BIOGRAPHICAL SKETCH

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NAME: GENG, QIBIN

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

POSITION TITLE: Postdoctoral Associate

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)	END DATE MM/YYYY	FIELD OF STUDY
Southern Medical University, GuangZhou, Guangdong	BS	07/2013	Biopharmaceutics, Biotechnology
Wuhan University, Wuhan, Hubei	MS	06/2016	Microbiology, Medical Virology
University of Minnesota, Twin Cities, Saint Paul, Minnesota	PHD	07/2022	Molecular Biology, Virology, Biochemistry, Structure Biology, Cell Biology, Immunology
Chinese Center for Disease Control and Prevention, Beijing	Other training	05/2016	Research Assistant, Intern
University of Minnesota, Twin Cities, Minneapolis, Minnesota	Other training	07/2017	Research Scholar, Technician
University of Minnesota, Twin Cities, Minneapolis, Minnesota	Postdoctoral Fellow	present	Molecular Biology, Virology, Biochemistry, Structure Biology, Cell Biology, Immunology; Drug discovery;

A. Personal Statement

I am a structural virologist with over 12 years of experience in virology, structural biology, and rational vaccine/drug design. My research has led to significant advances in our understanding of viral entry mechanisms and immunogen design. For example, my 2021 publication in PLoS Pathogens demonstrated the development of a virus-like nanoparticle (VLP) vaccine that protected animal models against the SARS-CoV-2 challenge—a breakthrough that directly resulted in a U.S. patent (US 2022/0001006 A1) for a novel lumazine synthase-based platform. Subsequent studies—including a 2022 Journal of Virology paper mapping the receptor recognition by the Omicron variant and my 2023 eLife publication—have further refined our understanding of conformation-specific viral infectivity and immune evasion. Collectively, these contributions have garnered over 10,000 citations, underscoring their significant impact in the field. In addition to my research accomplishments, I have actively mentored over eight undergraduate and graduate students in research projects, fostering their development as independent scientists and contributing to a collaborative research environment. My commitment to scientific service is reflected in my extensive record as a reviewer for more than 20 high-impact journals and as an editor for several special issues and volumes (e.g., the edited volume *Coronaviruses: Past, Present, and Future* just came out recently). These activities have not only enhanced the quality of published work in our field but have also kept me at the forefront of emerging scientific trends. My current work, including a forthcoming 2025 manuscript detailing an atomic (3.1 Å) cryo-EM structure of Sindbis virus, directly informs the objectives of my proposed K99/R00 project, *"Unraveling Alphavirus Structural Dynamics to Pioneer Novel Drug Discovery."* By integrating state-of-the-art cryo-electron microscopy/tomography with structure-based nanobody engineering and immunological assays, I will dissect the pH-triggered conformational changes of alphavirus glycoproteins and develop broadly neutralizing nanobodies. This integrated approach perfectly aligns with NIH's mission to advance infectious disease research and positions me well for a successful transition to an independent research career.

1. Qibin Geng, Zhang W. Cryo-EM Structure of Infective Sindbis Virus at 3.1 Å Resolution Reveals Insights into Alphavirus Host-Cell Entry and Assembly. In preparation. 2025.

2. Qibin Geng, Wan Y, Hsueh FC, Shang J, Ye G, Bu F, Herbst M, Wilkens R, Liu B, Li F. Lys417 acts as a molecular switch that regulates the conformation of SARS-CoV-2 spike protein. Elife. 2023 Nov 22;12 PubMed Central PMCID: PMC10695562.
3. Qibin Geng, Shi K, Ye G, Zhang W, Aihara H, Li F. Structural Basis for Human Receptor Recognition by SARS-CoV-2 Omicron Variant BA.1. Journal of Virology. 2022 April 27; 96(8):-. Available from: https://journals.asm.org/doi/10.1128/jvi.00249-22 DOI: 10.1128/jvi.00249-22
4. Qibin Geng, Tai W, Baxter V, Shi J, Wan Y, Zhang X, Montgomery S, Taft-Benz S, Anderson E, Knight A, Dinnon K, Leist S, Baric R, Shang J, Hong S, Drelich A, Tseng C, Jenkins M, Heise M, Du L, Li F. Novel virus-like nanoparticle vaccine effectively protects animal model from SARS-CoV-2 infection. PLOS Pathogens. 2021; 17(9):e1009897-. Available from: https://dx.plos.org/10.1371/journal.ppat.1009897 DOI: 10.1371/journal.ppat.1009897

