BIOGRAPHICAL SKETCH

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NAME: Liang, Bo

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

POSITION TITLE: Assistant Professor of Biochemistry, Tenure Track

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
University of Science and Technology of China, Hefei, Anhui	B.S.	07/2004	Biological Science
University of Science and Technology of China, Hefei, Anhui	B.E.	07/2004	Computer Science
Florida State University, Tallahassee, Florida	Ph.D.	08/2009	Molecular Biophysics
Harvard Medical School, Boston, Massachusetts	Postdoctoral Fellow	09/2016	Structural Cell Biology and Microbiology

A. Personal Statement

I have the motivation, expertise, leadership, and training essential to successfully complete the research projects in my laboratory. As a graduate student and two-time American Heart Association predoctoral fellow (0615182B & 0815118E) with Dr. Hong Li at Florida State University, and later as a postdoctoral fellow with Drs. Stephen Harrison and Sean Whelan at Harvard Medical School, I received outstanding training in structural biology, with specific expertise in cryo-electron microscopy (cryo-EM) and x-ray crystallography, as well as RNA biology and virology. My current research focuses on the structures and mechanisms of macromolecules with an emphasis on the RNA synthesis machinery of non-segmented negative-sense (NNS) RNA viruses, and neurobiological diseases-related proteins, including membrane receptors, ion channels, and neurodegenerative assemblies.

As an investigator on several NIH funded projects, I built the foundation for the proposed research by developing effective strategies of sample preparation, data acquisition, and analysis. In particular, I have comprehensive experience in single-particle cryo-EM, including specimen optimization, data collection, image processing, model interpretation, and validation. Additionally, I have rigorous training in biochemistry and x-ray crystallography, including protein and RNA purification, crystallization, synchrotron x-ray diffraction, data processing, model building, and refinement. I furthermore have an extensive background in RNA biology and virology.

I received a generous startup package and began my independent laboratory in the Biochemistry Department at Emory University School of Medicine in October 2016. Emory has purchased two state-of-the-art electron microscopes as part of my recruitment. Currently, I am the Co-Scientific Adviser of the Robert P. Apkarian Integrated Electron Microscopy Core (IEMC) at Emory. I have a dedicated mentoring committee that consists of established faculty Drs. Richard Kahn, Daniel Reines, Christine Dunham, and Anice Lowen at Emory. Drs. Stefan Sarafianos, Anita Corbett, David Steinhauer, Jeremy Boss (former interim chair), and Eric Sundberg (Chair) also provide critical feedback. Together, these colleagues have provided (and continue to provide) invaluable guidance on staffing and acquiring funding for my laboratory, prioritizing my research efforts, and ensuring that service and teaching commitments are appropriate for my independent career.

I received my first NIH R01 award in 2019. My lab has recently determined a 3.67 Å cryo-EM structure of the *apo* polymerase (L:P) complex of respiratory syncytial virus (RSV) using the Talos Arctica 200 kV (TEM) with BioQuantum/K2 direct electron detector (ThermoFisher) at Emory University. We want to continue the single-particle analysis of the RSV RNA synthesis machinery and therefore request the data collection resources at NCCAT.

B. Positions and Honors

Positions and Employment

2002-2003 Undergraduate Research Assistant, Department of Chemistry, University of Science and Technology of China, Hefei

2002-2004 Undergraduate Research Assistant, Department of Computer Science, University of Science and Technology of China, Hefei

2002-2004 Undergraduate Research Assistant, Key Laboratory of Structural Biology (Chinese Academy of Science), School of Life Science, University of Science and Technology of China, Hefei

2004-2009 Graduate Research Assistant, Institute of Molecular Biophysics, Florida State University, Tallahassee, FL

2009 Teaching Assistant, Florida State University, Tallahassee, FL

2009-2016 Postdoctoral Research Fellow, Biological Chemistry and Molecular Pharmacology (BCMP), and Microbiology and Immunobiology (MBIB), Harvard Medical School, Boston, MA

2015 Teaching Assistant, Harvard Medical School, Boston, MA

2016- Assistant Professor, Department of Biochemistry, Emory University School of Medicine, Atlanta, GA

2018- Co-Scientific Advisor, Robert P. Apkarian Integrated Electron Microscopy Core, Emory University, Atlanta, GA

Other Experience and Professional Memberships

2005- Member, The Biophysical Society

2005-2006 Treasurer, Students for the Effective Communication of Science, Florida State University

2006- Member, The RNA Society

2006-2007 Vice President, Chinese Students and Scholars Association, Florida State University

2007-2008 President, Chinese Students and Scholars Association, Florida State University

2008-2009 Senior Consultant, Chinese Students and Scholars Association, Florida State University

2009- Member, The Protein Society

2010-2016 Governing Board, HMS/HSDM Postdoctoral Association, Harvard Medical School

2011-2014 Co-Chair, HMS/HSDM Postdoctoral Association, Harvard Medical School

2013 Judge, American Society for Biochemistry and Molecular Biology Research Poster Competition

2013-2014 Associate Editors-in-Chief, the Journal of Postdoctoral Research

2013-2016 Trainee Committee, Biological Chemistry and Molecular Pharmacology, Harvard Medical School

