OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the applicant (student or fellow). DO NOT EXCEED FIVE PAGES.

NAME: Xu, Mengyuan
eRA COMMONS USER NAME (credential, e.g., agency login)**: MENGYUANXU**
POSITION TITLE: Graduate Student
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)	START DATE MM/YYYY	END DATE (or expected end date) MM/YYYY	FIELD OF STUDY
Nankai University	Bachelor of Science	09/2005	06/2009	Biological Science
Nankai University	Master of Science	09/2009	07/2012	Biochemistry, Molecular Biology, Structural Biology.
Case Western Reserve University	Doctor of Philosophy	07/2013	Expected 01/2020	Pharmacology

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A. Personal Statement:

I earned my bachelor's and master's degree from Nankai University, which is one of the top universities in China. The knowledge and research experience I have gained throughout the years there equipped me with the confidence and determination to continue my research career as a Ph.D. student. The hands-on research experience that I conducted during my undergraduate studies encouraged me to choose structural biology as a primary research interest. Due to the fact that structural biology usually requires solid mathematical background, I chose to study mathematics as my minor bachelor degree and finished it within two years. The knowledge, and most importantly, the spirit of mathematics would always benefit me for future research. Throughout my training, I have done exceptionally well in my academic coursework, which has helped me to advance to candidacy for the PhD degree. Furthermore, my master study focuses on FILIA, a member of the recently identified RNA binding related protein from oocyte/embryo expressed gene family. In that investigation, I solved the crystal structure of the N-terminal fragment of FILIA, which revealed a unique N-terminal extension beyond the canonical KH region that is well known for its RNA binding ability. This experience generated an interest in nucleic acid binding proteins and how they affect cell processes. Therefore, I decided to continue my research career as a PhD student in the Department of Pharmacology at Case Western Reserve University School of Medicine. Under the mentoring of Dr. Derek Taylor, I am working on my PhD project which focuses on understanding the function of telomere binding proteins in telomere maintenance. As a Ph.D. student, I have benefited from my research experience not only in experiment design and critical thinking, but also in communicating science by improving my writing and presentation skills. I would like to finish my Ph.D. work in the next year, then start a postdoc position in the similar field (telomere study or nucleic acid study). After several years postdoc experience, I would like to start my own lab

where I am able to combine my expertise in structural and biophysical methods with my newly acquired skills in cell biology.

B. Positions and Honors

Positions

ACTIVITY/ OCCUPATION	START DATE MM/YYYY	END DATE MM/YYYY	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Research Assistant	07/2012	06/2013	Biochemistry	Nankai University	Xinqi Liu

Professional Memberships
2016- American Heart Association

Honors
2010~2011 The Third Class Scholarship for Graduate Student, NKU
2009~2010 The First Class Scholarship for Graduate Student, NKU
2006~2007 The Third Class Scholarship for undergraduate Student, NKU
2005~2006 The First Class Scholarship for undergraduate Student, NKU

C. Contribution to Science

1. The primary focus of my Ph.D. work has focused on understanding the structure and function of the telomere binding protein complex called shelterin. Using structural, biophysical, and biochemical techniques, we have identified specific regions of the telomere TPP1 protein that function uniquely in telomere assembly and in regulating telomerase.

a. Zeng, X., Hernandez-Sanchez, W., **Xu, M.**, Whited, T.L., Baus, D., Zhang, J., Berdis, A.J., & Taylor, D.J. (2018) Induction of cancer cell death by telomerase-mediated incorporation of a nucleoside analog into telomeric DNA. Cell Reports. 23: 3031-3041.
b. Rajavel, M., Orban, T., **Xu, M.**, Hernandez-Sanchez, W., de la Fuente, M., Palczewski, K., & Taylor, D. J. (2016) Dynamic peptides of human TPP1 fulfill diverse functions in telomere maintenance (2016). *Nucleic Acids Research*. 2016 Dec 1; 44(21): 10467–10479.
c. Hernandez-Sanchez W.*, **Xu M.*,** & Taylor, D.J. (2016) Telomere maintenance and genome stability. In: Kovalchuk I and Kovalchuk O (Eds), Genome Stability. Cambridge: Elsevier Inc. *co-first author

2. In collaboration with Dr. Junran Zhang in Department of Radiation Oncology, I have contributed to understanding the role of RNF126, an E3 ubiquitin ligase, in regulating homologous recombination events. We demonstrate that RNF126 facilitates homologous recombination by promoting the expression of BRCA1, dependent on its promoter transcription factor E2F1.

a. Wang, Y., Deng, O., Feng, Z., Du, Z., Xiong, X., Lai, J., Yang, X., **Xu, M.**, Wang, H., Taylor, D. J., Yan, C., Chen, C., Difeo, A., Ma, Z. and Zhang, J. (2015) RNF126 promotes homologous recombination via regulation of E2F1-mediated BRCA1 expression. Oncogene.

