BIOGRAPHICAL SKETCH

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NAME: PENGHUA WANG

eRA COMMONS USER NAME (credential, e.g., agency login): PENGHUAWANG

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Sun Yat-sen University, Guangzhou, China	B.S	07/1992	Biochemistry
The National University of Singapore, Singapore	PHD	04/2006	Biochemistry & Molecular Biology
Yale University School of Medicine, CT, USA	Postdoc	06/2009	Immunology & Virology

A. Personal Statement

I am primarily interested in host-pathogen interactions, with a focus on RNA viruses in vivo and in vitro. Specifically, I attempt to understand pathogenic mechanisms of viral infection at the cellular and animal levels, and study the molecular function of host genes that influence viral pathogenesis and the disease outcomes. On the host end, I am keen on the innate immune system, detection of viruses and initiation of innate antiviral immune responses. On the viral end, I hope to understand the mechanisms of immune evasion and modulation of cellular functions by viral proteins.

- Jinzhu Ma, Harshada Ketkar, Tinting Geng, Emily Lo, Leilei Wang , Juemin Xi, Qiangming Sun, Zhanbo Zhu, Yudong Cui, Long Yang, Penghua Wang. Zika virus nonstructural protein 4A blocks the RLR-MAVS signaling. ***Frontiers in Microbiology***, doi: 10.3389/fmicb.2018.01350.
- Long Yang, Guang Yang, Leilei Wang, Shuang Cui, Harshada Ketkar, Dana Mordue, Toyoshi Fujimoto, Gong Cheng, Fuping You, Rongtuan Lin, Erol Fikrig, Penghua Wang. UBXN3B positively regulates STING mediated antiviral immune responses. ***Nat Commun***, DOI: 10.1038/s41467-018-04759-8.
- Penghua Wang, Shu Zhu, Long Yang, Shuang Cui, Wen Pan, Ruaidhri Jackson, Yunjiang Zheng, Anthony Rongvaux, Qiangming Sun, Guang Yang, Shandian Gao, Rongtuan Lin, Fuping You, Richard Flavell, Erol Fikrig. Nlrp6 regulates intestinal antiviral innate immunity. ***Science*** 2015. 350: 826-830.
- Shu Zhu, Siyuan Ding, Penghua Wang, Zheng Wei, Yi Yang, Geng Wang, Xuqiu Lei, Wen Pan, Noah W. Palm, Marcel de Zoete, Yujiao Zhao, Hua Yu, Kellie Jurado, Yunjiang Zheng, Jun Zhao, Ningguo Feng, Liang Shan, Yuval Kluger, Jun Lu, Clara Abraham, Erol Fikrig, Harry B. Greenberg, Richard A. Flavell. Nlrp9b inflammasome recognizes and restricts rotavirus infection in intestinal epithelial cells. ***Nature***. 2017 Jun 29;546(7660):667-670.

B. Positions and Honors

Positions and Employers

1992-1998: Research and Development Engineer and Manager, Haifeng Pharmaceuticals Co. Lt, Shandong, China
1998-2000: Production Engineer, Klenco (s) Pte Ltd, Singapore
2001-2006: Research Associate, Department of Biochemistry, the National University of Singapore, Singapore

2006-2009: Postdoctoral Associate, Internal Medicine, Yale University School of Medicine, New Haven, CT
2009-2015: Associate Research Scientist, Internal Medicine, Yale University School of Medicine, New Haven, CT
2015- : Adjunct Professor, Internal Medicine, Yale University School of Medicine, New Haven, CT
2015-2018: Assistant Professor, Department of Microbiology & Immunology, New York Medical College, Valhalla, NY
2018- : Assistant Professor, Department of Immunology, the University of Connecticut Health Center, Farmington, CT

Other Experience

Editor/Associate Editor

2015-present: Associated Editor, *Frontiers in Cellular and Infection Microbiology*, *Frontiers in Virology*
2018.1-2020.12: Member of Editorial Board of *Antimicrobial Agents and Chemotherapy,* American Society of Microbiology

***Ad hoc* Reviewer**

2008-present: ad hoc reviewer for PLoS Neglected Tropical Diseases, PLoS ONE, Progress in Neurobiology, Neuroscience, Arthritis & Rheumatism, Antimicrobial Agents and Chemotherapy, Scientific Reports, Cellular Immunology, Biochimica et Biophysica Acta, Journal of Virology, Autophagy

Participation on NIH study panels/others

2016/10: ZAI1 BLG-M (J2) Center of Human Tissue Models for Infectious Diseases (U19)
2016/08, 2017/05, 2018/01, 2018/05: ZRG1 IDM-V-12 & 81, Non-HIV Infectious Agent Detection/Diagnostics, Food Safety, Sterilization/Disinfection and Bioremediation Special Emphasis Panel,
2018/06: VIRB
2014-present: Hongkong Health and Medical Research Fund (HMRF)

Peer-Reviewed Presentations & Symposia Given at Meetings:

2016: Keystone Meeting on RNA viruses, Poster, Austin, USA
2015: American Society for Virology, Selected Oral Speaker, USA
2010: Dengue Workshop, Pacific Northwest Regional Center of Excellence, NIAID
2010: Howard Hughes Medical Institute Scientific Meeting on Inflammation, Innate Immunity and Infectious Diseases. Poster presentation.
2008: 6th Annual ASM Biodefense and Emerging Diseases Research Meeting, oral presentation
2008-2014: NIAID Immune Function and Biodefense in Children, Elderly, and Immunocompromised Populations Annual Meeting. Poster presentation.
2009: Northeast Biodefense Center Annual Meeting. Poster presentation.

