BIOGRAPHICAL SKETCH

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NAME: **Liang, Bo**

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

POSITION TITLE: **Co-Scientific Director and Associate 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.	12/2009	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 necessary to complete the proposed research program successfully. As a graduate student 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 and RNA biology, and virology. I built the foundation for the proposed research by developing effective sample preparation, data acquisition, and analysis strategies. I have comprehensive experience in cryo-EM, including specimen optimization, data collection, image processing, model interpretation, and validation. Additionally, I have rigorous biochemistry and x-ray crystallography training, 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. I am the Co-Scientific Director of the Robert P. Apkarian Integrated Electron Microscopy Core (IEMC) at Emory. My current research focuses on the structures and mechanisms of macromolecules, emphasizing the viral RNA synthesis machinery, neurobiological disease, and cancer-related assemblies. I am also a team player. Through collaboration, I am keen to exploit my expertise in structural biology (cryo-EM & crystallography) to elucidate the molecular machinery and associated mechanisms of traditionally challenging and exciting biological systems. I have successfully collaborated with many other researchers and produced several peer-reviewed publications from each project.

I have successfully determined multiple high-resolution structures of the polymerases from NNS RNA viruses using single-particle cryo-EM. My lab has successfully determined a 3.67 Å cryo-EM structure of the *apo* RSV polymerase (L:P) complex and multiple 2.5-3.5 Å cryo-EM structures of the RSV polymerase in complexes of RNA substrates (thanks to the previous support from NCCAT) in my lab. The primary goal of this proposal is to continue elucidating the structural basis of the RSV synthesis machine, mainly the initiation and elongation stages of RSV transcription carried out by the RSV polymerase complex. Therefore, we request additional data collection resources at NCCAT.

Ongoing and recently completed projects that I would like to highlight:

1R01GM130950, NIH/NIGMS 09/20/2019 - 07/31/2024
Structure and Regulation of The Respiratory Syncytial Virus Polymerase
Role: Liang (PD/PI)

1R01AI162267, NIH/NIAID 03/01/2021 - 02/28/2026
HIV-1 Fusion Peptide-directed Vaccine Design Using Virus-like Particles
Role: Liang (Co-Inv), Kong (PD/PI)

1R01AI162633, NIH/NIAID 05/01/2021 - 04/30/2026
SAMHD1 mediated dNTP regulation and HIV in myeloid cells
Role: Liang (Co-Inv), Kim (PD/PI)

IA-831472, American Lung Association Innovation Award 07/01/2021 - 06/30/2023
Structures and Shared Mechanisms of the RSV and SARS-CoV-2 Viral Polymerases
Role: Liang (PD/PI)

1R01AG079256, NIH/NIA 07/01/2022 - 06/30/2027
Understanding the functional impacts of Aβ variants in Alzheimer's disease with human brain organoids
Role: Liang (MPI), Wen (PD/PI)

B. Positions, Scientific Appointments, and Honors

Scientific Appointments

2022-	Associate Professor of Biochemistry, Emory University School of Medicine, Atlanta, GA
2018-	Co-Scientific Director, Robert P. Apkarian Integrated Electron Microscopy Core, Emory University, Atlanta, GA
2017-	Program Faculty Member, Discovery and Developmental Therapeutics (DDT) Research Program, Winship Cancer Institute, Emory University
2016-	Program Faculty Member, Microbiology and Molecular Genetics (MMG), Graduate Division of Biomedical and Biological Sciences (GDBBS), Emory University School of Medicine
2016-	Program Faculty Member, Biochemistry Cellular and Developmental Biology (BCDB), Graduate Division of Biomedical and Biological Sciences (GDBBS), Emory University School of Medicine
2016-2022	Assistant Professor of Biochemistry, Emory University School of Medicine, Atlanta, GA
2015	Teaching Assistant, Harvard Medical School, Boston, MA
2009-2016	Postdoctoral Research Fellow, Biological Chemistry and Molecular Pharmacology (BCMP), and Microbiology and Immunobiology (MBIB), Harvard Medical School, Boston, MA

Positions and Services

2023-	Member, Governance Committee, University Senate, Emory University
2022-	Member, University Senate Committee on the Environment, Emory University
2021-	Member, Faculty Development Advisory Committee, Emory University School of Medicine
2021-	Executive Committee, BCDB Graduate Program, Emory University
2021-	Member, GDBBS Web Advisory Committee, Emory University
2020-	Recruitment Committee, BCDB Graduate Program, Emory University
2020-	Funding & Resource Application Reviewer: NIH MSFB, NIH VIR SEP, NSF EPSCoR, NSF CAREER, AHA Microbiology, Auckland Medical Research Foundation (New Zealand), Emory URC, NCCAT GUPs, NCCAT GUPs, and BAGs
2018-	Annual Graduate Course Lecturer, Foundations of BCDB (BCDB 502), Emory University
2017-	Annual Graduate Course Lecturer, Virology (IBS 513), Emory University
2017-	Executive Committee, MMG Graduate Program, Emory University
2017-	Editorial Board Member, Journal of Molecular Cell Biology (2017-), Journal of Virology (2021-), Viruses (2022-)