3. During my Master's study, I worked with Dr. Xinqi Liu to determine the structure and function of a

novel identified KH domain containing protein Filia. In this study, we determine the structure of Filia N-terminus, which provides a novel model of the N-terminal extension beyond the canonical KH domain. We also demonstrate that the N-terminal extension plays critical roles in retaining RNA binding ability of Filia, providing new insight into the function of KH domain containing proteins.

a. J, Wang.*, **Xu, M.***, K, Zhu, L, Li., X, Liu. (2012) The N-terminus of FILIA Forms an Atypical KH Domain with a Unique Extension Involved in Interaction with RNA. PLoS One 7: e30209. *co-first author

D. Scholastic Performance

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE
	Nankai University				
2005-2006	advanced mathematics 2-1	99	**2005-2006**	Ideological and moral cultivation	86
	fundamental knowledge of computer system and C language 2-1	96		Physical education4-1	93
	College English band 1	84		Principles of Marxist philosophy	87
	Inorganic and analytical chemistry experiment	87		Physical education 4-2	87
	Inorganic and analytical chemistry	96		Military theory and training 2-1	85
	Advanced mathematics 2-2	99		Military theory and training 2-2	89.5
	Basic physics 2-1	95		Introduction to the world of the magical superconducting	84
	Fundamental knowledge of computer systems and C language	83		Demonstrate of physical experiment	89
	College English band 2	91		Appreciation of Classical English songs	85
	College English band 4	73	**2006-2007**	Introduction to Law	85
	Organic Chemistry	93		Taiji-quan	89
	Organic Chemistry experiment	88		Mathematical culture	87
2006-2007	Basic physics 2-2	93		Cognitive psychology	95
	Basic physics experiment	85		Principles of Marxist political economics	87
	Biochemistry	79		Wushu routine 2-2	90
	Experiment of Biochemistry	89		Teaching practice	97
	Experimental animal biology 2-1	86	**2007-2008**	Introduction to Mao Zedong thought	85
	Animal biology	91		Introduction to Deng Xiaoping thought	85
	Conservation biology	95	**2009-2010**	Marxist Theory I	85
	Basis of computer software technology	91		First Foreign Language (English)	P
	Cell biology	89		Marxist Theory II	83
	Experiment of cell biology	89			
	Experimental animal biology 2-2	88			
	Animal biology 2-2	81			

	Plant biology	81
	Plant biology experiment	88
	Entomology	90
	Taxonomy of medicine plant	91
	Computational Science and technique in biology system	94
	Progress in life science	94
2007-2008	Experiment of microbiology	88
	Genetics	92
	Genetics experiment	91
	Microbiology	85
	Physical chemistry	96.6
	General ecology	83
	Animal behavior	93
	Basic immunology	89
	Analytic geometry and higher algebra 2-1	88
	Mathematical analysis 3-1	69
	Molecular biology experiment	89
	Molecular biology	80
	Bio-medical Material	97
	Analytic geometry and higher algebra 2-2	83
	Probability theory	60
	Macro- and Micro-Economics	82
	Mathematical analysis 3-2	86
2008-2009	College Chinese	81
	Abstract algebra	78
	Mathematical analysis 3-3	60
	Ordinary differential equations	65
	Real analysis	60
	Graduation thesis	88
2009-2010	English scientific presentation and writing	86
	Advanced molecular Genetics I	82
	Molecular Cell Biology I	89.2
	Advanced Biochemistry	90
	Modern Biological technology	75
	Development and evolution and bioscience and biotechnology	89
	Teaching practice	P
	Introduction to structural biology	89
	Expression and regulation of eukaryotic gene	97
	Human genetics	94
	Cell biology: subcellular structure and function	93
	Molecular Virology	88
	Case Western Reserve University	
2013-2014	Physiology/Biophysics departmental seminar	P
	Protein structure and function	A
	Advanced structural biology-X ray	A
	Advanced structural biology-computational biology	B
	Journal club structural biology	P
	Pharmacology seminar series	A

	Principles of pharmacology I	A
	Being a professional Scientist	P
2014-2015	Pharmacology Seminar	B
	Principles of Pharmacology II	B
	Pharmacology Seminar	B

