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.)*

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 complete the proposed research successfully. My training background and broad expertise in the areas of virology, nucleic acids, biochemistry, and structural biology provide me with a unique combination of skills and determination necessary to tackle this challenging project. Throughout my career, I have repeatedly demonstrated that I can successfully work with viral and other ribonucleoprotein complexes using integrated tools. I am also a team player. I have successfully collaborated with many other researchers and produced several peer-reviewed publications from each project.

I have a successful track record of interdisciplinary research and creativity in my scientific career. I initially trained in dual disciplines of biology and computer science as an undergraduate student, and this training provided me with a strong background in biology and the skills in computer scripting and coding. In my Ph.D., I was mentored by a structural biologist (Prof. Hong Li) as an x-ray crystallographer and have expertise in the area of RNA biology, biochemistry, and structural biology of non-coding RNAs and ribonucleoprotein complexes. I determined a number of crystal structures of the box H/ACA ribonucleoprotein complexes (Rashid & Liang et al., Mol Cell 2006; Liang et al., Nat Struct Mol Biol 2007; Liang et al., Nat Struct Mol Biol 2009), and further dissected the function using fluorescence assays (Liang et al., RNA 2008). I was awarded two Predoctoral Fellowships from the American Heart Association. Many of my published studies have involved the assembly of protein and RNA into functional ribonucleoprotein complexes. I have used mutagenesis and structural characterizations extensively to derive the catalytic mechanisms of enzymes studied. These studies contributed significantly to our understanding of the multicomponent-mediated enzyme mechanism of the box H/ACA ribonucleoprotein, which is critical for ribosome and spliceosome biogenesis.

For my postdoctoral research, I was jointly mentored by a structural biologist (Prof. Stephen Harrison, Harvard Medical School, and Howard Hughes Medical Institute) and a virologist (Prof. Sean Whelan, Harvard Medical School). I continued my interests in structural biology and RNA biology and expanded my expertise in virology and electron microscopy. My recent focus involving a multifunction viral RNA polymerase, the L protein of vesicular stomatitis virus, represents a landmark in the evolution of cryo-electron microscopy (cryo-EM). The results were published in Cell entitled: “Structure of the L Protein of Vesicular Stomatitis Virus from Electron Cryomicroscopy” (Liang et al., Cell 2015). For the first time, I achieved near-atomic resolution by utilizing cryo-EM for an asymmetric protein less than 250 kDa, allowing a *de novo* atomic model to be built solely based on EM electron densities. This was also the first polymerase structure in the non-segmented negative-sense RNA virus order. My experiences involved preparation of challenging macromolecular complexes, so I am familiar with and prepared for the challenges to such experiments. My current research is an extension of that outstanding training as it focuses on the function and structure of macromolecules with an emphasis on the

machinery involved in viral replication and propagation. I have generous support from Drs. Harrison and Whelan on the proposed project and may consult with them though they have no plans to work on closely related projects.

Since setting up my independent laboratory at Emory, I have continued to focus on integrating single particle cryo-EM and x-ray crystallography to scrutinize challenging viral and RNA biology questions, in particular, the RSV RNA synthesis machinery. It is essential to note the productive environment at Emory and Atlanta area including Dr. Martin Moore, an expert in RSV biology and reverse genetics, and Dr. Richard Plemper, an expert in identification small molecule inhibitors for RNA viruses. The department is rich with biochemists and structural biologists who attend regular research meetings, where the ideas and data are exchanged. I have a dedicated mentoring committee that consists of established faculty Drs. Richard Kahn, Daniel Reines, Christine Dunham, and Anice Lowen at Emory. Dr. Anita Corbett and the interim departmental chair, Dr. Jeremy Boss, also provide critical feedback. Together, these colleagues have provided (and continue to provide) invaluable guidance on acquiring funding for my laboratory, prioritizing my research efforts, and ensuring that service and teaching commitments are minimal at this early stage of my independent career. In summary, this exciting proposal is innovative and will facilitate the rational design of novel antiviral drugs to treat the devastating diseases that these viruses cause.

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

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-	Single Particle 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
2017-	Scientific Advisor, The Robert P. Apkarian Integrated Electron Microscopy Core, Emory University
2018-	Member, The American Heart Association
2018-	Member, SouthEast Consortium for Microscopy of MacroMolecular Machines (SECM4)

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 key assembly and function stages of a novel family of RNA-guided modification enzyme.** My interests in the macromolecular machine composed of RNA and proteins began with my graduate studies in professor Hong Li's laboratory, where I focused on box H/ACA ribonucleoproteins (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 major components of telomerase, and a set of non-coding guide RNAs to capture ribosomal RNAs and snRNAs for chemical modification. My primary contribution was to determine a set of crystal structures which represent key stages of the box H/ACA RNP assembly and function, including a complex of Cbf5:Nop10:Gar1, one substrate-bound and one functional box H/ACA RNP. I also devised a fluorescence assay to dissect the accurate placement of the substrate RNA and contributed significantly to analyze 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.

