BIOGRAPHICAL SKETCH

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NAME: Mears, Jason A.

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

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)	END DATE MM/YYYY	FIELD OF STUDY
Indiana University, Bloomington, IN	BS	05/1999	Biochemistry
University of Alabama at Birmingham, Birmingham, AL	PHD	05/2005	Biochemistry and Molecular Genetics
National Institute of Diabetes, Digestive and Kidney Diseases, NIH, Bethesda, MD	Postdoctoral Fellow	06/2010	Biochemistry and Structural Biology

A. Personal Statement

The central goal of my research is to investigate proteins that regulate mitochondrial dynamics and provide detailed mechanistic insight about the mitochondrial fission machinery and its ability to regulate membrane-remodeling events in eukaryotic cells. Mitochondrial dynamics has recently come to the forefront as a therapeutic target in several degenerative diseases, including neurodegeneration, cancer, and aging. But the lack of insight into the regulation of this process is a major limitation. To address this shortcoming, my lab has been at the leading edge of research that has characterized the functional roles of proteins that contribute to mitochondrial fission. We have also identified novel mechanistic features of this process by showing that this protein machinery actively constricts membranes to drive ensuing fission. The innovative goals of this proposal are to: 1) provide mechanistic insight into the cytosolic regulation of Drp1 assembly and recruitment to mitochondria, 2) resolve divergent data about the extent to which Drp1 can promote final scission, and 3) correlate changes in the fission proteins with altered mitochondrial physiology. Our group utilizes a multifaceted approach to address these questions, including cryo-EM, biophysical and biochemical methods, and bioenergetic analyses with intact cells and isolated protein complexes. We are fortunate to have regular interactions with mitochondrial, structural and cell biologists that continue to support our research interests. With this support, I am eager to resolve long-standing questions about the key factors that alter mitochondrial structure and physiology, leading to organelle dysfunction in human pathologies.

This research environment also fosters the development of young scientists, which is a critical objective in my group. Trainees at all levels have significant interactions within the lab, the department, the Center for Mitochondrial Diseases and the Cleveland Center for Membrane and Structural Biology. Regular seminars, data meetings and journal clubs in these groups encourage collaborative interactions with senior colleagues and other trainees at various stages of their careers. Additionally, I value and promote diversity to inject different perspectives in our research setting. As a graduate student, I served as a McNair Scholar mentor at the University of Alabama at Birmingham. Through my postdoctoral training, I mentored students and trainees from diverse cultural backgrounds. In my own lab, I have trained graduate, post-graduate, post-baccalaureate, undergraduate and high school scientists from diverse cultural and ethnic backgrounds as well as trainees with physical disabilities to offer research experiences and provide mentoring opportunities for future leaders. This range of experience and perspectives creates an environment that fosters diverse interactions and enhances our research efforts.

Ongoing projects that I would like to highlight include:

R01 GM125844
Mears (PI)

02/01/18 – 01/31/2023
Defining Molecular Interactions that Drive Mitochondrial Fission

R01 CA208516
Mears (PI)
09/01/17 – 08/31/2022
Mitochondrial dynamics in Brain Tumor Initiating Cells

Publications Relevant to this proposal:

1. Robertson GL, Riffle SN, Patel M, Marshall A, Beasley H, Garza-Lopez E, Shao J, Vue Z, Hinton A Jr., Mears JA, and Gama V. DRP1-mediated mitochondrial fission is essential to maintain cristae morphology and bioenergetics. *bioRxiv 2021.12.31.474637* [Preprint] January 9, 2022. Available from: https://doi.org/10.1101/2021.12.31.474637
2. Clinton RW, Bauer BL, and Mears JA. (2020) Purification of dynamin-related protein 1 for structural and functional studies. *Methods in Mol. Biol.* 2159: 41-53. PMCID: PMC8018536
3. Francy CA, Clinton RW, Fröhlich C, Murphy C, and Mears JA. (2017) Cryo-EM Studies of Drp1 Reveal Cardiolipin Interactions that Activate the Helical Oligomer. *Sci. Rep.*, **7**: 10744. PMCID: PMC5587723
4. Fröhlich C, Grabiger S, Schwefel D, Faelber K, **Mears J**, Rocks O, and Daumke O (2013) The crystal structure of human dynamin 1-like protein reveals an alternative oligomerization mode. *EMBO J.,* **32**: 1280-92. PMID: 2358453

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 -	Associate Professor (tenured), Department of Pharmacology, CWRU School of Medicine (SOM), Cleveland, OH
2017 -	Member, Case Comprehensive Cancer Center (CCCC), CWRU SOM, Cleveland, OH
2010 -	Member, Cleveland Center for Membrane and Structural Biology (CCMSB) , CWRU SOM, Cleveland, OH
2010 -	Member, Center for Mitochondrial Diseases, CWRU SOM, Cleveland, OH
2010 - 2019	Assistant Professor, Department of Pharmacology, CWRU SOM, Cleveland, OH
2005 - 2010	Postdoctoral Fellow, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD
2002 - 2005	Research Technician II, Georgia Institute of Technology, Atlanta, GA
1999 - 2005	Graduate Research Assistant, University of Alabama at Birmingham, Birmingham, AL
1995 - 1999	Undergraduate Research Assistant, Indiana University, Bloomington, IN