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Taylor, Derek J

eRA COMMONS USER NAME (credential, e.g., agency login): WADS117

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Fort Lewis College	B.S.	1993-1997	Biochemistry; Cell & Molecular Biology
University of California, San Diego	Ph.D.	1999-2003	Biochemistry; Virology; Structural Biology
The Wadsworth Center	Post-Doc	2004-2008	Computational Biology; Molecular Imaging
University of Colorado at Boulder	Visiting Scientist	2008-2009	Biochemistry; Structural Biology

A. Personal Statement

My lab relies on the accessibility of state-of-the-art cryo electron microscopy (cryoEM) and detection equipment in order to probe the three-dimensional structure of macromolecular complexes. My diverse training in electron microscopy, x-ray crystallography, biochemistry, and molecular biology places me in a unique position to engage in a multifaceted approach for investigating these structures. As a graduate student I was trained in molecular virology, x-ray crystallography, and macromolecular biophysics under Dr. Jack Johnson (The Scripps Research Institute). Later, during my postdoctoral tenure, my research concentrated on understanding ribosome dynamics and the independent steps required for protein synthesis. Using cryoEM and single particle reconstruction, I determined the three-dimensional structure of factors bound to the eukaryotic ribosome at subnanometer resolution. I was fortunate to learn cryoEM under the tutelage of Dr. Joachim Frank (now at Columbia Univ), a pioneer in the EM field and together we published specialized papers describing cryoEM related techniques. After my postdoctoral career, I spent one year working with Dr. Tom Cech (Univ. of Colorado), a leader in the RNA field and Nobel Laureate, investigating the structure and function of telomere and telomerase nucleoprotein complexes. I have continued to use electron microscopy as a primary tool in my independent lab, now at Case Western Reserve University. Specifically, my lab uses electron microscopy to probe the structures of assemblies that are important to mRNA 3' processing, telomere complexes, functional ribosome complexes, the ABCA4 transporter, and Protein Phosphatase 2A.

B. Positions and Honors

Positions and Employment

1995 Undergraduate Student Research Assistant, Fort Lewis College
1996 Undergraduate Student Research Assistant, University of Georgia
1997-1999 R&D Chemist, Rosemont Pharmaceutical Inc., Denver, CO
1999-2003 Graduate Student Research Assistant, University of California, San Diego with Dr. John E. Johnson
2004-2008 HHMI Postdoctoral Fellow, Health Research Inc., The Wadsworth Center with Dr. Joachim Frank
2008-2009 Visiting Scientist, University of Colorado at Boulder with Dr. Thomas R. Cech
2009 – 2017 Assistant Professor, Department of Pharmacology, Case Western Reserve University
2017 – Associate Professor with tenure, Department of Pharmacology, Case Western Reserve University

Professional Memberships

2010 – American Association for the Advancement of Sciences
2010 – American Society for Pharmacology and Experimental Therapeutics
2007 – Microscopy Society of America
2005 – Biophysical Society

Honors and Awards

2013 National Institutes of Health Director's New Innovator Award
2013 American Cancer Society – Research Scholar Award
2011 Case Western Reserve University School of Medicine – Mt. Sinai Scholar
2011 American Heart Association – Young Investigator Award
2004-2008 Howard Hughes Medical Institute Postdoctoral Fellow
2002 The Scripps Research Institute Society of Fellows Poster Award
2000-2003 University of California, San Diego Excellence in Teaching Award
1997 Fort Lewis College Senior in Chemistry Award
1997 Magna Cum Laude, Fort Lewis College
1996-1997 Beta Beta Beta Biological Honor Society

C. Contributions to Science

1. Work from my lab has contributed toward an understanding of the interactions that occur between telomere end-binding proteins and telomere DNA. The POT1-TPP1 heterodimer binds selectively to single-stranded DNA exhibiting telomere sequence. In addition to preventing illicit induction of the DNA damage response, POT1-TPP1 interacts intimately with telomerase to localize it to the telomere and to enhance its ability to synthesize telomere DNA. Work from my lab has demonstrated that the binding of multiple POT1-TPP1 proteins unfolds DNA secondary structure and compacts the telomere DNA into globular structures, where the protein likely surrounds the DNA to provide more protection. Together, these data provide insight into how POT1-TPP1 proteins interact with telomere DNA to protect it from degradation and regulate telomerase-mediated extension.

