BIOGRAPHICAL SKETCH

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NAME: Zhang, Yi

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

POSITION TITLE: Assistant 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
Peking University, Beijing	B.S	06/2010	Chemistry
Peking University, Beijing	Ph.D.	07/2015	Biochemistry and Molecular Biology
University of Colorado Anschutz Medical Campus, Aurora, CO	Postdoctoral	06/2021	Structural Biology and Epigenetics

A. Personal Statement

I am a tenure-track assistant professor who just started this summer with a long-standing research interest focuses on elucidating the molecular basis of cellular pathways important for human health and disease biology. My past work mainly focused on determining the molecular mechanisms and biological consequences of reading out epigenetic marks. I have co-authored more than 30 publications in the past five years on different aspects of chromatin biology. Examples of my contribution include characterizing the ZZ domain as a new epigenetic reader and a degradation signal sensor, which expanded into the awarded K99/R00 proposal that aims to understand the basic biology of p62, particularly the structure-function relationship and regulation of p62 in the cytosol. Other examples of my contribution include extensive characterization of nuclear condensates *in vitro* and in cell, which is another research focus in my group.

Research in my lab investigates topics at the interface of chemistry and biology, focusing on elucidating the molecular basis of cellular pathways important for human health and disease biology. We employ integrative approaches to study the structure and behavior of macromolecules, understand their functions, and then predict and validate their roles in different cellular contexts. In this pilot project, I propose to determine the structural mechanisms of ATE1-catalyzed protein arginylation using cryo-EM. Together with our ongoing research on the mechanisms and regulation of ATE1 and arginylated-protein receptor p62, preliminary data generated by this grant will be critical to support my R01 applications (planned for submission in October 2023 to both NCI and NIGMS) aiming at an in-depth mechanistic study.

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

Citations:

1. **Zhang Y**[*], Mun SR[*], Linares JF, Ahn J, Towers CG, Ji CH, Fitzwalter BE, Holden MR, Mi W, Shi X, Moscat J, Thorburn A, Diaz-Meco MT, Kwon YT, Kutateladze TG. ZZ-dependent regulation of p62/SQSTM1 in autophagy. Nat Commun. 2018 10 22; 9(1):4373.
2. **Zhang Y**, Mun SR, Linares JF, Towers CG, Thorburn A, Diaz-Meco MT, Kwon YT, Kutateladze TG. Mechanistic insight into the regulation of SQSTM1/p62. Autophagy. 2019 Apr; 15(4):735-737.
3. Mi W*, **Zhang Y***, Lyu J, Wang X, Tong Q, Peng D, Xue Y, Tencer AH, Wen H, Li W, Kutateladze TG, Shi X. Recognition of histone H3 by the ZZ-type zinc finger of ZZZ3 modulates ATAC-mediated histone acetylation and gene activation. Nat Commun. 2018 Sep 14;9(1):3759. PubMed PMID: 30217978.
4. **Zhang Y***, Xue Y*, Shi J, Ahn J, Mi W, Ali M, Wang X, Klein BJ, Wen H, Li W, Shi X, Kutateladze TG. The ZZ domain of p300 mediates specificity of the adjacent HAT domain for histone H3. Nat Struct Mol Biol. 2018 Aug 27; PubMed PMID: 30150647.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2021-	Assistant Professor, SOM-Biochemistry, Case Western Reserve University, Cleveland, OH
2022-	Member, Case Western Reserve University Comprehensive Cancer Center
2015-2021	Postdoctoral Fellow, University of Colorado Anschutz Medical Campus, Aurora, CO

Other Experience and Professional Memberships

2018-Present	Member, American Society for Biochemistry and Molecular Biology
2018-Present	Member, Genetics Society of America
2018-2020	GENETICS Early Career Reviewer

Honors

2019	James Maller Memorial postdoc award, Dept. of Pharmacology, CU Anschutz
2018	Post-doctoral Award for Outstanding Achievement, Dept. of Pharmacology, CU Anschutz
2014	National Fellowship for graduate students, China

