BIOGRAPHICAL SKETCH

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NAME: **Chuan Xiao**

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POSITION TITLE: **Associate Professor of Biochemistry**

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
Fudan University, Shanghai, China	B.S.	08/1996	Biochemistry
Fudan University, China	M.S.	08/1998	Biochemistry
Purdue University, West Lafayette, Indiana, USA	Ph.D.	12/2005	Structural Biochemistry
Purdue University, West Lafayette, Indiana, USA	Postdoc	08/08	Structural Biochemistry

A. Personal Statement

Because of my training and achievement in traditional biochemistry and structural biology, I am well qualified to serve as a co-investigator in the BBRC RCMI's basic research project.

Training Experiences: Beginning in 1992, I received training in recombinant DNA and modern molecular biology techniques in the Chinese Rice Genome Project, where I cloned and sequenced hundreds of expressed sequence tags (ESTs) for genomic mapping. I also completed cDNA and genomic sequencing of three Rice genes, including the house keeping gene glyceraldehyde 3-phosphate dehydrogenase (GAPDH). In addition to obtaining a BS degree in biochemistry, I also obtained a minor BS degree in electronic engineering where I acquired my computer skills. In 1998, I joined the laboratory of Dr. Michael Rossmann, at Purdue University, where I acquired systematic training in X-ray crystallography and cryo-electron microscopy (cryoEM). My Ph.D. research was focused on studying several human common cold viruses and their interaction with cellular receptors. After receiving my PhD in 2005, I remained in Dr. Rossmann's lab as a post-doctoral fellow. The reason I chose to stay with the same group is because I wanted to take on the challenge of working on giant virus structures. The size of giant viruses makes their structural investigation extremely challenging using current structural determination techniques. Several experts in the field even had predicted that theoretical limits of current techniques make it impossible to solve the structure of giant viruses. Nevertheless, given my expertise in cryoEM data collection and computational analysis, I had the expertise and experience to work on this challenging project. After three years of hardworking of collecting cryoEM data on three thousand films and solving many computational problems, I was able to determine the first cryo-EM structure of the world's largest virus at that time, the Mimivirus. During my research career at Purdue, I published eight first-author, peer-reviewed papers and co-authored six others.

Academic career development and achievement: My career goal is to apply my expertise in structural biochemistry to fundamental biomedical research that will enhance our understanding of biological processes, based on which developing new diagnosis, treatment and prevention methods can be developed. Since arriving at UTEP in 2008 as a faculty member, my research has expanded to many different areas to study various important biological macromolecules while continuing to explore different viruses using X-ray and cryo-EM. Other novel techniques have also been integrated into my research such as CD (circular dichroism) and SAXS (small angle X-ray scattering). Beside the mammalian circadian project mentioned above, currently other active

projects are listed here as examples: (1) Structural studies of giant marine viruses; (2) Dissecting the molecular regulatory mechanism of mammalian circadian core components; (3) Structural and Functional Studies of a Viral SUMOylation Inhibitor, Gam1; and (4) Structural and functional studies of a virophage integrase. I have collaborative projects working with anthrax toxin, TB, plant photosynthetic system, and interaction between potential drugs with their targeting metabolism proteins. Since arriving at UTEP, I have 18 publications with four more in preparation and one under review. I have been PI of one, co-PI of two, and local institutional PI of two federal grants. I am currently supervising research of one post-doctoral fellow, one Ph.D. student, one master student, and twelve undergraduate students. I have taught more than 2,100 undergraduate students for their biochemistry classes and was awarded "Undergraduate Student Choice Award for Outstanding Teaching" at the department level twice and at the college level once. I have supervised research of three Ph.D. students, two unfinished Ph.D. student (who quit due to severe sickness), five M.S. students, 70 undergraduate students, and nine high school students. I am currently serving or have served on committees of 19 M.S. students and 16 Ph.D. students.