    a. Hernandez-Sanchez, W., Huang, W., Plucinsky, B., Garcia-Vazquez, N., Robinson, N.J., Schiemann, W.P., Berdis, A.J., Skordalakes, E., & **Taylor, D.J.** (2018) A non-natural nucleotide uses a specific pocket to selectively inhibit telomerase activity. *PLOS Biology.* Epub: April 5, 2019. https://doi.org/10.1371/journal.pbio.3000204. PMID: 30951520.
    b. Zeng, X., Hernandez-Sanchez, W., Xu, M., Whited, T.L., Baus, D., Zhang, J., Berdis, A.J., & **Taylor, D.J.** (2018) Induction of cancer cell death by telomerase-mediated incorporation of a nucleoside analog into telomeric DNA. *Cell Reports.* 23: 3031-3041. PMID: 29874588.
    c. Rajavel, M., Orban, T., Xu, M., Hernandez-Sanchez, W., de la Fuente, M., Palczewski, K., & **Taylor, D.J.** (2016) Dynamic peptides of human TPP1 govern diverse functions in maintaining telomeres. *Nucl. Acids. Res*. 44(21): 10467-10479. PMID: 27655633.
    d. Mullins, M.R., Rajavel, M., Hernandez-Sanchez, W., de la Fuente, M., Biendarra, S., Harris, M.E., & **Taylor, D.J.** (2016) POT1-TPP1 binding to telomere DNA discriminates against G-quadruplex structural morphology. *J. Mol. Biol.* Epub: 428(13): 2695-2708. PMID: 27173378.
    e. Rajavel, M., Mullins, M.R., & **Taylor, D.J.** (2014) Multiple facets of TPP1 in telomere DNA maintenance. *Biochim Biophys Acta Proteins & Proteomics.* 1844:1550-1559. PMID: 24780581

2. My work has also focused on understanding the intricate details of ribosome-catalyzed, protein synthesis in eukaryotes. Years before being solved by x-ray crystallography, I was able to use cryo-EM to detail one of the first structures of a eukaryotic 80S ribosome at sub-nanometer resolution that included the full sequence of ribosomal RNA and many of the ribosomal proteins. My work also revealed, in molecular detail, how specific factors interact with the eukaryotic ribosome to perform distinct functions. Bacterial toxins, including exotoxin A and diphtheria toxin, exert cytotoxicity by adding an ADP-ribosylation (ADPR) moiety to a uniquely modified diphthamide residue residing at the tip of eukaryotic elongation factor 2 (eEF2). In separate studies, I used cryo-EM to understand how eukaryotic release factors coordinate to bind the mammalian ribosome when a STOP codon exists in its A-site. Finally, we have shown how stress conditions stall protein translation in eukaryotic cells by causing 80S ribosomes to enter a reversible state of hibernating dimeric structures.

a. **Taylor, D.**, Unbehaun, A., Li, W., Das, W., Lei, S., Lao, H., Grassucci, R.A., Pestova, T.V., & Frank, J. (2012) Cryo-EM structure of the mammalian eRF1-eRF3-associated termination complex. *Proc Natl Acad Sci U S A*, 109, 18413-8. PMID: 23091004.
b. Krokowski, D., Gaccioli, F., Majumder, M., Mullins, M.R., Yuan, C.L., Papadopoulou, B., Merrick, W.C., Komar, A.A., **Taylor, D.**, & Hatzoglou, M. (2011) Characterization of hibernating ribosomes in mammalian cells. *Cell Cycle.* 10(16):1-12. PMID: 21768774.
c. **Taylor, D. J.**, Devkota, B., Huang, A., Topf, M., Narayanan, E., Sali, A., Harvey, S., & Frank, J. (2009) Comprehensive Molecular Structure of the Eukaryotic Ribosome. *Structure.* 17, 11591-1604. PMID: 20004163.
d. Frank, J., Gao, H., Sengupta, J., Gao, N., & **Taylor, D.J.** (2007) The process of mRNA-tRNA Translocation. *Proc Natl Acad Sci U S A*, 104, 19671-8. PMID: 18003906.
e. **Taylor, D.J.**, Nilsson, J., Merrill, A.R., Andersen, G.R., Nissen, P., and Frank, J. (2007) Structures of modified eEF2•80S ribosome complexes reveals the role of GTP hydrolysis in translocation. *EMBO J.* 26, 2421-2431. PMID: 17446867.