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022 -	Postdoctoral Associate, University of Minnesota, Twin Cities, Minneapolis, MN
2017 - 2022	Research Assistant, PhD student/candidate, University of Minnesota, Twin Cities, Department of Veterinary and Biomedical Sciences, Saint Paul, MN
2016 - 2017	Research Scholar, University of Minnesota, Twin Cities, Department of Pharmacology, Minneapolis, MN
2015 - 2016	Research Assistant, Intern, Chinese Center for Disease Control and Prevention, Beijing
2013 - 2016	Research Assistant, Master Student on Microbiology, Wuhan University, College of Life sciences, Wuhan
2013 - 2014	Teaching Assistant of Experimental class of Immunology, Wuhan University, College of Life sciences, Wuhan

Honors

2023	Pharmacology Publication Award, University of Minnesota, Twin Cities
2016	The Outstanding M.S. (Master of Science) Thesis, Wuhan University
2014	The University-level Third-class scholarship, Wuhan University
2013	The GUOZEWEI Science and Technology Innovation Scholarship, Southern Medical University
2012	The University-level Second-class scholarship, Southern Medical University
2012	The University-level Outstanding Student, Southern Medical University

C. Contribution to Science

1. During my postdoctoral training at the University of Minnesota, I also contributed to the molecular mechanisms and evolutionary trajectory of SARS-CoV-2, particularly the Omicron variant, and to novel vaccine strategies to combat emerging variants. I edited a comprehensive volume on COVID-19 research, which encompasses 32 papers covering multiple fields such as epidemiology, diagnostics, therapeutics, immunology, and Long COVID. In parallel, I also contributed to structural biology studies using crystallography and biochemical assays to pinpoint how specific amino acid changes in the Omicron receptor-binding domain (RBD) adapt to human and mouse ACE2, clarifying how both animal reservoirs and immune pressures drive viral evolution. Moreover, I collaborated on developing and assessing a “spike cocktail” vaccination approach that conferred broad protection against Omicron subvariants and other variants of concern. Collectively, these contributions advance our understanding of Omicron’s evolutionary patterns and support the design of next-generation vaccines and therapeutics against SARS-CoV-2.

    a. Qibin Geng (Editor). Coronaviruses: Past, Present, and Future. MDPI. 2025. ISBN 978-3-7258-3059-6 (PDF); ISBN978-3-7258-3060-2 (Hardback). Available from: https://www.mdpi.com/books/reprint/10455-coronaviruses-past-present-and-future DOI: 10.3390/books978-3-7258-3059-6

b. Shi J, Wang G, Zheng J, Verma A, Guan X, Malisheni M, Qibin Geng, Li F, Perlman S, Du L. Effective vaccination strategy using SARS-CoV-2 spike cocktail against Omicron and other variants of concern. npj Vaccines. 2022 December 19; 7(1):-. Available from: https://www.nature.com/articles/s41541-022-00580-z DOI: 10.1038/s41541-022-00580-z

c. Zhang W, Shi K, Qibin Geng, Ye G, Aihara H, Li F. Structural basis for mouse receptor recognition by SARS-CoV-2 omicron variant. Proc Natl Acad Sci U S A. 2022 Nov;119(44):e2206509119. PubMed Central PMCID: PMC9636943.

d. Zhang W*, Shi K*, Qibin Geng*, Ye G, Aihara H, Li F. (*Co-first authors are marked with**) Structural basis for mouse receptor recognition by SARS-CoV-2 omicron variant. Proceedings of the National Academy of Sciences. 2022 October 18; 119(44):-. Available from: https://pnas.org/doi/10.1073/pnas.2206509119 DOI: 10.1073/pnas.2206509119

2. During my doctoral studies, I investigated the structural biology and entry mechanisms of coronaviruses—work that laid critical groundwork for understanding how these viruses infect host cells, evolve, and evade immune defenses. In particular, I focused on revealing how spike glycoproteins interact with host receptors, such as angiotensin-converting enzyme 2 (ACE2), and how spike proteins undergo conformational changes critical for viral entry and immune evasion. Using X-ray crystallography and cryo-electron microscopy (cryo-EM), I helped determine high-resolution spike structures from diverse coronaviruses (e.g., SARS-CoV-2, porcine deltacoronavirus, and infectious bronchitis coronavirus), unveiling core similarities in membrane fusion machinery as well as genus-specific differences in receptor binding. These findings explained why some coronaviruses exhibit stronger receptor affinity or rely on preactivation by proteases, ultimately influencing infection efficiency and pathogenicity. Collectively, my Ph.D. work illuminated key evolutionary trajectories of coronavirus spikes and provided a foundation for designing vaccines and therapeutics targeting these pivotal viral proteins.