Roles in the proposed research: The proposed research is a continuation of the collaboration between Drs. Robert Kirken, Georgialina Rodriguez, Lin Li and me. This project began in 2016 as a BBRC pilot grant and we have worked on homology modeling of full-length JAK3 in order to understand its phosphorylation regulation. By combining several available domain structures of JAK family proteins, we were able to generate a full-length JAK3 model. In 2018, new faculty Dr. Li joined the team for his expertise in dynamic simulation and analyses of charge-charge interactions. Using the modeled structures, we were able to raise hypotheses about the regulatory mechanisms of some conserved tyrosine residues. In this proposed research, I will continue to provide my knowledge by analyzing available structures and the homology modeled structures. In addition, I will use my extensive training in structural biology, especially in the field of cryo-electron microscopy, to determine and analyze structures of JAK3 so that we can understand its mechanism of phosphorylation regulation and how cancer phenotype SNPs may alter JAK3 function. Other JAK proteins may be modeled as well. The resultant high-resolution structures obtained from the project not only will deepen our understanding of JAK3 regulatory mechanism but also will provide new drug targets for cancer therapy. This project matches very well with my career goals.

B. Positions and Honors

Positions and Employment

2005-2008	Postdoctoral Research Associate, Dept of Biological Science, Purdue University, West Lafayette, IN
2008-2015	Assistant Professor of Biochemistry, Department of Chemistry, UTEP, El Paso, TX
2015-	Associate Professor of Biochemistry, Department of Chemistry, UTEP, El Paso, TX
2009-	Committee member, Institutional Biosafety Committee, UTEP, El Paso, TX
2014-2016	Co-Vice Chair, Institutional Biosafety Committee, UTEP, El Paso, TX

Other Experience and Professional Memberships

2001-	ASV: American Society for Virology
2001-	MSA: Microscopy Society of America
2008-2010	AAAS: American Association for the Advancement of Science
2009-2010	Sigma Xi, serve in admissions committee of UTEP chapter
2010-2012	ACS: American Chemical Society
2010	NSF-MRI Review Panel One, reviewer
2012	NSF-OCE Review Panel, ad hoc reviewer
2015-	SRBR: Society for Research on Biological Rhythms
2016-	ASBMB: American Society for Biochemistry and Molecular Biology

Honors

2001	Graduate student travel grant award, 20th Annual Meeting of American Society for Virology, Madison, Wisconsin, USA
2002	MSA Presidential Student Award of Microscopy & Microanalysis, Quebec City. Canada.
2003	Committee Appreciation Poster Award, 3rd International Conference on Structural Analysis of Supramolecular Assemblies by Hybrid Methods, Lake Tahoe, CA, USA

2007 One of three selected talks from poster session, Workshop on Advanced Topics in EM Structure Determination, San Diego, CA, USA

2008 Postdoctoral travel grant award, 27th Annual Meeting of American Society for Virology, Ithaca, NY, USA

2008 The University of Texas System's Science and Technology Acquisition and Retention Program (STAR) Award

C. Contribution to Science

1. My research career started when I joined the Satellite Laboratory of Chinese Rice Genome Project at Fudan University, Shanghai, in 1992 as a sophomore undergraduate student. I obtained intensive training for molecular biological experiments to clone and sequence hundreds of Rice cDNA clones using the original Sanger methods. These cDNA sequences were used as expressed sequence tags to complete the physical map of the Rice genome. After obtaining my bachelor's degree, I continued to pursue my master's degree program in the same group where I completed cDNA and genomic sequencing of three Rice genes for the first time, including the house keeping gene glyceraldehyde 3-phosphate dehydrogenase (GAPDH), the c subunit of the V-ATPase and a calmodulin with C-terminal prenylation.
   a. **Xiao, C.**, Xin, H., Dong, A., Sun, C. and Cao, K. (1999). "A novel calmodulin-like protein gene in rice which has an unusual prolonged C-terminal sequence carrying a putative prenylation site." *DNA Res* 6(3): 179-81. PMID: 10470849
   b. **Xiao, C.**, Liu, X., Zhan, S., Wang, X. and Cao, K. (1998). "Rice Glyceraldehyde-3-phosphate Dehydrogenase cDNA Structure Analyze and Molecular Evolution Properties." *Progress in Natural Science* 8(4): 411-419.
   c. Database contributions: Genomic sequence of a new calmodulin-like protein (GenBank, AF064456, June, 1998); cDNA sequence of GAPDH (GenBank, U31676, August, 1996); cDNA sequence of 16kDa subunit of Vacuolar H^+-ATPase (GenBank, U27098, June, 1996); cDNA sequence of A new calmodulin-like protein (GenBank, U37936, May, 1996); About 323 ESTs of Rice in GenBank (1996-1998).