2014-2016 Secretary, Harvard Medical Postdoctoral Association, Harvard Medical School

2017 Faculty Search Committee, Department of Biochemistry, Emory University School of Medicine

2017- Cryo-EM Scientist Search Committee, Electron Microscopy Core, Emory University

2017- Cryo-EM Planning Committee, Electron Microscopy Core, Emory University

2017- Editorial Board, Journal of Molecular Cell Biology

2017- Co-director, Biochemistry Departmental Seminar Program, Emory University School of Medicine

2017- Executive Committee, Microbiology and Molecular Genetics Graduate Program, Emory University

2018- Member, The American Heart Association

2018- Member, SouthEast Consortium for Microscopy of MacroMolecular Machines (SECM4)

2019- Member, Midwest Consortium for High Resolution Cryoelectron Microscopy

Honors

2002 Excellent Undergraduate Research Project, University of Science and Technology of China

2002 Outstanding Student Scholarship, University of Science and Technology of China

2006 Predoctoral Fellowship, Florida/Puerto Rico Affiliate, American Heart Association

2008 Kasha Award, Florida State University

2008 Predoctoral Fellowship, Greater Southeast Affiliate, American Heart Association

2009 Chinese Government Award for Outstanding Self-financed Students Abroad, China Scholarship Council

2009 Protein Science Young Investigator Travel Grant, The Protein Society

C. Contributions to Science

1. **Illustrated the molecular basis of key assembly stages of a novel family of RNA-guided RNA modification enzyme.** My interest in ribonucleoprotein (RNP) machinery began with my graduate studies in Professor Hong Li's laboratory, where I focused on box H/ACA RNPs that are essential for ribosome and spliceosome maturation. Box H/ACA RNPs utilize the same four proteins, Cbf5, Nop10, Gar1, and L7Ae, which are also core components of the telomerase, and a set of non-coding guide RNAs to capture ribosomal RNAs and snRNAs for chemical modification. My primary contribution was to illustrate the molecular basis of key assembly stages of the box H/ACA RNP assembly and function with a set of crystal structures, including one complex of Cbf5:Nop10:Gar1 (2.1 Å), one substrate-bound (2.87 Å) and one functional (2.35 Å) box H/ACA RNP. I also devised a fluorescence assay to dissect the accurate placement of the substrate RNA and analyzed the impact of chemical substitutions with biochemical and structural approaches and dynamic simulations. These findings, as papers cited below, collectively had a significant impact on understanding the multistep and multicomponent-mediated enzyme activity of the box H/ACA RNP.
   - **B. Liang**, J. Zhou, E. Kahen, R. M. Terns, M. P. Terns & H. Li. Structure of a functional ribonucleoprotein pseudouridine synthase bound to a substrate RNA. ***Nat Struct Mol Biol*** (2009) *16*, 740-6; PMC5706466.
   - **B. Liang**, E. J. Kahen, K. Calvin, J. Zhou, M. Blanco & H. Li. Long-distance placement of substrate RNA by H/ACA proteins. ***RNA*** (2008) *14*, 2086-94; PMC2553744.
   - **B. Liang**, S. Xue, R. M. Terns, M. P. Terns & H. Li. Substrate RNA positioning in the archaeal H/ACA ribonucleoprotein complex. ***Nat Struct Mol Biol*** (2007) *14*, 1189-95; doi:10.1038/nsmb1336.
   - R. Rashid, **B. Liang**, D. L. Baker, O. A. Youssef, Y. He, K. Phipps, R. M. Terns, M. P. Terns & H. Li. Crystal structure of a Cbf5-Nop10-Gar1 complex and implications in RNA-guided pseudouridylation and dyskeratosis congenita. ***Mol Cell*** (2006) *21*, 249-60; doi:10.1016/j.molcel.2005.11.017.