   a. Shang J, Wan Y, Luo C, Ye G, Qibin Geng, Auerbach A, Li F. Cell entry mechanisms of SARS-CoV-2. Proceedings of the National Academy of Sciences. 2020 May 06; 117(21):11727-11734. Available from: https://pnas.org/doi/full/10.1073/pnas.2003138117 DOI: 10.1073/pnas.2003138117

   b. Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, Qibin Geng, Auerbach A, Li F. Structural basis of receptor recognition by SARS-CoV-2. Nature. 2020 March 30; 581(7807):221-224. Available from: https://www.nature.com/articles/s41586-020-2179-y DOI: 10.1038/s41586-020-2179-y

   c. Shang J, Zheng Y, Yang Y, Liu C, Qibin Geng, Luo C, Zhang W, Li F. Cryo-EM structure of infectious bronchitis coronavirus spike protein reveals structural and functional evolution of coronavirus spike proteins. PLOS Pathogens. 2018; 14(4):e1007009-. Available from: https://dx.plos.org/10.1371/journal.ppat.1007009 DOI: 10.1371/journal.ppat.1007009

   d. Shang J, Zheng Y, Yang Y, Liu C, Qibin Geng, Tai W, Du L, Zhou Y, Zhang W, Li F. Cryo-Electron Microscopy Structure of Porcine Deltacoronavirus Spike Protein in the Prefusion State. Journal of Virology. 2018 February 15; 92(4):-. Available from: https://journals.asm.org/doi/10.1128/JVI.01556-17 DOI: 10.1128/JVI.01556-17

3. During my postdoctoral training/doctoral studies, I also contributed to how coronaviruses—particularly SARS-CoV-2—utilize their spike glycoproteins to mediate entry into host cells and how subunit vaccine strategies can be optimized to elicit potent and broadly neutralizing immune responses. By identifying immunodominant yet non-neutralizing epitopes on receptor-binding domains (RBDs), I helped develop an innovative “glycan shielding” approach that masked these regions, thereby refocusing the immune response on more protective, neutralizing epitopes. This strategy significantly enhanced the breadth and efficacy of candidate vaccines against multiple SARS-CoV-2 variants, including Omicron. I also contributed to the molecular basis of antibody-dependent enhancement (ADE), revealing how certain neutralizing antibodies can paradoxically facilitate viral entry via Fc receptor-mediated pathways when present at sub-neutralizing concentrations. These findings informed the design and dosing regimens of monoclonal antibodies and vaccine candidates to minimize ADE risks. Beyond coronaviruses, I extended these principles to other emerging viruses, exemplified by my rational design of a Zika virus subunit vaccine that achieved improved efficacy through epitope shielding. Collectively, the work above established foundational insights into coronavirus spike structure, viral entry mechanisms, and subunit vaccine

optimization. These discoveries inform the ongoing development of next-generation vaccines and antibody-based countermeasures against emerging viral threats.

a. Shi J, Zheng J, Tai W, Verma A, Zhang X, Qibin Geng, Wang G, Guan X, Malisheni M, Odle A, Zhang W, Li F, Perlman S, Du L. A Glycosylated RBD Protein Induces Enhanced Neutralizing Antibodies against Omicron and Other Variants with Improved Protection against SARS-CoV-2 Infection. Journal of Virology. 2022 September 14; 96(17):-. Available from: https://journals.asm.org/doi/10.1128/jvi.00118-22 DOI: 10.1128/jvi.00118-22
b. Zhang W, Huang L, Ye G, Qibin Geng, Ikeogu N, Harris M, Dileepan G, Burrack K, Du L, Frosch A, Li F. Vaccine booster efficiently inhibits entry of SARS-CoV-2 omicron variant. Cell Mol Immunol. 2022 Mar;19(3):445-446. PubMed Central PMCID: PMC8785151.
c. Wan Y, Shang J, Sun S, Tai W, Chen J, Qibin Geng, He L, Chen Y, Wu J, Shi Z, Zhou Y, Du L, Li F. Molecular Mechanism for Antibody-Dependent Enhancement of Coronavirus Entry. Journal of Virology. 2020 February 14; 94(5):-. Available from: https://journals.asm.org/doi/10.1128/JVI.02015-19 DOI: 10.1128/JVI.02015-19
d. Tai W, Chen J, Zhao G, Qibin Geng, He L, Chen Y, Zhou Y, Li F, Du L. Rational Design of Zika Virus Subunit Vaccine with Enhanced Efficacy. Journal of Virology. 2019 September; 93(17):-. Available from: https://journals.asm.org/doi/10.1128/JVI.02187-18 DOI: 10.1128/JVI.02187-18