2. In 1998, I joined the laboratory of Dr. Michael Rossmann at Purdue University, where I acquired systematic training in X-ray crystallography and cryo-electron microscopy (cryo-EM). My Ph.D. research was focused on studying several human common cold viruses and their interaction with their cellular receptors. I solved the atomic structure of a common cold virus called Coxsackievirus A21 (CVA21) by X-ray crystallography. In addition, I ultimately improved the resolution of cryo-EM reconstruction of the CVA21/ICAM-1 complex to 8Å, the highest resolution of a virus-receptor complex at that time. This work was published in *Structure*, together with a commentary on this accomplishment titled "Viruses Rock and Roll with Their Receptors." I also improved the resolution of the cryo-EM reconstructions of two other common cold viruses complexed with ICAM-1. My analyses of these complexes have since deepened our understanding of virus-receptor interactions that facilitate the development of anti-cold drugs.
   a. **Xiao, C.**, McKinlay, M. A. and Rossmann, M. G. (2010). "Design of Capsid-binding Antiviral Agents against Human Rhinoviruses". in *Structural Virology* M. Agbandje and R. McKenna, Editors, Book Sales Department, Royal Society of Chemistry:Cambridge. p. 319-337.
   b. **Xiao, C.**, Bator-Kelly, C. M., Rieder, E., Chipman, P. R., Craig, A., Kuhn, R. J., Wimmer, E. and Rossmann, M. G. (2005). "The crystal structure of coxsackievirus A21 and its interaction with ICAM-1." *Structure (Camb)* 13(7): 1019-33. PMID: 16004874.
   c. **Xiao, C.**, Tuthill, T. J., Bator Kelly, C. M., Challinor, L. J., Chipman, P. R., Killington, R. A., Rowlands, D. J., Craig, A. and Rossmann, M. G. (2004). "Discrimination among rhinovirus serotypes for a variant ICAM-1 receptor molecule." *J Virol* 78(18): 10034-44. PMID: 15331736; PMCID: PMC514980.
   d. Database contributions: Crystal Structure of Coxsackievirus A21 (PDB, 1Z7S, August, 2005); Human Coxsackievirus A21 complex with ICAM-1KilifiFc (EMDB, 1114, August, 2004); Cryo-EM structure of human Coxsackievirus A21 complexed with five domain ICAM 1KilifiFc (PDB, 1Z7Z, August, 2005)

3. Achieving sub-nanometer (less than 10Å) resolution in cryo-EM in the 1990s was a considerable challenge. To meet this challenge, I developed and improved much of the laboratory software used for image processing and 3D reconstructions. I also developed a new program called RIVEM for plotting and analyzing amino acids on a spherical virus surface, a program that has been widely used in the field.

a. Hafenstein, S., Palermo, L. M., Kostyuchenko, V. A., **Xiao, C.**, Morais, M. C., Nelson, C. D., Bowman, V. D., Battisti, A. J., Chipman, P. R., Parrish, C. R. and Rossmann, M. G. (2007). "Asymmetric binding of transferrin receptor to parvovirus capsids." *Proc Natl Acad Sci U S A* 104(16): 6585-9. PMID: 17420467; PMCID: PMC1871829.
b. Rossmann, M. G., Arisaka, F., Battisti, A. J., Bowman, V. D., Chipman, P. R., Fokine, A., Hafenstein, S., Kanamaru, S., Kostyuchenko, V. A., Mesyanzhinov, V. V., Shneider, M. M., Morais, M. C., Leiman, P. G., Palermo, L. M., Parrish, C. R. and **Xiao, C.** (2007). "From structure of the complex to understanding of the biology." *Acta Crystallogr D Biol Crystallogr* 63(Pt 1): 9-16. PMID: 17164521; PMCID: PMC2483488.
c. **Xiao, C.** and Rossmann, M. G. (2007). "Interpretation of electron density with stereographic roadmap projections." *J Struct Biol* 158(2): 182-7. PMID: 17116403; PMCID: PMC1978246.
d. Programs that were developed are listed at: http://utminers.utep.edu/cxiao/My_programs.htm