C. Contributions to Science

1. Histone proteins, which compact genomic DNA, can be heavily decorated with PTMs, which are also referred to as epigenetic marks. Chemical nature and location of these marks correlate with every aspect of DNA templated processes and, therefore, vitally important for normal development and in disease. My earlier publications aimed to define the functions of 'reader' domains, which selectively recognize these marks, ensuring the correct readout of epigenetic landscape. For example, we found the CW domain of MORC3 is a specific reader for H3K4me3 mark, the ZZ domain binds to the exposed N-terminus of H3 tail, whereas the PHD domain of PHF23 recognizes H3K4me3 mark. These publications reinforced the idea that chromatin interacting proteins utilize specific structural modules to bind corresponding histone marks, leading to proper enrichment at their target genomic sites. I served as the primary investigator or co-investigator in all of these studies.
   a. Andrews FH, Tong Q, Sullivan KD, Cornett EM, **Zhang Y**, Ali M, Ahn J, Pandey A, Guo AH, Strahl BD, Costello JC, Espinosa JM, Rothbart SB, Kutateladze TG. Multivalent Chromatin Engagement and Inter-domain Crosstalk Regulate MORC3 ATPase. Cell Rep. 2016 Sep 20;16(12):3195-3207. PubMed PMID: 27653685.
   b. Mi W*, **Zhang Y***, Lyu J, Wang X, Tong Q, Peng D, Xue Y, Tencer AH, Wen H, Li W, Kutateladze TG, Shi X. Recognition of histone H3 by the ZZ-type zinc finger of ZZZ3 modulates ATAC-mediated histone acetylation and gene activation. Nat Commun. 2018 Sep 14;9(1):3759. PubMed PMID: 30217978.
   c. Klein BJ, Vann KR, Andrews FH, Wang WW, Zhang J, **Zhang Y**, Beloglazkina AA, Mi W, Li Y, Li H, Shi X, Kutateladze AG, Strahl BD, Liu WR, Kutateladze TG. Structural insights into the p-p-p stacking mechanism and DNA-binding activity of the YEATS domain. Nat Commun. 2018 11 01; 9(1):4574.
   d. **Zhang Y**, Guo Y, Gough SM, Zhang J, Vann KR, Li K, Cai L, Shi X, Aplan PD, Wang GG, Kutateladze TG. Mechanistic insights into chromatin targeting by leukemic NUP98-PHF23 fusion. Nat Commun. 2020 Jul 03; 11(1):3339. PMID: 32620764.

2. Epigenetics is a fundamental mechanism that regulates chromatin structure and gene transcription. Reader domains are rarely present as single modules in proteins and more often function in combination with other readers or writer domains. How separate modules cooperate is not well understood. In addition to simple 'reading' events, I also studied how reader domains regulate the activity of adjacent effector domains, in other words, the direct consequence following reading out the epigenetic marks. For instance, the ZZ domains of p300 and ZZZ3 bind histone H3 tail, leading to selective acetylation of H3K18 and H3K27 by p300 but H3K9 acetylation by ZZZ3 containing ATAC complex. For MORC3, the CW domain binds to the H3 tail, releasing its autoinhibition state and activating the chromatin remodeler. These studies emphasize a context-dependent role of chromatin reader domains, particularly in directing the enzymatic activity of chromatin modifiers.
   a. Gatchalian J, Wang X, Ikebe J, Cox KL, Tencer AH, **Zhang Y**, Burge NL, Di L, Gibson MD, Musselman CA, Poirier MG, Kono H, Hayes JJ, Kutateladze TG. Accessibility of the histone H3 tail in the nucleosome for binding of paired readers. Nat Commun. 2017 Nov 14; 8(1):1489. PMID: 29138400.

b. **Zhang Y***, Xue Y*, Shi J, Ahn J, Mi W, Ali M, Wang X, Klein BJ, Wen H, Li W, Shi X, Kutateladze TG. The ZZ domain of p300 mediates specificity of the adjacent HAT domain for histone H3. Nat Struct Mol Biol. 2018 Aug 27; PubMed PMID: 30150647.
c. **Zhang Y**, Klein BJ, Cox KL, Bertulat B, Tencer AH, Holden MR, Wright GM, Black J, Cardoso MC, Poirier MG, Kutateladze TG. Mechanism for autoinhibition and activation of the MORC3 ATPase. Proc Natl Acad Sci U S A. 2019 03 26; 116(13):6111-6119.
d. Klein BJ, Jang SM, Lachance C, Mi W, Lyu J, Sakuraba S, Krajewski K, Wang WW, Sidoli S, Liu J, **Zhang Y**, Wang X, Warfield BM, Kueh AJ, Voss AK, Thomas T, Garcia BA, Liu WR, Strahl BD, Kono H, Li W, Shi X, Côté J, Kutateladze TG. Histone H3K23-specific acetylation by MORF is coupled to H3K14 acylation. Nat Commun. 2019 Oct 17; 10(1):4724. PMID: 31624313.