4. During my Ph.D. training, I also investigated virus-host interactions that shape both viral tropism and the host immune response. A significant portion of my work focused on coronaviruses, where I helped uncover how lysosomal proteases in different species and tissues activate coronavirus spike proteins, thus influencing which hosts and tissues these viruses can infect. I also contributed to identifying novel bat coronaviruses capable of using the same receptor as MERS-CoV, underscoring bats as potential reservoirs for emerging human pathogens. In parallel, during my M.Sc. training, I helped examine the innate immune response to RNA viruses, such as Enterovirus 71 (EV71). Through these studies, I helped characterize how cellular factors (e.g., HRS, HERP) modulate TLR7 and TBK1 signaling cascades, thereby orchestrating type I and type III interferon production and inflammatory responses. Together, these discoveries broaden our understanding of cross-species viral transmission, tissue tropism, and the molecular underpinnings of innate antiviral defenses—key insights that inform both surveillance strategies and the development of targeted therapeutics.

a. Zheng Y, Shang J, Yang Y, Liu C, Wan Y, Qibin Geng, Wang M, Baric R, Li F. Lysosomal Proteases Are a Determinant of Coronavirus Tropism. Journal of Virology. 2018 December 15; 92(24):-. Available from: https://journals.asm.org/doi/10.1128/JVI.01504-18 DOI: 10.1128/JVI.01504-18
b. Luo C, Wang N, Yang X, Liu H, Zhang W, Li B, Hu B, Peng C, Qibin Geng, Zhu G, Li F, Shi Z. Discovery of Novel Bat Coronaviruses in South China That Use the Same Receptor as Middle East Respiratory Syndrome Coronavirus. Journal of Virology. 2018 July; 92(13):-. Available from: https://journals.asm.org/doi/10.1128/JVI.00116-18 DOI: 10.1128/JVI.00116-18
c. Ge M, Luo Z, Qiao Z, Zhou Y, Cheng X, Qibin Geng, Cai Y, Wan P, Xiong Y, Liu F, Wu K, Liu Y, Wu J. HERP Binds TBK1 To Activate Innate Immunity and Repress Virus Replication in Response to Endoplasmic Reticulum Stress. The Journal of Immunology. 2017 November 01; 199(9):3280-3292. Available from: https://journals.aai.org/jimmunol/article/199/9/3280/109815/HERP-Binds-TBK1-To-Activate-Innate-Immunity-and DOI: 10.4049/jimmunol.1700376
d. Luo Z, Ge M, Chen J, Qibin Geng, Tian M, Qiao Z, Bai L, Zhang Q, Zhu C, Xiong Y, Wu K, Liu F, Liu Y, Wu J. HRS plays an important role for TLR7 signaling to orchestrate inflammation and innate immunity upon EV71 infection. PLOS Pathogens. 2017; 13(8):e1006585-. Available from: https://dx.plos.org/10.1371/journal.ppat.1006585 DOI: 10.1371/journal.ppat.1006585

5. During my MSc training, my research primarily focused on understanding the epidemiological characteristics and burden of acute gastroenteritis—particularly rotavirus- and norovirus-associated diarrhea—across different age groups in China. By analyzing extensive surveillance data from multiple hospital sentinel sites, I helped characterize prevalence trends, seasonal patterns, and genotype distributions of key pathogens. Notably, we identified the rapid emergence of G9P[8] as a predominant rotavirus strain in children under five and demonstrated the considerable impact of norovirus infections,

both in the community and outpatient settings. In addition, our findings underscored risk factors among the elderly population, revealing that norovirus and diarrheagenic E. coli were leading causes of acute diarrhea in older adults. These studies have provided critical insights into the need for continued surveillance and informed potential vaccine and public health strategies to mitigate diarrheal disease in China.