4. After receiving my Ph.D. in 2005, I remained in Dr. Rossmann's lab as a post-doctoral fellow taking on an extremely challenging project to determine the first cryo-EM structure of the world's largest virus at that time, the Mimivirus. Due to its size (~7500Å in diameter) and complexity (many layers of structures) approaching that of a small cell, the project was very challenging, requiring large data collection and technique development. By combining with atomic force microscopy, I was able to determine a 65Å resolution structure of this massive virus.
   a. Xiao, C. §, Fischer, M. G., Bolotaulo, D. M., Ulloa-Rondeau, N., Avila, G. A., and Suttle, C. A. (2017). "Cryo-EM reconstruction of the Cafeteria roenbergensis virus capsid suggests novel assembly pathway for giant viruses." Sci Rep 7(1): 5484. PMID: 28710447; PMCID: PMC5511168.
   b. **Xiao, C**, Rossmann, M. G. (2011) "Structures of giant icosahedral eukaryotic dsDNA viruses." *Current Opinion in Virology* 1(2): 101-109. PMID: 21909343. PMCID: PMC3167175
   c. Kuznetsov, Y. G., **Xiao, C.**, Sun, S., Raoult, D., Rossmann, M. and McPherson, A. (2010). "Atomic force microscopy investigation of the giant mimivirus." *Virology* 404(1): 127-37. PMID: 20684838.
   d. **Xiao, C.**, Kuznetsov, Y. G., Sun, S., Hafenstein, S. L., Kostyuchenko, V. A., Chipman, P. R., Suzan-Monti, M., Raoult, D., McPherson, A. and Rossmann, M. G. (2009). "Structural studies of the giant mimivirus." *PLoS Biol* 7(4): e92. PMID: 19402750. PMCID: PMC2671561.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/chuan.xiao.1/bibliography/47304953/public/?sort=date&direction=ascending

D. Additional Information: Research Support and Scholastic Performance

Ongoing Research Support

U24GM116787 Chiu (PI) 06/01/16-05/31/21
CryoEM Data Collection Facility Consortium at NCMI
The goal of this proposal is to provide the highest quality of images acquired in our facility using DDD cameras, as measured by the extent of isotropic data resolution (i.e. computer spectrum and SNR) after frame re-alignment, and also the preservation of both low and high resolution signal for each imaged specimen area to allow accurate particle orientation/tilt image alignment determination leading to the best possible resolution single particle reconstructions or tomograms.
Role: Local institutional PI

U24GM116792 Zhou (PI) 06/01/16-05/31/21
West/Midwest Consortium for High-Resolution Cryo Electron Microscopy
The goal of the consortium is to offer 19 cryoEM users from 10 regional institutes free access to a high-end cryoEM facility with proven high-resolution capabilities located in the California NanoSystems Institute (CNSI) at University of California, Los Angeles (UCLA). UCLA will act as host institute and provide investigators in these cryoEM laboratories access to its highly productive Titan Krios cryo electron microscope recently upgraded with a Volta phase plate, a Gatan imaging filter (GIF), and pre- and post-GIF direct electron detectors. A highly experienced staff with proven records of cryoEM-derived atomic structures will provide on-site assistance to collect data and provide streamlined "movie" pre-processing for our consortium user laboratories. The establishment of this consortium will immediately empower our users with high-resolution cryoEM capabilities for a broad range of biological samples, enabling them to understand mechanisms of action and identify new targets for the development of new therapeutics.

Role: Local institutional PI

Completed Research Support

SC3 GM109870-01 Xiao (PI) 04/01/14-04/30/18
Dissecting the Molecular Regulatory Mechanism of Mammalian Circadian Core Component
The primary goal of this research is to characterize the molecular interactions among the core regulatory components central to mammalian circadian rhythm which will be used to identify potential targets for therapeutics and to suggest strategies for interventions against circadian-linked diseases.
Role: PI

NSF-DBI 1429708 Li (PI) 08/15/14-07/31/18
MRI: Development of a scan-less temporal focusing two-photon fluorescence microscope for high-speed three-dimensional imaging
The goal of the research is to develop a high-speed optical microscope for imaging fluorescent objects and thereafter simultaneously track their fast motion in three-dimensional (3D) space.
Role: Co-PI