2. **Determined the first structure of the multifunctional L protein of a non-segmented negative-strand RNA virus with cryo-EM.** My subsequent work in the laboratories of Professors Stephen Harrison and Sean Whelan at Harvard Medical School directly visualized the atomic structure of the multifunctional RNA polymerase of vesicular stomatitis virus (VSV), a model non-segmented negative-sense (NNS) RNA virus. NNS RNA viruses are a group of viruses containing many significant human pathogens, including Ebola, rabies, and respiratory syncytial virus (RSV). The RNA synthesis by the RNA polymerase of these viruses is central to their life cycle. The RNA polymerase, constituted of the large protein (**L**) and the phosphoprotein (**P**), contains multiple distinct activities of RNA-dependent RNA polymerase, polyribonucleotidyl transferase, and RNA methyltransferase. I have successfully prepared and biochemically characterized the L complexes. My colleagues and I obtained the first architectures of L alone and its complexes using negative-stain EM. Importantly, I obtained a 3.8 Å cryo-EM structure of VSV L and performed the *de novo* model building of this 2109-residue polypeptide. Two significant contributions resulted from this work: 1) the determination of the first atomic structure of an asymmetric protein of less than 250 kDa using cryo-EM; 2) the first atomic view of the RNA polymerase of NNS RNA viruses. Further, I have successfully expressed and purified the L protein of rabies virus (RABV) and adapted an *in vitro* transcription assay from VSV to RABV.
   - S. Jenni, L. Bloyet, R. Diaz-Avalos, **B. Liang**, S. P. J. Whelan, N. Grigorieff, S. C. Harrison. Structure of the Vesicular Stomatitis Virus L Protein in Complex with Its Phosphoprotein Cofactor. ***Cell Reports*** (2019) Accepted.
   - B. Morin, **B. Liang**, E. Gardner, R. A. Ross & S. P. Whelan. An In Vitro RNA Synthesis Assay for Rabies Virus Defines Ribonucleoprotein Interactions Critical for Polymerase Activity. ***J Virol*** (2017) *91*; PMC5165209.
   - **B. Liang**, Z. Li, S. Jenni, A. A. Rahmeh, B. M. Morin, T. Grant, N. Grigorieff, S. C. Harrison & S. P. J. Whelan. Structure of the L Protein of Vesicular Stomatitis Virus from Electron Cryomicroscopy. ***Cell*** (2015) *162*, 314-27; PMC4557768.
   - A. A. Rahmeh, B. Morin, A. D. Schenk, **B. Liang**, B. S. Heinrich, V. Brusic, T. Walz & S. P. Whelan. Critical phosphoprotein elements that regulate polymerase architecture and function in vesicular stomatitis virus. ***Proc Natl Acad Sci U S A*** (2012) *109*, 14628-33; PMC3437890.

3. **Illustrated the structure and regulation of the respiratory syncytial virus RNA synthesis machine.** After being independent, I switched the focus to the structure and regulation of the RNA synthesis machine of RSV, a pathogenic NNS RNA virus. The **L** protein and an essential tetramer of **P** constitute the polymerase that acts on the viral genome, which is a complex of genomic RNA tightly coated by nucleoprotein (**N**). In

some cases, additional viral proteins (VP30 in Ebola, and **M2-1** in RSV) are necessary for full polymerase processivity. Thus far, (**1**) We adapted and set up the RSV RNA polymerization assay in the lab and provided new mechanistic insights into the initiation and elongation of RSV RNA synthesis. (**2**) We have determined a 3.67 Å cryo-EM structure of the *apo* RSV polymerase (L:P) complex. (**3**) We established a protocol to obtain RNA-free N protein (N^0) and successfully demonstrated the *in vitro* trackable assembly of N with RNA into nucleocapsid-like particles (NCLPs) for in-depth mechanistic analyses. (**4**) We determined a 2.7 Å co-crystal structure of RSV M2-1 bound to a short RNA oligo and provided a structural basis for the recognition of RNA by M2-1.

a. Y. Gao, D. Cao, H. M. Ahn, A. Swain, S. Hill, C. Ogilvie, M. Kurien, T. Rahmatullah & **B. Liang***. *In vitro* trackable assembly of RNA-specific nucleocapsids of the respiratory syncytial virus. ***J Biol Chem*** (2019); doi:10.1074/jbc.RA119.011602.
b. D. Cao, Y. Gao, C. Roesler, S. Rice, P. D'Cunha, L. Zhuang, J. Slack, M. Domke, A. Antonova, S. Romanelli, S. Keating, G. Forero, P. Juneja & **B. Liang***. Cryo-EM structure of the respiratory syncytial virus RNA polymerase. ***Nat Comm*** (2019) Accepted.
c. Y. Gao, D. Cao, H. M. Ahn, J. M. Ha, P. Parikh, C. Ogilvie, A. Yang, A. Bell, A. Salazar, **B. Liang***. Structural basis for RNA recognition by M2-1 protein of the human respiratory syncytial virus. In revision.
d. D. Cao, Y. Gao, C. Roesler, P. D'Cunha, L. Zhuang, J. Slack, S. Romanelli, **B. Liang***. RNA elongation and fine mapping of the promoter sequence of the respiratory syncytial virus polymerase. In revision.

Complete Publication List:
https://www.ncbi.nlm.nih.gov/myncbi/bo.liang.2/bibliography/public/

D. Additional Information: Research Support and Scholastic Performance

Ongoing Research Support

Emory University, Start-Up Fund Liang (PD/PI) 10/01/2016-09/30/2020
Research Start-Up Fund
Goal: Set up the PI's laboratory and fund preliminary studies for extramural research support.
Role: PI

NIH/NIGMS 1R01GM130950-01A1 Liang (PD/PI) 09/20/2019-07/31/2024
Structure and Regulation of The Respiratory Syncytial Virus Polymerase
Goal: Elucidate the molecular mechanisms of the RSV polymerase, and provide functional and structural insights into RSV RNA synthesis
Role: PI

Research Support Completed During the Last Three Years
None