (Mar. 2014)
Reviewer, Special emphasis panel, Cooperative Centers on Human Immunology (U19), NIAID, NIH (Jan. 2014)
Reviewer, Transformative Research Award Special emphasis panel, NIAID, NIH (Feb. 2014)
Reviewer, Defense Threat Reduction Agency basic Research Program (Jul. 2011)

Editorial Board:

Journal of Tropical Diseases & Public Health (2012 – present)
Journal of Biowar and Defense (2013 – present)

Ad hoc Reviewer:

Journal of Virology, Virology, Journal of General Virology, PLoS Pathogens, Emerging Infectious Diseases, Clinical Infectious Diseases, Journal of Molecular Biology, Antiviral Research, Virus Research, Trends in Microbiology, Journal of Virological Methods, Journal of Biomedical Science, Archives of Medical Research, Journal of Microbiology, Immunology and Infection, and Tropical Medicine and International Health.

**C.Selected Peer-Reviewed Publications** (from 49 peer-reviewed publications)

Most relevant to the current application


1. Lai CY, Tsai WY, Lin SR, Kao CL, Hu SP, King CC, Wu HC, **Wang WK.** 2008. Antibodies to envelope glycoprotein of dengue virus during the natural course of infection are predominantly cross-reactive and recognize epitopes containing highly conserved residues at the fusion loop of domain II. J Virol 82:6631-6643.
2. Hsieh SC,Tsai WY, **Wang WK.** 2010. The length and non-hydrophobic residues in transmembrane domain of dengue virus envelope protein critical for its retention and assembly in endoplasmic reticulum J Virol 84:4782-4797.
3. Lin SR, Zou G, Hsieh SC, Qing M, Tsai WY, Shi PY, **Wang WK.** 2011. The stem region of envelope protein of dengue virus is involved in virus assembly and entry. J Virol 85:5159-5171.
4. Hsieh SC, Zou G, Tsai WY, Qing M, Chang GJ, Shi PY, **Wang WK.** 2011. The C-terminal helical domain of dengue virus precursor membrane protein is involved in virus assembly and entry. Virology 410:170-180.
5. Tsai WY, Hsieh SC, Lai CY, Lin HE, Nerurkar VR, **Wang WK.** 2012. The C-terminal helical domains of dengue virus type 4 E protein affect the expression/stability of prM protein and conformation of prM and E proteins. PLoS One 7:e52600.


Additional recent publications of importance to the field (in chronological order)

1. **Wang WK**, Dudek T, Zhao YZ, Brumblay HG, Essex M, Lee TH. 1998. CCR5 co-receptor utilization involves a highly conserved arginine of human immunodeficiency virus type 1 gp120. Proc Natl Acad Sci USA. 95:5740-5745.
2. **Wang WK**, Dudek T, Essex M, Lee TH. 1999. Hypervariable region 3 residues of HIV type 1 gp120 involved in CCR5 coreceptor utilization: therapeutic and prophylactic implication. Proc Natl Acad Sci USA. 96:4558-4562.
3. **Wang WK**, Lin SR, Lee CM, King CC, Chang SC. 2002. Dengue-3 virus in plasma is a population of closely related genomes: quasispecies. J Virol 76:4662-4665.
4. Lin SR, Hsieh SC, Yueh YY, Lin TH, Chao DY, Chen WJ, King CC, **Wang WK.** 2004. Study of sequence variation of dengue-3 virus in naturally infected mosquitoes and human hosts: implications for transmission and evolution. J Virol 78:12717-12721.
5. **Wang WK,** Chen HL, Yang CF, Hsieh SC, Juan CC, Chang SM, Yu CC, Lin LH, Huang JH, King CC. 2006. Slower rates of clearance of viral load and virus-containing immune complexes in patients with dengue hemorrhagic fever. Clin Infect Dis 43:1023-1030.
6. Hsieh SC, Liu IJ, King CC, Chang GJ, **Wang WK.** 2008. A strong signal for retention in the endoplasmic reticulum in the stem-anchor region of envelope glycoprotein of dengue virus type 2 affects the production of subviral particles. Virology 374:338-350.
7. de Alwis R, Beltramello M, Messer WB, Sukupolvi-Petty S, Wahala WM, Kraus A, Olivarez NP, Pham Q, Brian J, Tsai WY, **Wang WK**, Halstead S, Kliks S, Diamond MS, Baric R, Lanzavecchia A, Sallusto F, de Silva AM. 2011. In-depth analysis of the antibody response of individuals exposed to primary dengue virus infection. PLoS Negl Trop Dis 5:e1188.
8. Lin HE, Tsai WY, Liu IJ, Li PC, Liao MY, Tsai JJ, Wu YC, Lai CY, Lu CH, Huang JH, Chang GJ, Wu HC, **Wang WK.** 2012. Analysis of epitopes on dengue virus envelope protein recognized by monoclonal antibodies and polyclonal human sera by a high throughput assay. PLoS Negl Trop Dis 6:e1447.
9. Tsai WY, Lai CY, Wu YC, Lin HE, Edwards E, Jumnainsong A, Kliks S, Halstead S, Mongkolsapaya J, Screaton GR, **Wang WK.** 2013. High avidity and potent neutralizing cross-reactive human monoclonal antibodies derived from secondary dengue virus infection. J Virol. 87:12562-12575.
10. Lai CY, Williams KL, Wu YC, Knight S, Balmaseda A, Harris E, **Wang WK.** 2013. Analysis of cross-reactive antibodies recognizing the fusion loop of envelope protein and correlation with neutralizing antibody titers in Nicaraguan dengue cases. PLoS Negl Trop Dis. 7:e2451.