a. Yu J*, Lai S*, Qibin Geng*, Ye C, Zhang Z, Zheng Y, Wang L, Duan Z, Zhang J, Wu S, Parashar U, Yang W, Liao Q, Li Z. (*Co-first authors are marked with**) Prevalence of rotavirus and rapid changes in circulating rotavirus strains among children with acute diarrhea in China, 2009–2015. Journal of Infection. 2019 January; 78(1):66-74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0163445318302160 DOI: 10.1016/j.jinf.2018.07.004
b. Zhang Z, Lai S, Yu J, Qibin Geng, Yang W, Chen Y, Wu J, Jing H, Yang W, Li Z. Etiology of acute diarrhea in the elderly in China: A six-year observational study. PLOS ONE. 2017; 12(3):e0173881-. Available from: https://dx.plos.org/10.1371/journal.pone.0173881 DOI: 10.1371/journal.pone.0173881
c. Yu J, Ye C, Lai S, Zhu W, Zhang Z, Qibin Geng, Xue C, Yang W, Wu S, Hall A, Sun Q, Li Z. Incidence of Norovirus-Associated Diarrhea, Shanghai, China, 2012–2013. Emerging Infectious Diseases. 2017 February; 23(2):312-315. Available from: http://wwwnc.cdc.gov/eid/article/23/2/16-1153_article.htm DOI: 10.3201/eid2302.161153
d. Qibin Geng, Sheng-jie LAI, Jian-xing YU, Zi-ke ZHANG, Wan-qi YANG, Zhong-jie LI, Jian-guo WU, Wei-zhong YANG. Epidemiological characteristics of rotavirus caused diarrhea in children aged 5 years in 26 provinces in China, 2011-2014. Disease Surveillance. 2016; 31(6):463. Available from: http://www.jbjc.org/en/article/id/153bc089-0106-48aa-8926-5cb823c0ac1c DOI: 10.3784/j.issn.1003-9961.2016.06.006

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BIOGRAPHICAL SKETCH

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NAME: Zhang, Wei

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

POSITION TITLE: Associate 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)	END DATE MM/YYYY	FIELD OF STUDY
Nankai University, Tianjin	BS	07/1989	Biophysics
Institute of Biophysics, Chinese Academy of Science, Beijing	MS	07/1992	Biophysics
Purdue University, West Lafayette, Indiana	PHD	05/2001	Structural Biology
Purdue University, West Lafayette, Indiana	MS	05/2002	Computer Science
Purdue University, West Lafayette, Indiana	Postdoctoral Fellow	07/2002	Structural Biology

A. Personal Statement

I have been doing fundamental research on structural virology for 28 years and will continue to work vigorously on mechanistic studies of enveloped virus assembly and infection, two important stages of the virus life cycle. I have a deep interest in using cryo-electron microscopy (cryo-EM) to understand how structural information of macromolecules is preserved, transformed, detected, verified, reconstituted via computation, and how the structural information is used in deciphering the cellular functions of macromolecules and their roles in biological processes. My research expertise and interest were grounded in my training in physical science as an undergraduate student, the training in computer science as a graduate student, and my Ph.D. training from several key scientists in the world-renowned structural biology group at Purdue University, including Drs. Timothy Baker (Ph.D. mentor), Michael Rossmann, Richard Kuhn and Jue Chen.

One research direction in my lab is to study the dynamic structural changes when the viral membrane fuses with the cellular membrane. We use alphaviruses, as a model system for studying membrane fusion driving by the class II viral fusion proteins. My lab has established reliable and reproducible virus-liposome fusion assays that reveal the alphavirus pre-fusion intermediate and the post- fusion state on the TEM grids. We have hardware and software platforms that support single-particle reconstruction, cryo-electron tomography, and sub-tomogram averaging computations. Through collaboration with Dr. Guichuan Yu, we actively develop computation methods to achieve innovative image processing solutions to challenging problems. We aim to determine the structures of the critical viral proteins at several discernable steps of the membrane fusion. In addition, we propose to further investigate the significance and impact of the specific structure properties of these proteins to the success of the membrane fusion in both *in vitro* and *in vivo* assays. Dr. Chanakha Navaratnarajah from Mayo Clinic is a molecular virologist who has extensive experience in studying the fusion mechanism in several virus systems. This collaborative work will potentially lead to breakthrough discoveries and deepens our understanding of this important biological process.