Professional Memberships

2015-present: Member, American Society for Virology

Honors

2010: Travel award, NIAID Dengue Virus Workshop, Portland, Oregon
2009: Best Poster Award at Northeast Biodefense 2009 Annual Meeting
2009: Northeast Biodefense Center, Career Development Award (2009-2011)
2001: National University of Singapore Research Graduate Scholarship (2001-2005)
1990: Sun Yat-sen University Scholarship for Outstanding Students
1989: Sun Yat-sen University Scholarship for Outstanding Students

C. Contributions to Science

1. **Cholesterol homeostasis**. During the candidature of my Ph.D. studies, I studied intracellular cholesterol metabolism and membrane trafficking through biochemical, genetic, molecular, and cell biological approaches. The mechanisms underlying cholesterol biosynthesis and uptake are well understood, however, intracellular cholesterol homeostasis and transport between membrane compartments are less clear. A large family of conserved proteins, oxysterol binding protein (OSBP),

plays an important role in maintaining cholesterol homeostasis, but is poorly characterized. Using the unicellular eukaryote yeast, I found that yeast OSBPs are directly involved in cholesterol homeostasis, probably vesicle-independent cholesterol transport. Furthermore, for the first time, I discovered that OSBPs both physically and functionally interact with a subfamily of AAA ATPases, and these proteins function together to regulate cholesterol transport.

- Penghua Wang, Wei Duan, Alan L. Munn and Hongyuan Yang. Molecular Characterization of Osh6p, an Oxysterol Binding Protein Homolog in the Yeast *Saccharomyces cerevisiae.* ***FEBS J****.* 2005, 272: 4703-15.
- Penghua Wang, Yong Zhang, Hongzhe Li, Hai Kee Chieu, Alan L. Munn and Hongyuan Yang. AAA ATPases Regulate Membrane Association of Yeast Oxysterol Binding Proteins and Sterol Metabolism. ***EMBO J****.* 2005, 24: 2989-2999. PMCID: PMC1201346

2. **Pathogenesis of Lyme arthritis**. Lyme disease is caused by a spirochete, *B. burgdorferi*, which displays differential gene expression patterns during its life cycle, tick-mammal-tick. During my postdoctoral training, I found that the bacterium also changes its gene expression profile in different organs, which may facilitate bacterial colonization and survival. Specifically, I found that two genes, *bmpA* and *bmpB*, are preferentially expressed in joints compared with other tissues. This joint-specific expression pattern correlates with the bacterium's ability to colonize and elicit arthritis. This finding highlights the complex strategies that *B.burgdorferi* uses to adapt to different tissue environments and thus provides us with new measures to prevent Lyme arthritis.

   - Pal U, Wang P (co-first), Bao F, Yang X, Samanta S, Schoen R, Wormser GP, Schwartz I, Fikrig E. Borrelia burgdorferi basic membrane protein BmpA/B are critical for Lyme arthritis. ***J. Exp. Med***. 2008, 205(1): 133-41. PMCID: PMC2234379.
   - Jianfeng Dai, Penghua Wang, Sarojini Adusumilli, Carmen Booth, Justin D. Radolf, Sukanya Narasimhan, Juan Anguita, and Erol Fikrig. Antibodies against a tick protein, Salp15, protect mice from the Lyme disease agent. ***Cell Host & Microbe*** 2009, 6(5):482-92.
   - Joppe W.R. Hovius, Maarten F. Bijlsma , W. Joost Wiersinga, Gerritje J van der Windt, Bas Boukens , Jeroen Coumou, Anneke Oei, Regina de Beer, Alex F. de Vos, Cornelius van 't Veer, Alje P. van Dam, Penghua Wang, Erol Fikrig, Marcel M. Levi, Joris J. Roelofs, Tom van der Poll. The Urokinase receptor (uPAR) Facilitates Clearance of *Borrelia burgdorferi*. ***PLoS Pathogen*** 2009, 5(5):e1000447.
   - Yang X, Izadi H, Coleman AS, Wang P, Ma Y, Fikrig E, Anguita J, Pal U. Borrelia burgdorferi lipoprotein BmpA activates pro-inflammatory responses in human synovial cells through a protein moiety. **Microbes Infect**. 2008,10(12-13):1300-8.

3. **Pathogenesis of flaviviral diseases**. The *Flaviviridae* family consists of a large number of ssRNA viruses that cause fatal human diseases. For example, West Nile virus (WNV) is the culprit of over 20,000 of encephalitis/meningitis cases and 1,700 deaths since 1999. I attempt to identify novel host factors that restrict or facilitate viral pathogenesis *in vivo* and *in vitro*. These factors may be regulators of host antiviral immune pathways or important factors of viral life cycle including surface receptors mediating viral entry. Understanding the molecular mechanisms underlying the pathogenesis of these disease conditions and virus specific host immune response can advance the development of specific antiviral therapeutics and vaccines.