3. While analyzing the molecular interactions between epigenetic reader domains and histone tail, it became clear that most of these interactions require only 4-8 amino acids in length. Considering the thousands of genes in the human genome, I started to deliberately search for the non-canonical sequences that histone reader domains may recognize. We found that a PHD finger of MLL4 can specifically read out histone H4K16ac mark, using the same binding pocket which typically binds to H3K4me3 mark in other PHD finger domains. We also found an influenza peptide mimicking histone H3 and hijacking the CW domain of MORC3. These studies highlight the potential crosstalk between epigenetic and cellular/viral pathways, integrating gene regulation with other cellular processes.
   a. **Zhang Y**[*], Jang Y[*], Lee JE, Ahn JW, Xu L, Holden MR, Cornett EM, Krajewski K, Klein BJ, Wang SP, Dou Y, Roeder RG, Strahl BD, Rothbart SB, Shi X, Ge K, Kutateladze TG. Selective binding of the PHD6 finger of MLL4 to histone H4K16ac links MLL4 and MOF. Nat Commun. 2019 05 24; 10(1):2314.
   b. **Zhang Y**, Ahn JW, Green KJ, Vann KR, Black J, Brook CB, Kutateladze TG. MORC3 is a target of the Influenza A viral protein NS1. Structure. 2019 Jun 04; 27(6):1029-1033.e3.

4. Another field emerging from my earlier work involves the phase transition of chromatin-modifying enzymes. These studies found both chromatin remodeler MORC3 and histone acetyltransferase p300 form nuclear condensates possessing liquid/gel-like property. The number and size of MORC3 condensates are regulated through the cell cycle; whereas for p300, condensates formation attenuates its catalytic activity. This body of work shows an exciting new layer of chromatin regulation through forming local compartments by phase transition.
   a. **Zhang Y**, Bertulat B, Tencer AH, Ren X, Wright GM, Black J, Cardoso MC, Kutateladze TG. MORC3 Forms Nuclear Condensates through Phase Separation. iScience. 2019 Jul 26; 17:182-189.
   b. **Zhang Y**, Kutateladze TG. Liquid-liquid phase separation is an intrinsic physicochemical property of chromatin. Nat Struct Mol Biol. 2019 Dec; 26(12):1085-1086. PMID: 31695191.
   c. **Zhang Y**[#], Narlikar GJ[#], Kutateladze TG[#]. Enzymatic Reactions inside Biological Condensates. J Mol Biol. 2020 Aug 14. PMID: 32805219. ([#]Corespondance)
5. **Zhang Y**, Brown K, Yu Y, Ibrahim Z, Zandian M, Xuan H, Ingersoll S, Lee T, Ebmeier CC, Liu J, Panne D, Shi X, Ren X, Kutateladze TG. Nuclear Condensates of p300 formed through the structured catalytic core can act as a storage pool of p300 with reduced HAT activity. Nat Commun. 2021 Jul 29; 12, 4618

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/yi.zhang.11/bibliography/public/

D. Research Support

Completed Research Support
K99 CA241301
Zhang (PI)
07/01/19-6/30/21
p62 in Cancer: Mechanism and Regulation

Active Research Support:
R00 CA241301
Zhang (PI)
08/1/21-7/31/24
p62 in Cancer: Mechanism and Regulation

BIOGRAPHICAL SKETCH

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NAME: Taylor, Derek J

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

POSITION TITLE: 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

A primary focus of my lab is to understand the molecular architecture and functional interactions that govern assembly, regulation, and mechanism of proteins and complexes that control fundamental biological events. An overarching goal is to use the detailed, mechanistic insight gained from structural analysis and molecular function to design small molecules that can be used to manipulate these processes in cancer cells. As an example, my group has investigated how telomere end-binding proteins interact exclusively with telomere DNA to prevent illicit induction of the DNA damage response and in regulating telomerase. We designed small molecule inhibitors that promoted telomere shortening in cancer cells and we developed new strategies for telomerase to selectively deliver small molecule toxins exclusively to the telomeres of cancer cells. This ongoing project was initially supported by an NIH Innovator Award. In more recent years, we have been working to understand the molecular interactions that regulate post-translational modifications, with a primary focus on phosphatase activity. We have recently helped to uncover a unique mode of action for a small molecule to selectively reactivate a PP2A (protein phosphatase 2A) tumor suppressor serine-threonine phosphatase complex. The basic science and structural information we generated has enabled us to evolve and design a new series of first-in-class PP2A activators. As phosphatases have conventionally been viewed as ‘undruggable’ targets, our achievements have reinvigorated the realistic potential of advancing our new series of activators into the clinic. We are now extending an analogous approach to help define how, at a molecular level, small DNA tumor viruses interfere with host machinery and how that process leads to cell transformation. We hope to use our knowledge and past experience to help develop small molecules that are designed to interfere with viral-host protein-protein interactions and to eventually be used as a means of treating or preventing certain types of cancer that are associated with virus infection.