I have a strong commitment to instrumentation and mentoring graduate students and post-doctoral scientists. I am the PI of several NIH- or university-funded instrumentation grants that upgraded cryo-EM technology on campus. I have mentored and co-mentored five post-doc scientists and several graduate students. Two of the post-doc scientists I mentored and co-mentored have started their independent research positions, as principal investigators. I believe that an effective graduate and post-doctoral training program should not only teach knowledge and methodology relevant to the specific research field but also coach the students' critical scientific skills that include identifying significant research questions, utilizing various theoretical or experimental modalities, integrating information obtained from different sources, critical reasoning, effective communication, and good work ethics. I will cultivate these skills and positive work habits when I mentor graduate students and post-doctoral scientists.

Ongoing research projects include the following:

R21 DE032878, NIH Mansky, Louis (PI); Joachim Mueller & Wei Zhang (Co-I's)
05/01/23-04/30/25

Imaging of HTLV-1 by cryo-CLEM
The goal of this project is to analyze HTLV-1 assembly at cell-cell contact by using cryo-CLEM and cell micropatterning technologies.

R01 AI177264, NIH Mansky, Louis (contact PI) and Mueller, Joachim (PI); Wei Zhang (Co-I)
07/01/23-06/30/28

HIV Gag Lattice Morphology and Particle Biogenesis
This project is to investigate the HIV-2 Gag protein trafficking, virus particle structure and assembly.

R01AI162699-01, NIH Zhang, Wei (PI), Navaratnarajah, Chanakha (Co-I) 04/22/22-03/30/27
Structural Mechanisms of Alphavirus Membrane Fusion
This project studies the conformational changes of Alphavirus structural proteins during membrane fusion

U19AI171954, NIH Harris, Reuben (PI), Li, Fang (Co-I) 05/16/22-04/30/25
Midwest AViDD Center
This center grant conducts the basic and translational research on small molecules against emerging viruses.
Role: Co-Investigator in the Structural Biology Core

Recently completed projects:

R21 AI148328, NIH Zhang, Wei Zhang (contact) and Mansky, Louis (PI)
08/21/20-07/31/23 (in no-cost extension)

Cryo-ET Guided Single Particle Reconstruction of HIV
This project aims to develop an imaging and computation method to study HIV immature particle structure

Citations:

1. Talledge N, Yang H, Shi K, Coray R, Yu G, Arndt WG, Meng S, Baxter GC, Mendonça LM, Castaño-Díez D, Aihara H, Mansky LM*, **Zhang W***. HIV-2 Immature Particle Morphology Provides Insights into Gag Lattice Stability and Virus Maturation. J Mol Biol. 2023 Aug 1;435(15):168143. PMID: 37150290.

   Significance: This study presents the first evidence for a novel stabilization interface mediated by the HIV-2 CA-CTD and provides important clues for explaining differences between HIV-1 and HIV-2 immature particle morphology, as well as insights into Gag lattice stabilization and virus maturation.

2. Shang J, Zheng Y, Yang Y, Liu C, Geng Q, Tai W, Du L, Zhou Y, **Zhang W***, Li F*. Cryo-Electron Microscopy Structure of Porcine Deltacoronavirus Spike Protein in the Prefusion State. J Virol. 2018 Feb 15;92(4) PubMed Central PMCID: PMC5790952.

   Significance: Cryo-EM reconstruction of Deltacoronavirus spike protein at 3.3Å resolution.

3. Cao S, Maldonado JO, Grigsby IF, Mansky LM*, **Zhang W*.** Analysis of human T-cell leukemia virus type 1 particles by using cryo-electron tomography. J Virol. 2015 Feb;89(4):2430-5. PubMed Central PMCID: PMC4338869.

   Significance: First cryo-tomographic study of authentic HTLV-1 particles.

4. Cao S, **Zhang W.** Characterization of an early-stage fusion intermediate of Sindbis virus using cryo-electron microscopy. Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13362-7. PubMed Central PMCID: PMC3746934.

   Significance: Discovery that at the initial stage of membrane fusion, Sindbis virus E2 stays as a trimer conformation when E1 attaches to a target membrane.