   - Liu Y, Liu J, Du S, Shan C, Nie K, Zhang R, Li XF, Zhang R, Wang T, Qin CF, Wang P, Shi PY, Cheng G. Evolutionary enhancement of Zika virus infectivity in Aedes aegypti mosquitoes. ***Nature***. 2017 May 25;545(7655):482-486.
   - Leilei Wang, Long Yang, Erol Fikrig, Penghua Wang. An essential role of PI3K in the control of West Nile virus infection. ***Sci Rep***. 2017 Jun 16;7(1):3724.
   - Penghua Wang (correspondence author), Fengwei Bai , Lauren A. Zenewicz, Jianfeng Dai, Long Yang, David Gate, Eric Cheng, Richard A. Flavell, Terrence Town, Erol Fikrig. IL-22 contributes to West Nile virus encephalitis via neutrophils. ***PLoS ONE*** 2012, 7(8): e44153. PMICD: PMC3429482.

- Wang P**,** Dai J, Bai F, Kong KF, Wong SJ, Montgomery RR, Madri JA, Fikrig E. Matrix Metalloproteinase 9 Facilitates West Nile Virus Entry into the Brain. ***J. Virol****.* 2008, 82(18):8978-85. PMCID: PMC2546894.

4. **Regulation of pathogen pattern receptor signaling.** Toll like receptors (TLRs)/RIG-I like receptors (RLRLs)/NOD-like receptors (NLRs) are important pathogen sensing receptors that are critical for induction of innate immune response and activation of adaptive immunity. I attempt to understand their functions during viral infection and how are they regulated.

- Shu Zhu, Siyuan Ding, Penghua Wang, Zheng Wei, Yi Yang, Geng Wang, Xuqiu Lei, Wen Pan, Noah W. Palm, Marcel de Zoete, Yujiao Zhao, Hua Yu, Kellie Jurado, Yunjiang Zheng, Jun Zhao, Ningguo Feng, Liang Shan, Yuval Kluger, Jun Lu, Clara Abraham, Erol Fikrig, Harry B. Greenberg, Richard A. Flavell. Nlrp9b inflammasome recognizes and restricts rotavirus infection in intestinal epithelial cells. ***Nature***. 2017, 546(7660):667-670.
- Penghua Wang, Shu Zhu, Long Yang, Shuang Cui, Wen Pan, Ruaidhri Jackson, Yunjiang Zheng, Anthony Rongvaux, Qiangming Sun, Guang Yang, Shandian Gao, Rongtuan Lin, Fuping You, Richard Flavell, Erol Fikrig. Nlrp6 regulates intestinal antiviral innate immunity. ***Science*** 2015. 350: 826-830.
- Penghua Wang, Long Yang, Gong Cheng, Erol Fikrig and Richard Sutton. UBXN1 interferes with RIG-I like receptor signaling by targeting MAVS. ***Cell Rep****.* 2013, 3 (4): 1057-1070. NIHMSID: 485145.
- Fuping You, Penghua Wang, Long Yang, Guang Yang, Erol Fikrig. ELF4 is a transactivator of type IFNs. ***Nature Immunology*** 2013; 14:1237-1246.
- Penghua Wang, Alvaro Arjona, Yue Zhang, Hameeda Sultana, Jianfeng Dai, Long Yang, Philippe LeBlanc, Karine Doiron, Maya Saleh, Erol Fikrig. Caspase-12 controls West Nile virus infection via the RNA receptor RIG-I. ***Nat. Immunol****.* 2010, 11(10): 912-919. NIHMSID: 485117

Complete List of Published Work in MyBibliography (39 publications):

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41366467/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01AI132526-01A1 Wang (PI) 01/03/2018-12/31/2022
Title: The role of UBXNs in antiviral immunity
Synopsis: This project is to characterize the physiological function of UBXN3B in herpes simplex virus and Chikungunya virus pathogenesis and antiviral immune responses in mice
Role: PI

Completed Research Support

R21 AI103807 Wang (PI) 04/10/2014-3/31/2016
Title: A critical role of NLRP6 in West Nile virus pathogenesis in mice
Synopsis: This project is to characterize the physiological function of NLRP6 during West Nile virus infection and its antiviral mechanism in vivo and in vitro
Role: PI

R03 AI099625 Wang (PI) 01/01/2013-12/31/2014
Title: Roles of interleukin 22 in West Nile virus pathogenesis
Synopsis: This project is to test the prophylactic/therapeutic potential of interleukin-22 antagonists and investigate how IL-22 influences West Nile virus pathogenesis using a mouse model
Role: PI

Northeast Biodefense Center Wang (PI) 3/01/2009-02/28/2011
Career Development Award
Title: Roles of Autophagy in Flaviviral Immunity
Synopsis: This project is to investigate the role of autophagy in West Nile virus pathogenesis and immunity
Role: PI