Prof. Liwang Chi
Professor
Penn State University, USA

BIOGRAPHICAL SKETCH

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NAME: Liwang Cui

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

POSITION TITLE: 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
Shenyang Agricultural University, China	BS	07/1984	Plant protection
Moldova Agricultural University, Moldova Academy of Sciences, USSR	PhD	12/1991	Biology
University of Kentucky, Lexington, KY	PhD	05/1996	Entomology (Virology)
Walter Reed Army Institute of Research, Washington DC	Postdoc	11/1998	Parasitology/Entomolog

A. Personal Statement

I have more than 15 years of research experience on malaria and led several NIH-funded grants to study developmental biology and drug resistance of the malaria parasites. My laboratory has an established record of productivity in many areas of malaria researc

h, with more than 170 peer-reviewed papers. My research covers both basic and applie d aspects of malaria, with a focus on malaria epidemiology, mechanisms and population genetics of drug resistance, gene regulation and sexual development. This broad researc h portfolio and my extensive training in entomology make me qualified to direct the ICE MR program, which integrates studies on parasites, vectors and human populations.

Throughout my career, I have fostered important international collaborations. Especially duri ng the current ICEMR, I have built a strong collaborative network in malaria research in sev eral countries of the Greater Mekong Subregion (GMS). I have overcome various challenges and gained tremendous experience in directing an international research center. I have succ essfully managed budgets and coordinated the development and execution of a realistic rese arch plan to ensure that milestones of all projects are met in a timely manner. I have also fa cilitated timely dissemination of our research results to both malaria research and contr ol communities and coordinated the publication of more than 80 peer-reviewed manuscri pts as a direct result of the current ICEMR. This renewal application *"Southeast Asia M alaria Research Center"*, built on the achievements of our current ICEMR, aims to achieve a comprehensive understanding of malaria transmission in the GMS though systemat ic studies of malaria epidemiology, vector biology, and drug resistance. This Center includes study sites in three countries of the GMS (Myanmar, China and Thailand) with drastically di fferent patterns of malaria epidemiology. We focus on malaria transmission along internation al borders, a problem that is pertinent to many countries pursuing malaria elimination. My pr evious experiences have prepared me to meet future challenges in our continuous endeavor in malaria research within the framework of the Southeast Asia ICEMR. Thus, I am confiden t that the proposed collaborative studies in this renewal will make more significant cont ributions to our understanding of malaria transmission in different endemic settings and have greater impacts on the regional malaria elimination campaign.

B. Positions and Honors.

Positions and Employment

1984-86 Research Assistant, Institute of Sericulture, Chinese Academy of Agricultural Sciences.

1987-91 Graduate Fellow, Moldova Agricultural University, Moldova Academy of Sciences.

1992-94 Marion Johnson Fellow, T.J. Headlee Fellow, Department of Entomology, Rutgers University.

1995-96 Graduate Research Assistant, Department of Entomology, University

of Kentucky.

1997-98 Postdoctoral Fellow, Walter Reed Army Institute of Research, Washington, DC.

12/98-3/00 Research Assistant Professor, Department of Preventive Medicine, F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences.

04/00-05/06 Assistant Professor, Department of Entomology, The Pennsylvania State University.

07/06-06/09 Associate Professor, Department of Entomology, The Pennsylvania State University.

07/2009- Professor, Department of Entomology, The Pennsylvania State University.

Honors

1992-93 Marion Johnson Graduate Fellowship, Rutgers University.

1993-94 T. J. Headlee Memorial Graduate Fellowship, Department of Entomology, Rutgers University.

1995 Winner of the Student Paper Competition, Ohio Valley Entomology Association, Lexington, KY.

1995 President's Award, Student Paper Competition, Section B (Physiology, Biochemistry, and Toxicology), National Meeting of the Entomological Society of America, Las Vegas, Nevada.

1995-96 Graduate Research Assistantship, University of Kentucky.

1998 U.S. Patent: Viral and insect genes that inhibit the immune system and method of use thereof.

2000 Faculty Development Award, College of Agriculture, Penn State University.

2000-05 Member, Tropical Medicine and Parasitology study section, NIAID, NIH.

2002-06 Ad hoc Member, Suborganismal Entomology/Nematology panel, USDA NRI.

2006-11 Member, Pathogenic Eukaryotes Study Section (PTHE), NIAID, NIH.

2007-08 Senior Fulbright Scholar to Thailand, lecture and research on infectious diseases.