**D. Research Support**

Ongoing Research Support

8P20GM103516-08 Yanagihara (PI) 09/30/2003 – 06/30/2015
NIH/NIGMS
Pacific Center for Emerging Infectious Disease Research
Project 1: Stem Region of Envelope Protein of Dengue Virus and Re-emerging Flaviviruses
The objective of the project is to explore the stem region of the E protein of dengue virus and other disease-causing flaviviruses as novel targets for the development of antiviral compounds.
Role: Project Investigator

R01 AI110769-01 Wang (PI) 04/01/2014 – 03/31/2019
NIH/NIAID
Mature virus-like particles as a new strategy for dengue virus vaccines
The objective of the project is to investigate the superiority of mature dengue virus-like particles over mixed particles as dengue vaccines.
Role: Principal Investigator

Completed Research Support

Cooperative Research Agreement Wang (PI) 04/01/2010 – 12/31/2010
International Vaccine Institute/Pediatric Dengue Vaccine Initiative (IVI/PDVI)
ELISA Based Assay for Detection of Neutralizing Antibodies in Polyclonal Dengue Antisera
The main objective of this project is to develop a prototype VLPs-capture ELISA to detect neutralizing antibodies in polyclonal human sera after dengue virus infection or vaccination.
Role: Principal Investigator

NSC95-2320-B-002-084-MY3 Wang (PI) 08/01/2006 – 07/31/2009
National Science Council, Taiwan
Development of Dengue Reporter Viruses to Study the Phenotypic Properties of the Precursor Membrane (PrM)/E Proteins of Four Serotypes of Dengue Viruses from the Field
The overall goal of this project is to establish a pseudotype reporter viral system for four serotypes of dengue virus by using the luciferase reporter gene in lentiviral vector and to employ it to study the function of PrM/E proteins of dengue viruses in the field.
Role: Principal Investigator

NSC96-3112-B-002-038 Wang (PI) 05/01/2007 – 04/30/2009
National Science Council, Taiwan
Study of the Roles of Heparin/Heparan Sulfate Interacting Protein (HIP) in the Entry of Dengue Virus
The objective of this project is to study a candidate cellular protein, HIP, involved in the entry of dengue virus. Since heparan sulfate has been shown as attachment factor for dengue virus, the role of HIP, which was discovered by cDNA substraction of two clones of 293T cells with different susceptibility to dengue virus infection, was investigated.
Role: Principal Investigator

NSC95-2745-B-002-007 Wang (PI) 08/01/2006 – 07/31/2009
National Science Council, Taiwan
Rapid Detection and Quantification of Type A Influenza Viruses During the Course of Infection
The main objective of this project is to establish a quantitative RT-PCR assay for rapid detection, quantification and typing of influenza A virus in clinical samples during the course of infection.
Role: Principal Investigator