Ongoing projects that I would like to highlight include:

R01 GM133841
Role: PI
07/01/2019 – 06/30/2023
Molecular interactions and regulatory events of telomere proteins

R01 CA240993
Role: Co-PI (PI: Narla)

6/01/2019 – 5/31/2024
Structural and molecular determinants of protein phosphatase 2A function in lung cancer

RM1 GM142002
Role: Co-PI (PI: Ready)
7/01/2021 – 6/30/2026
Chemical, Structural and Cell-Signaling Interrogation of 15-Prostanglandin Dehydrogenase in Tissue Repair and Regeneration.

I confirm that I have not published under a different name

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2021	Professor with tenure, Depts. of Pharmacology & Biochemistry, Case Western Reserve University
2019	Co-Founder, Consultant, and Vice-President of Biology for Rappta Therapeutics LLC
2017	Associate Professor w/ tenure, Pharmacology & Biochemistry, Case Western Reserve University
2009-2017	Assistant Professor, Depts of Pharmacology & Biochemistry, Case Western Reserve University
2008-2009	Visiting Scientist, University of Colorado at Boulder with Dr. Thomas R. Cech
2004 2008	HHMI Postdoctoral Fellow, Health Research Inc., The Wadsworth Center with Dr. Joachim Frank
1999-2003	Graduate Student Research Assistant, University of California, San Diego with Dr. John E. Johnson
1997-1999	R&D Chemist, Rosemont Pharmaceutical Inc., Denver, CO
1996	Undergraduate Student Research Assistant, University of Georgia
1995	Undergraduate Student Research Assistant, Fort Lewis College

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

2021	*Nature* Spin-off Prize ‘Ones to Watch’
2021	Work recognized as “one of 20 huge advances in the year 2020” by BBC News Science Focus: 20 Positive Science News Stories from 2020
2020	Finalist for the John S. Diekhoff Award for Distinguished Graduate Mentoring
2013	American Cancer Society – Research Scholar Award
2013	National Institutes of Health Director’s New Innovator Award
2011	American Heart Association – Young Investigator Award
2011	Case Western Reserve University School of Medicine – Mt. Sinai Scholar
2004-2008	Howard Hughes Medical Institute Postdoctoral Fellow
2002	The Scripps Research Institute Postdoctoral Fellow
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. My group implements a structure- and mechanistic-based approach to develop small-molecule drugs and strategies for manipulating abrogated processes that are associated with human afflictions. My group has used the structural and molecular information related to telomeres and telomerase to develop small molecule compounds that inhibit or exploit telomerase activity to be used as putative chemotherapeutic agents. Additionally, the cryo-EM structure of a small molecule activator of PP2A (SMAP) bound to PP2A identifies a novel mode of action for a new class of chemotherapeutic compounds. In antivirals, we have identified and characterized a broad range of nanobodies that block infection of SARS-CoV-2.

a. Sun, D., Sang, Z., Kim, J., Xiang, Y., Cohen, T., Belford, A., Huet, A., Sun, J., Conway, J., Schneidman-Duhovny, D., **Taylor, D.**, Zhang, C., Huang, W., & Shi, Y. (2021). Potent neutralizing nanobodies resist convergent circulating variants of SARS-CoV-2 by targeting novel and conserved epitopes. *Nat. Comm.* **12**, Article Number 4676. PMID: 33758850
b. Leonard, D.*, Huang, W.*, Izadmehr, S., O'Connor, C.M., Wiredja, D., Wang, Z., Zaware, N., Chen, Y., Schlatzer, D., Kiselar, J., Vasireddi, N., Schuchner, S., Perl, A.L., Galsky, M., Xu, W., Brautigan, D., Ogris, E., **Taylor, D.J.**†, & Narla, G.† (2020). Small molecule selectively enhances phosphatase function through biased heterotrimer stabilization. *Cell.* 181(3): 688-701.E16. PMID: 32315618.
c. Hernandez-Sanchez, W., Huang, W., Plucinsky, B., Garcia-Vazquez, N., Robinson, N.J., Schiemann, W.P., Berdis, A.J., Skordalakes, E., & **Taylor, D.J.** (2019) A non-natural nucleotide uses a specific pocket to selectively inhibit telomerase activity. *PLOS Biology.* Apr 5; 17(4):e3000204. PMID: 30951520.
d. 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.