2000- Ad hoc reviews (Journals): Trends Parasitol., Mol. Med., Parasitology, Int. J. Parasitol., Mol. Biochem. Parasitol., Am. J. Trop. Med. Hyg., Exp. Parasit

ol., Insect Biochem. Mol. Biol., Arch. Insect Physiol. Biochem., J. Med. Entomol., Biomolecular Engineering, J. Virol. Meth., J. Gen. Virol., Cell. Microbiol., Mol. Cell. Biol., Eukaryotic Cell, Antimicriob. Agents Chemother.

2009- Editorial board, “Malaria Research and Treatment”.

11-12/2009 Senior Researcher, Japan Society for the Promotion of Science (JSPS) "Invitational Training Program for Japanese Advanced Research Institutes 2009".

2010 Alex and Jessie C. Black Award for Excellence in Research, Penn State University.

C. Contribution to Science

1. My research in the field of drug resistance addresses the emergence of artemisinin resistance in the Greater Mekong Sub-region, where artemisinin drugs have been used for over three decades. In the China-Myanmar border region with co-endemicity of *P. falciparum* and *P. vivax* malaria, we assessed the efficacy of chloroquine-primaquine for treating *P. vivax* malaria as well as artemisinin-combination therapy for the treatment of *P. falciparum* malaria. Using longitudinally archived parasite samples, we comprehensively profiled *P. falciparum* in vitro sensitivities to a panel of 10 commonly used antimalarial drugs. We used individual gene-based correlation approach as well as genome-wide association studies, we determined the association of pfnhe1 with resistance to quinine, and pfmrp1 to piperaquine and other drugs. We also used population genetics approaches to determine whether recently identified molecular markers (such as Pfatp6 and K13) mediate artemisinin resistance in the study parasite populations. Laboratory selection of resistance also identified genes and pathways potentially involved in artemisinin resistance. These studies provided a thorough evaluation of the complexity of drug resistance in field parasite populations and identified potential drug resistance mechanisms.

    a. Yang, Z., Li, C., Miao, M., Zhang, Z., Sun, X., Meng, H., Li, J., Fan Q., Cui, L. 2011. Multidrug-resistant genotypes of *Plasmodium falciparum*, Myanmar. Emerg. Infect. Dis. 17, 498-501.
    b. Cui, L., Wang, Z., Miao, J., Miao, M., Chandra, R., Jiang, H., Su, X, Cui, L. 2012. Mechanisms of in vitro resistance to dihydroartemisinin in Plasmodium falciparum. Mol. Microbiol. 86, 111–128.
    c. Gupta, B., Xu, S., Wang, Z., Sun, L., Miao, J., Cui, L., Yang, Z. 2014. Plasmodium falciparum multidrug resistance protein 1 (Pfmrp1) gene and its

association with in vitro drug susceptibility of parasite isolates from northeast Myanmar. J. Antimicrob. Chemother. 69, 2110-2117.

d. Wang, Z., Wang, Y., Cabrera, M., Zhang, Y., Gupta, B., Wu, Y., Kemirembe, K., Hu, Y., Liang, X., Brashear, A., Shrestha, S., Li, X., Miao, J., Sun, X., Yang, Z., Cui, L. 2015. Artemisinin resistance at the China-Myanmar border and association with mutations in the K13-propeller gene. Antimicrob Agents Chemother. 59, 6952-6959.

2. My research on the biology of the malaria parasite *Plasmodium falciparum* addresses epigenetic regulation of gene expression in this parasite. These studies first identified the histone isoforms and extensive modifications of histone residues. We further evaluated the importance of different histone modification enzymes including the lysine acetyltransferases GCN5 and MYST, arginine methyltransferase PRMT1, and SET domain histone lysine methyltransferases. This body of work has firmly established the role of epigenetics in regulating gene expression in malaria parasites, and justified certain histone modification enzymes as potential chemotherapeutic targets. I served as the primary investigator in these studies.

a. Cui, L., Miao, J., Furuya, T., Li, X., Su, X.-z., Cui, L. 2007. PfGCN5 mediated histone H3 acetylation plays a key role in gene expression in Plasmodium falciparum. Eukaryot. Cell 6, 1219-1227.
b. Fan, Q., Miao, J., Cui, L., Cui, L. 2009. Characterization of protein arginine methyltransferase I from Plasmodium falciparum. Biochem. J. 421,107-118.
c. Miao, J., Fan, Q., Cui, L., Li, X., Wang, H., Ning, G., Reese, J.C., Cui, L. 2010. The MYST family histone acetyltransferase regulates gene expression and cell cycle in malaria parasite Plasmodium falciparum. Mol. Microbiol. 78, 883–902.
d. Miao, J., Lawrence, M., Parker, D., Jeffers, V., Ge, Y., Sullivan Jr., W. J., Cui, L. 2013. Extensive lysine acetylation occurs in evolutionarily conserved metabolic pathways and parasite-specific functions during Plasmodium falciparum intraerythrocytic development. Mol. Microbiol. 89, 660-675.