B. Positions and Honors

Positions and Employment

2023 -	Associate Professor, Department of Diagnostic and Biological Sciences, University of Minnesota, Minneapolis, MN
2020 -	Research Professor, Department of Diagnostic and Biological Sciences, University of Minnesota, Minneapolis, MN
2016 - 2020	Research Associate Professor, Department of Diagnostic and Biological Sciences, University of Minnesota, Minneapolis, MN
2008 -	Scientist, Characterization Facility, University of Minnesota, Minneapolis, MN
2008 - 2016	Research Assistant Professor, Department of Diagnostic and Biological Sciences, University of Minnesota, Minneapolis, MN
2004 - 2008	Associate Research Scientist, Department of Biological Scientist, Purdue University, West Lafayette, MN
2002 - 2004	Assistant Research Scientist, Department of Biological Sciences, Purdue University, West Lafayette, IN
2001 - 2002	Postdoctoral Research Scientist, Department of Biological Sciences, Purdue University, West Lafayette, IN
1996 - 2001	Graduate Research Assistant, Department of Biological Sciences, Purdue University, West Lafayette, IN
1994 - 1996	Graduate Teaching Assistant, Department of Psychology, Purdue University, West Lafayette, IN
1992 - 1994	Research Associate, Department of Neurobiology, Institute of Biophysics, Chinese Academy of Science, Beijing

Other Experience and Professional Memberships

1997 -	Member, Microscopy Society of America
2002 -	Member, Biophysical Society of America
2003 -	Member, American Society for Virology

Honors

1988	Shen Shou-Chun Experimental Physics 1st Prize, Nankai University, China
1994	Neuroscience Program Graduate Fellowship, Purdue University
1999	Presidential Student Award, Microscopy Society of America
2000	Purdue Research Foundation Grant, Purdue University
2001	Elected as a member, ΤΠΕ - Honor Society in the Computing Sciences
2002	Postdoctoral Travel Award, American Society for Virology 22nd Annual Meeting, Davis, CA
2002	Young Investigator Travel Award, FASEB Summer Research Conference on Virus Assembly, Saxtons River, VT

C. Contribution to Science

1. **Retrovirus assembly and morphogenesis**: This study was done in collaboration with Drs. Joachim Mueller (quantitative super-resolution fluorescence microscopy) and Louis Mansky (virology) at the University of Minnesota. Our interdisciplinary research team employs coordinated biochemical, biophysical and virology approaches to address fundamental questions in retrovirus assembly. We determined the first cryo-ET reconstruction of authentic HTLV-1 particles (ref. d). We also characterized the morphology of retrovirus virus-like particles by cryo-EM, including HTLV-1, HIV-1, HIV-2, Rous sarcoma virus, Mason- Pfizer monkey virus, bovine leukemia virus, walleye dermal sarcoma virus, murine leukemia virus, and human foamy virus (ref. b and c). The following papers are selected from 14 peer-reviewed publications:

    a. Talledge N, Yang H, Shi K, Coray R, Yu G, Arndt WG, Meng S, Baxter GC, Mendonça LM, Castaño-Díez D, Aihara H, Mansky LM*, **Zhang W***. HIV-2 Immature Particle Morphology Provides Insights into Gag Lattice Stability and Virus Maturation. J Mol Biol. 2023 Aug 1;435(15):168143. PMID: 37150290.

Significance: This study presents the first evidence for a novel stabilization interface mediated by the HIV-2 CA_{CTD} and provides important clues for explaining differences between HIV-1 and HIV-2 immature particle morphology, as well as insights into Gag lattice stabilization and virus maturation

b. Yang H, Arndt WG, **Zhang W***, Mansky LM*. Determinants in the HTLV-1 Capsid Major Homology Region that are Critical for Virus Particle Assembly. J Mol Biol. 2024 Dec 15;436(24):168851. PubMed Central PMCID: PMC11637902.

Significance: First comprehensive analysis about the MHR region of the HTLV-1 capsid.

c. Martin JL, Mendonça LM, **Zhang W***, Mansky LM*. Distinct particle morphologies revealed through comparative parallel analyses of retrovirus-like particles. J Virol. 2016 Sep15; 90(18): 8074-84. PMID: 27356903; PMCID: PMC5008088.

Significance: Cryo-EM description of the distinct morphological features that exist among retrovirus-like particles in a comparative, parallel analysis.

d. Cao S, Maldonado JO, Grigsby IF, Mansky LM*, **Zhang W***. Analysis of human T-cell leukemia virus type 1 particles by using cryo-electron tomography. J Virol. 2015 Feb;89(4):2430-5. PubMed Central PMCID: PMC4338869.