   a. **Liang B**, Zhou J, Kahen E, Terns RM, Terns MP, Li H. Structure of a functional ribonucleoprotein pseudouridine synthase bound to a substrate RNA. ***Nat Struct Mol Biol****.* 2009 Jul;16(7):740-6. PubMed PMID: 19478803.
   b. **Liang B**, Kahen EJ, Calvin K, Zhou J, Blanco M, Li H. Long-distance placement of substrate RNA by H/ACA proteins. ***RNA***. 2008 Oct;14(10):2086-94. PubMed PMID: 18755842; PubMed Central PMCID: PMC2553744.
   c. **Liang B,** Xue S, Terns RM, Terns MP, Li H. Substrate RNA positioning in the archaeal H/ACA ribonucleoprotein complex. ***Nat Struct Mol Biol***. 2007 Dec;14(12):1189-95. PubMed PMID: 18059286.
   d. Rashid R, **Liang B,** Baker DL, Youssef OA, He Y, Phipps K, Terns RM, Terns MP, Li H. Crystal structure of a Cbf5-Nop10-Gar1 complex and implications in RNA-guided pseudouridylation and dyskeratosis congenita. ***Mol Cell****.* 2006 Jan 20;21(2):249-60. PubMed PMID: 16427014.

2. **Determined the first atomic cryo-EM structure of the multifunctional polymerase of a non-segmented negative-strand RNA virus.** My subsequent work in the laboratories of Professors Stephen Harrison and Sean Whelan at Harvard Medical School directly visualized the multifunctional large enzyme L protein that encodes the RNA-dependent RNA polymerase, polyribonucleotidyl transferase, and RNA methyltransferase activities 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 rabies, Ebola, respiratory syncytial virus (RSV). The RNA synthesis by the RNA polymerase, comprising of the large protein (L) and the phosphoprotein (P), of these viruses, is central to their life cycle. I have successfully prepared and biochemically characterized the L protein complexes. My colleagues and I obtained the first structural insights using negative-stain EM: L protein forms a ring-like "core" decorated by three globular appendages, and the polymerization activity maps to the core. We showed that the addition of P protein causes the globular appendages to reorganize into a compact tail. Importantly, I obtained a single particle cryo-EM

structure of VSV L at 3.8 Å resolution and performed the *de novo* model building of the 2109-residue polypeptide. Two significant contributions resulted from this work: 1) the determination of the first atomic structure of an asymmetric protein with less than 250 kDa using cryo-EM; 2) the first atomic view of the RNA synthesis machinery of NNS RNA viruses. Recently, I have successfully prepared the Rabies L protein and adapted an *in vitro* transcription assay from VSV to Rabies.

a. Morin B, **Liang B**, Gardner E, Ross RA, Whelan SP. An *In Vitro* RNA Synthesis Assay for Rabies Virus Defines Ribonucleoprotein Interactions Critical for Polymerase Activity. ***J Virol***. 2017 Jan; 91(1): e01508-16. PubMed PMID: 27795419; PubMed Central PMCID: PMC5165209.
b. **Liang B,** Li Z, Jenni S, Rahmeh AA, Morin BM, Grant T, Grigorieff N, Harrison SC, Whelan SP. Structure of the L Protein of Vesicular Stomatitis Virus from Electron Cryomicroscopy. ***Cell***. 2015 Jul 16;162(2):314-27. PubMed PMID: 26144317; PubMed Central PMCID: PMC4557768.
c. Rahmeh AA, Morin B, Schenk AD, **Liang B**, Heinrich BS, Brusic V, Walz T, Whelan SP. Critical phosphoprotein elements that regulate polymerase architecture and function in vesicular stomatitis virus. ***Proc Natl Acad Sci U S A***. 2012 Sep 4;109(36):14628-33. PubMed PMID: 22908284; PubMed Central PMCID: PMC3437890.
d. Rahmeh AA, Schenk AD, Danek EI, Kranzusch PJ, **Liang B**, Walz T, Whelan SP. Molecular architecture of the vesicular stomatitis virus RNA polymerase. ***Proc Natl Acad Sci U S A***. 2010 Nov 16;107(46):20075-80. PubMed PMID: 21041632; PubMed Central PMCID: PMC2993402.

Complete Publication List:
https://www.ncbi.nlm.nih.gov/sites/myncbi/bo.liang.2/bibliography/9974920/public/?sort=date&direction=descending

D. Additional Information: Research Support and Scholastic Performance

Ongoing Research Support

Departmental Start-Up Grant, Emory University Liang (PI) 10/01/2016-09/30/2020

Research Start-Up Funds

Goal: The purpose of this grant is to set up the PI's laboratory and fund preliminary studies needed to be competitive for extramural research support.

Role: PI

Overlap: None

Research Support Completed During the Last Three Years

None