2017-2021 Co-director, Biochemistry Departmental Seminar Program, Emory University School of Medicine
2017, 2021 Faculty Search Committee, Department of Biochemistry, Emory University School of Medicine
2014-2016 Secretary, Harvard Medical Postdoctoral Association, Harvard Medical School
2013-2016 Trainee Committee, Biological Chemistry and Molecular Pharmacology, Harvard Medical School
2013-2014 Associate Editors-in-Chief, the Journal of Postdoctoral Research
2011-2014 Co-Chair, HMS/HSDM Postdoctoral Association, Harvard Medical School
2010-2011 Governing Board, HMS/HSDM Postdoctoral Association, Harvard Medical School

Honors

2021 Hidden Gems, Faculty Excellence Award, Emory University School of Medicine
2021 Scholarly Writing and Publishing Award, Emory University
2020 MP3 (Molecules and Pathogens to Populations and Pandemics) Award, Emory University
2020 The University Research Committee (URC) Award, Emory University
2009 Protein Science Young Investigator Travel Grant, The Protein Society
2008 Kasha Award, Florida State University

Professional Memberships

Member, The RNA Society
Member, The American Society for Biochemistry and Molecular Biology
Member, The American Society of Virology
Member, The American Crystallographic Association
Member, The Microscopy Society of America

C. Contributions to Science

- **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.
  - **Liang B.**, Zhou J., Kahen E., Terns R. M., Terns M. P., Li H. Structure of a functional ribonucleoprotein pseudouridine synthase bound to a substrate RNA. ***Nat Struct Mol Biol*** 16, 740-746 (**2009**) | PMC5706466.
  - **Liang B.**, Kahen E. J., Calvin K., Zhou J., Blanco M., Li H. Long-distance placement of substrate RNA by H/ACA proteins. ***RNA*** 14, 2086-2094 (**2008**) | PMC2553744.
  - **Liang B.**, Xue S., Terns R. M., Terns M. P., Li H. Substrate RNA positioning in the archaeal H/ACA ribonucleoprotein complex. ***Nat Struct Mol Biol*** 14, 1189-1195 (**2007**) | 10.1038/nsmb1336.
  - Rashid R., **Liang B.**, Baker D. L., Youssef O. A., He Y., Phipps K., Terns R. M., Terns M. P., Li H. Crystal structure of a Cbf5-Nop10-Gar1 complex and implications in RNA-guided pseudouridylation and dyskeratosis congenita. ***Mol Cell*** 21, 249-260 (**2006**) | 10.1016/j.molcel.2005.11.017.

- **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.

- Jenni S., Bloyet L. M., Diaz-Avalos R., **Liang B.**, Whelan S. P. J., Grigorieff N., Harrison S. C. Structure of the Vesicular Stomatitis Virus L Protein in Complex with Its Phosphoprotein Cofactor. ***Cell Rep*** 30, 53-60 e55 (**2020**) | PMC7049099.
- Morin B., **Liang B.**, Gardner E., Ross R. A., Whelan S. P. J. An *In Vitro* RNA Synthesis Assay for Rabies Virus Defines Ribonucleoprotein Interactions Critical for Polymerase Activity. ***J Virol*** 91, (**2017**) | PMC5165209.
- **Liang B.**, Li Z., Jenni S., Rahmeh A. A., Morin B. M., Grant T., Grigorieff N., Harrison S. C., Whelan S. P. J. Structure of the L Protein of Vesicular Stomatitis Virus from Electron Cryomicroscopy. ***Cell*** 162, 314-327 (**2015**) | PMC4557768.
- Rahmeh A. A., Morin B., Schenk A. D., **Liang B.**, Heinrich B. S., Brusic V., Walz T., Whelan S. P. Critical phosphoprotein elements that regulate polymerase architecture and function in vesicular stomatitis virus. ***Proc Natl Acad Sci U S A*** 109, 14628-14633 (**2012**) | PMC3437890.

- **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 significant pathogenic NNS RNA virus. The **L** protein and an essential tetramer of **P** constitute the polymerase that acts on the viral genome, 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 transcription assay in the lab, analyzed the template variations, 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 the protocol and optimized the conditions 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 recognizing RNA by M2-1.
  - Gao, Y., Raghavan, A., Deng, B., Lee, J., **Liang B.*** Optimal Conditions for *In Vitro* Assembly of Respiratory Syncytial Virus Nucleocapsid-like Particles. ***Viruses*** 15, (**2023**), 344. DOI: 10.3390/v15020344 | PMID: 36851557 | PMCID: PMC9962444.
  - Cao D., Gooneratne I., Mera C., Vy J., Royal M., Huang B., Park Y., Manjunath A., **Liang B.*** Analysis of Template Variations on RNA Synthesis by Respiratory Syncytial Virus Polymerase. ***Viruses*** 15, (**2022**). DOI: 10.3390/v15010047 | PMID: 36680087 | PMCID: 10.3390/v15010047.
  - Gao Y., Cao D., Pawnikar S., John K., Ahn H. M., Ha J. M., Parikh P., Ogilvie C., Yang A., Bell A., Salazar A., Miao Y.*, **Liang B.*** Structure of the human respiratory syncytial virus M2-1 protein in complex with a short positive-sense gene-end RNA. ***Structure*** 28, 979-990 e974 (**2020**) | PMC7484405.
  - Cao D., Gao Y., Roesler C., Rice S., D'Cunha P., Zhuang L., Slack J., Domke M., Antonova A., Romanelli S., Keating S., Forero G., Juneja P., **Liang B.*** Cryo-EM structure of the respiratory syncytial virus RNA polymerase. ***Nat Commun*** 11, 368 (**2020**) | PMC6969064.

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