3. My studies addressing translational control in the malaria parasites focus on the process of sexual development (gametocytogenesis), which is obligatory for parasite transmission through mosquito vectors. We focused on evolutionarily conserved Puf family proteins in *P. falciparum*. We determined their differential expression during development stage transition in the parasites, and demonstrated the functions of this protein family in

repressing mRNA translation and maintaining mRNA stability in gametocytes. Especially, PfPuf2 is required for the translation repression of a number of transcripts in gametocytes including two genes encoding the transmission-blocking vaccine candidates Pfs25 and Pfs28. Whereas studies to date support a paradigm of Puf-mediated translation regulation through 3' untranslated regions (UTRs) of target mRNAs, we identified, for the first time, the presence of Puf binding elements in the 5'UTR of pfs25. These studies revealed the significance of translation regulation in parasite development, especially during stage transition of parasites between different hosts. I served as the primary investigator in these studies.

a. Cui, L., Fan, Q., Li, J. 2002. The malaria parasite Plasmodium falciparum encodes members of Puf RNA binding protein family with conserved RNA binding activity. Nucleic Acids Res. 30, 4607-4617.
b. Miao, J., Li, J., Fan, Q., Li, X.-L., Li, X.-Y., Cui, L. 2010. The Puf family RNA-binding protein PfPuf2 regulates sexual development and sex differentiation in the malaria parasite Plasmodium falciparum. J. Cell Sci. 123, 1039-49.
c. Miao, J., Fan, Q., Parker, D., Li, X., Li, J., Cui, L. 2013. Puf mediates translation repression through 5'UTR in a transmission blocking vaccine candidate of the malaria parasite. PLoS Pathogens 9, e1003268.
d. Cui, L., Lindner, S., Miao, J. 2015. Translational regulation during stage transitions in malaria parasites. Ann. NY Acad. Sci. 1342, 1-9.

Complete List of Published Work in MyBibliography (>200 referred publications):
http://www.ncbi.nlm.nih.gov/sites/myncbi/liwang.cui.1/bibliography/40448557/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

U19AI089672 Cui (PI)

07/01/2011-06/30/2017 5.5 months

NIAID, NIH

"Southeast Asia Malaria Research Center"

This project involves a consortium of multiple institutions and focuses on malaria epidemiology, vector biology, and epidemiology of drug resistance in three countries in Southeast Asia, namely Thailand, Myanmar and China.

Role: PD; co-PDs: Jetsumon Sattabongkot, Guiyun Yan

D43TW006571 Cui (PI)
03/01/2014-2/28/2019 1.2 months
Fogarty International Center, NIH
"Enhancing Vivax Malaria Research in Thailand"
This is a collaborative training project with Mahidol University in Thailand, which will train PhD students, postdocs and junior faculty from the Mekong region of Southeast Asia in malaria research.
Role: PI; co-PI: Jetsumon Sattabongkot

R01AI104946 Cui (PI)
08/01/2014-07/31/2018 1.0 month
NIAID, NIH
"Puf-Mediated Translation Control in Plasmodium"
This project studies the Puf family RNA binding proteins and their roles in malaria parasite development.
Role: PI.

R21 AI1239301 Cui (PI)
04/01/2016-03/31/2018 0.5 months
NIAID, NIH
"Transcriptomes and Proteomes of Plasmodium vivax"
This collaborative project aims to use humanized mice and vivax parasites collected from Thai field sites for the determination of transcriptomes and proteomes of the vivax parasites.
Role: PI; Co-PI: Roobsong W.

Completed Research Support

1R21AI09805 Cui (PI)
03/01/2012-02/28/2014
NIAID, NIH
"Sex-Specific Gene Expression in Malaria Parasite *Plasmodium falciparum*"
This R21 project studies the transcriptomes and proteomes of the male and female *P. falciparum* gametocytes.

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