2. 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 telomere proteins interact with telomere DNA to protect it from degradation and regulate telomerase-mediated extension. We have additionally helped to uncover the role of SLX4IP, an understudied protein, in regulating telomere maintenance mechanisms.

a. Xu, M., Axhemi, A., Malgowska, M., Chen, Y., Leonard, D., Srinivasan, S., Jankowsky, J., & **Taylor, D.J.** (2021). Active and passive destabilization of G-quadruplex DNA by the telomere POT1-TPP1 complex. *J Mol Biol.* 2021 Feb 4;433(7):166846. doi: 10.1016/j.jmb.2021.166846. PMID: 33549587
b. Mangosh, T.L., Awadallah, W.N., Grabowska, M.M., & **Taylor, D.J.** (2020). SLX4IP-mediated telomere maintenance is essential for androgen receptor-independent castration- resistant prostate cancer. *Mol Cancer Res.* doi: 10.1158/1541-7786.MCR-20-0314. PMID: 33188147.
c. Robinson, N.J., Morrison-Smith, C.D., Gooding, A.J., Schiemann, B.J., Chang, J., Jackson, M.W., **Taylor, D.J.,** & Schiemann, W.P. (2020). SLX4IP regulates telomere maintenance and Wnt signaling to control breast cancer metastasis. *Life Sciences Alliance.* Feb. 18;3(4). PMID: 32071280
d. Xu, M., Kiselar, J., Whited, T.L., Hernandez-Sanchez, W., & **Taylor, D.J.** (2019) POT1-TPP1 differentially regulates telomerase via POT1 His266 and as a function of single-stranded telomere DNA length. *PNAS.* Nov 19; 116(47):23527-23533. PMID: 31685617.

3. In addition to the specific complexes described in detail above, my lab has used cryo-electron microscopy to solve the structures of other important cellular assemblies that are involved in fundamental processes such as post-translational modifications, DNA packaging, serotonin signaling, and interferon response. Our contributions include near-atomic resolution structures of the bacterial efflux pumps that are responsible for antibiotic resistance, ligand gated ion channels, and viral/bacteriophage infection machinery. Many of these examples represent the most comprehensive structures of fully assembled and functional complexes to-date.

a. Wang, Y., Song, Q., Huang, W., Lin, Y., Wang, X., Wang, C., Willard, B., Zhao, C., Nan, J., Holvey-Bates, E., Wang, Z., **Taylor, D**., Yang, J., & Stark, G.R. Phosphorylation of STAT2 on T404 is critical for interferon-mediated antiviral defense. *Cell Res* (2020). https://doi.org/10.1038/s41422-020-0386-6.
b. Su, C-C., Kambakam, S., Rajavel, M., Morgan, C.E., Scott, H., Huang, W., Emerson, C., **Taylor, D.J**, Stewart, P.L., Bonomo, R., & Yu, E.W. (2019). Cryo-EM structure of an *Acinetobacter baumanii* multidrug efflux pump. *mBio.* July 2;10(4). PMID: 31266873.
c. 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.
d. 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.

4. I have made key contributions to the structural biology field, specifically through training in cryo-EM and in structure determination of large, complex viruses using x-ray crystallography. My involvement in generating detailed protocols has benefited cryo-EM users throughout the world by providing them with technical training and documentation for doing so. In addition, I have contributed to understanding the structure, function, assembly and maturation of eukaryotic viruses. In addition to structural investigation, I have used genetic mutations and biophysical analysis to characterize viral assembly, maturation, and infectivity.

    a. Grassucci, R. A., **Taylor, D.**, and Frank, J. (2008) Visualization of Macromolecular Complexes using Cryo-Electron Microscopy with FEI Tecnai Transmission Electron Microscopes. *Nat Protoc.,* 3:330-339. PMID: 18274535.
    b. Grassucci, R. A., **Taylor, D. J.**, and Frank, J. (2007) Preparation of Macromolecular Complexes for Cryo-Electron Microscopy. *Nat Protoc.,* 2:3239-3246. PMID: 18079724.
    c. **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.
    d. **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.

5. 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 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). The ADPR modification completely inhibits protein synthesis in the infected host and results in cell death. Through my work, we were able to show how the ADPR moiety interferes with ribosome decoding of the messenger RNA during protein synthesis. Furthermore, we were able to use the ADPR as a novel density marker to better understand the GTP-induced conformational changes eEF2 undergoes to catalyze the movement of the mRNA-tRNA duplex from the A- and P-sites of the ribosome to the P- and E-sites, respectively. In separate studies, we used cryo-EM to understand how eukaryotic release factors 1 and 3 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. **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.
    c. 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.
    d. **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.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/16E_oA59hirQC/bibliography/46016877/public/?sort=date&direction=descending