Significance: First cryo-ET study of authentic HTLV-1 particles

* co-corresponding author

4. **Structure studies on alphavirus and flavivirus assemblies:** my research in this area has led to several influential discoveries: (1) The first cryo-EM structure of Sindbis virus that resolved the shape of both E1 and E2 protein densities on the viral membrane (ref. a); (2) The first flavivirus (dengue virus) structure that revealed the molecular arrangement of the surface E proteins and densities of M proteins illustrating the tetramer organization of E and M (ref. b and c). This result and method developed in this paper paved the way for the structural studies on other prominent flaviviruses including West Nile virus and Zika virus. (3) The membrane fusion intermediate structure of Sindbis virus when attaching to a target membrane at the low pH condition (ref. d). The following papers are chosen from 15 peer-reviewed research papers:

a. **Zhang W**, Mukhopadhyay S, Pletnev SV, Baker TS, Kuhn RJ, Rossmann MG. Placement of the structural proteins in Sindbis virus. J Virol. 2002 Nov;76(22):11645-58. PubMed Central PMCID: PMC136788.

b. **Zhang W**, Chipman PR, Corver J, Johnson PR, Zhang Y, Mukhopadhyay S, Baker TS, Strauss JH, Rossmann MG, Kuhn RJ. Visualization of membrane protein domains by cryo-electron microscopy of dengue virus. Nat Struct Biol. 2003 Nov;10(11):907-12. PubMed Central PMCID: PMC4148076.

Significance: 9Å resolution reconstruction map that confirmed the fitted atomic model of Dengue virus

c. Yu IM, **Zhang W**, Holdaway HA, Li L, Kostyuchenko VA, Chipman PR, Kuhn RJ, Rossmann MG, Chen J. Structure of the immature dengue virus at low pH primes proteolytic maturation. Science. 2008 Mar 28;319(5871):1834-7. PubMed PMID: 18369148.

Significance: Deciphering the structural changes during Dengue virus maturation

d. Cao S, **Zhang W**. Characterization of an early-stage fusion intermediate of Sindbis virus using cryoelectron microscopy. Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13362-7. PubMed Central PMCID: PMC3746934.

4. **Technique development:** I have a great interest in developing novel methods to expedite cryo-EM image processing and to solve challenging problems. Some of the computation tools are disseminated after publication and used by others in the field. Technology development will be one of the principal research themes in my lab. My original computation work includes: (1) Using microscope contrast transfer function as a weighting function in resolving 3D reconstruction maps: this approach significantly improved the resolution of the reconstruction map from data sets with limited variation of under-focus conditions; (2) Particle orientation determination for elongated Geminivirus particles (ref. a): this approach led to the first reconstruction map of a geminate virus particle. (3) Analyzing the curvature of the viral membrane in flavivirus and alphavirus (ref. c): this work demonstrates an algorithm that computes curvature, a property derived from the differential equation in positions of pixelated cryo-EM maps. (4) Determining the liposome- binding site on the surface of an icosahedral particle at low pH (ref. d): this work led to characterization of an early-state fusion intermediate of Sindbis

virus. The following papers are selected from 7 peer-reviewed research papers that reported these image processing methods:

a. **Zhang W**, Olson NH, Baker TS, Faulkner L, Agbandje-McKenna M, Boulton MI, Davies JW, McKenna R. Structure of the Maize streak virus geminate particle. Virology. 2001 Jan 20;279(2):471-7. PMID: 11162803.

   Significance: Establishing an orientation determination method that led to the first reconstruction map of a Geminivirus

b. Ji Y, Marinescu DC, **Zhang W**, Zhang X, Yan X, Baker TS. A model-based parallel origin and orientation refinement algorithm for cryoTEM and its application to the study of virus structures. J Struct Biol. 2006 Apr;154(1):1-19. PMID: 16459100; PMCID: PMC4147871.

   Significance: Reporting a parallel origin orientation determination and refinement software package

c. **Zhang W**, Kaufmann B, Chipman PR, Kuhn RJ, Rossmann MG. Membrane curvature in flaviviruses. J Struct Biol. 2013 Jul;183(1):86-94. PMID: 23602814; PMCID: PMC4091808.

   Significance: Implementing an algorithm that determines the membrane curvature from pixelated cryo-EM reconstruction density maps

d. Cao S, **Zhang W**. Characterization of an early-stage fusion intermediate of Sindbis virus using cryoelectron microscopy. Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13362-7. PMID: 23898184; PMCID: PMC3746934.

   Significance: Elucidating an algorithm that determines the unique liposome-binding site on an icosahedral Sindbis virus particle

Complete List of PubMed Cited Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/wei.zhang.11/bibliography/public/