3. In addition to the ribosome and telomere complexes mentioned above, my lab has used electron microscopy to define the structural architecture of assemblies that are important for DNA packaging, mRNA 3' processing and membrane transport. Combining x-ray crystallography and electron microscopy, we assembled a complete model of the P22 bacteriophage tail needle and demonstrated a pH-induced dependence on its structural organization. The structural data of the human pre-mRNA 3' processing complex remains the most comprehensive analysis of the fully assembled complex. Similarly, the three-dimensional structure of the ABCA4 ATP transporter is the most complete structure of this receptor to-date. The structural analysis of the ABCA4 transporter combined with immunolabeling provided the precise localization of the individual domains of the transporter to fully define its molecular organization. The structure of ACBA4 in ATP-bound and ADP-bound states further identified conformational changes in the transporter that are responsible for its function.

    a. Basak, S., Gicheru, Y., Samanta, A., Molugu, S., Huang, W., de la Fuente, M., Hughes, T., **Taylor, D.J.**, Nieman, M., Moiseenkova-Bell, V., & Chakrapani, S. (2018) Cryo-EM structure of the full-length 5-HT3A receptor in its resting conformation. *Nat. Comm.* Epub: 2018 Feb 6;9(1):514. PMID: 29410406.
    b. Scott, H., Kim, J-K., Yu, C., Huang, L. Qiao, F., & **Taylor, D.J.** (2017) Spatial organization and molecular interactions of the *Schizosaccharomyces pombe* Ccq1-Tpz1-Poz1 shelterin complex. *J. Mol Biol.* 429:2863-2872. PMID: 28807855.
    c. Bhardwaj, A., Sankhala R.S., Olia, A.S., Brooke, D., Casjens, S.R., **Taylor, D.J.**, Prevelige Jr., P.E., & Cingolani, G. (2016) Structural plasticity of the protein plug that traps newly packaged genomes in *Podoviridae virions*. *J. Biol. Chem*. 291:215-226. PMID: 26574546.
    d. Tsybovsky, Y., Orban, T., Molday, R.S., **Taylor, D.**, & Palczewski, K. (2013) Molecular organization and ATP-induced conformational changes of ABCA4, the photoreceptor-specific ABC transporter. *Structure*, 854-860. PMID: 23562398
    e. Shi, Y., Di Giammartino, D.C., **Taylor, D.**, Sarkeshik, A., Rice, W.J., Yates III, J.R., Frank, J., & Manley, J.L. (2009) Molecular Architecture of the Human pre-mRNA 3' Processing Complex. *Mol. Cell.* 33, 365-376. PMID: 19217410.

4. My Ph.D. thesis focused on understanding the structure, function, assembly and maturation of small, non-enveloped eukaryotic viruses. I worked primarily on *Nudaurelia capensis* ω virus (NωV), a *T=4* icosahedral virus that shares structural homology with poliovirus and exhibits an auto-catalytic cleavage of its coat protein that is similar to that of reovirus. I used genetic mutations and biophysical analysis, which included cryo-EM, to characterize NωV maturation and autocatalytic cleavage. We discovered that the autocatalytic cleavage event "locks" the NωV capsid in its mature state. However, I showed that mutating the asparagine residue at the scissile bond made the pH-induced maturation of NωV reversible, while other mutations abrogated proper assembly of the virion. As a potential antiviral approach, we identified small molecule compounds that would block maturation of NωV. Finally, during my Ph.D. training, I was able to use x-ray crystallography to solve the structure of Providence virus that, like NωV, is a member of the *Tetraviridae* Family.

    a. Speir, J.A., **Taylor, D.J.**, Natarajan, P., Pringle, F.M., Ball, L.A. & Johnson J. E. (2010) Evolution in Action: N and C Termini of Related T=4 Viruses Exchange Roles as Molecular Switches. *Structure.* 18:700-709. PMID: 20541507.

b. **Taylor, D.J.**, Speir, J.A., Reddy, V., Cingolani, G., Pringle, F.M., Ball, L.A., and Johnson, J.E. (2006) Preliminary x-ray characterization of authentic providence virus and attempts to express its coat protein gene in recombinant baculovirus. *Arch Virol*, 151, 155-165. PMID: 16211330.
c. **Taylor, D.J.**, and Johnson, J.E., (2005) Folding and Particle Assembly are Disrupted by Single Point Mutations near the Auto-catalytic Cleavage Site of *Nudaurelia capensis* ω *virus* Capsid Protein *Protein Sci.* 14, 401-408. PMID: 15659373.
d. Lee, K.K., Tang, J., **Taylor, D.**, Bothner, B., Johnson, J.E. (2004) Small compounds targeted to subunit interfaces arrest maturation in a nonenveloped, icosahedral animal virus. *J. Virol.*, 13, 7208-7216. PMID: 15194797.
e. **Taylor, D.J.**, Krishna, N.K., Canady, M.A., Schneemann, A., and Johnson, J.E. (2002) Large Scale, pH-Dependent, Quaternary Structure Changes in an RNA Virus Capsid are Reversible in the Absence of Subunit Autoproteolysis. *J. Virol.*, 76, 9972-9980. PMID: 12208973.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/16E_oA59hirQC/bibliography/46016877/public/?sort=date&direction=descending