Other Experience and Professional Memberships

2000 - 2002	Mentor, McNair Scholars Program, University of Alabama at Birmingham
2002 -	Member, *Biophysical Society (2002-)*, *American Society for Cell Biology (2006-)*, *Chesapeake Society for Microscopy (2006-2010)*, *American Society for Pharmacology and Experimental Therapeutics (2011-)*, *Microscopy Society of America (2011-)*, *Microscopy Society of Northeast Ohio (2011-)*, *American Society for Biochemistry and Molecular Biology (2015-)*
2007 - 2008	Fellows Editorial Board, NCI/CCR, National Institutes of Health
2009 -	Ad Hoc Reviewer for over 35+ journals, including *J Cell Biol, PNAS,* eLife, *Hum Mol Gen, J Biol Chem, Mol Biol Cell, Nucleic Acids Research, Clin Trans Med, Cell Mol Life Sci, Commun Biol, Sci Rep, Biochem J, Endocrinology, Cell Biol Toxicol, Protein Sci, PLoS Comp Biol, PLoS ONE, Mol Biol Evol, Front Cell Dev Biol, Front Oncol, Int Rev Cell and Mol Biol, Aging, Antioxidants, Biomolecules, Cancers, Cells, J Clin Med* and more

2012 - Chair of Scientific Sessions at National Meetings: Scientific Symposium: Structure of membrane-shaping proteins, Microscopy and Microanalysis Meeting, Phoenix, AZ (2012); Platform session: Protein assemblies, Biophysical Society 62nd Annual Meeting, San Francisco, CA (2018); Cryo-EM Subgroup Symposia, Biophysical Society 63rd Annual Meeting, Baltimore, MD (2019, elected)

2016 - Ad Hoc Grant Reviewer for *National Institutes of Health: NCI Scientific Review Group (2018/05 ZCA1 SRB-K (M2)*, *2019/01 ZCA1 RTRB-U (J1)) and NIGMS Scientific Review Group* (*2021/06 MBPP), American Heart Association (Transformational Project Award: 2019, 2020 & 2022), Wellcome Trust UK, Israel Science Foundation*, and *The Netherlands Organization for Scientific Research (NWO)*

Honors

1998	E.G. Sturdevant Summer Research Fellowship, Indiana University
2002	McKibben Young Investigator Award, University of Alabama at Birmingham
2005 - 2010	NIDDK Nancy Nossal Fellowship Award, NIDDK, National Institutes of Health
2012	American Heart Association SDG Award, American Heart Association
2021, 2022	John S. Diekhoff Mentoring Award Finalist, Case Western Reserve University

C. Contribution to Science

1. The main focus of my research is to examine the role of dynamin superfamily proteins (DSPs) in mitochondrial membrane fission and fusion events. As a postdoc, I determined the helical structure of the yeast mitochondrial fission DSP, Dnm1p, on a lipid template using cryo-EM. Additionally, I found that Dnm1p polymers constrict underlying lipid bilayers upon addition of GTP to impart the contractile force needed for membrane fission (Mears et al., 2011). This work provided the first evidence that mitochondrial DSPs mediate membrane constriction using GTP hydrolysis to trigger this process. When starting my own lab, I focused on molecular interactions that drive assembly of the human mitochondrial fission machinery and the key mediator of this complex, dynamin-related protein 1 (Drp1). We identified key structural features of Drp1 using x-ray and cryo-EM methods (Frohlich et al., 2013; Francy et al., 2017; Rochon et al., *in preparation*). My group also determined the functional roles of distinct sequence domains that regulate assembly of the fission complex and facilitate mitochondrial membrane constriction (Francy et al., 2015). In this way, we have identified the core protein machinery needed to constrict membranes. Moreover, our protocols are the gold-standard for isolating these functional proteins and complexes (Clinton et al., 2020), so we are optimally positioned to address ongoing controversies about the roles of mitochondrial fission proteins in membrane remodeling and sustaining mitochondrial health.
    a. Clinton RW, Bauer BL, Mears JA. (2020) Affinity Purification and Functional Characterization of Dynamin-Related Protein 1. *Methods Mol. Biol*. 2159:41-53. PMCID: PMC8018536.
    b. Francy CA, Alvarez FJ, Zhou L, Ramachandran R, Mears JA. (2015) The mechanoenzymatic core of dynamin-related protein 1 comprises the minimal machinery required for membrane constriction. *J. Biol. Chem.*, 290(18):11692-703. PMCID: PMC4416870.
    c. Fröhlich C, Grabiger S, Schwefel D, Faelber K, Rosenbaum E, Mears J, Rocks O, Daumke O. (2013) Structural insights into oligomerization and mitochondrial remodelling of dynamin 1-like protein. *EMBO J.*, 32(9):1280-92. PMCID: PMC3642683.
    d. Mears JA, Lackner LL, Fang S, Ingerman E, Nunnari J, Hinshaw JE. (2011) Conformational changes in Dnm1 support a contractile mechanism for mitochondrial fission. *Nat. Struct. Mol. Biol.*, 18(1):20-6. PMCID: PMC3059246.

2. Importantly, we have incorporated lipid and protein factors to build on the complexity of our *in vitro* reconstitution experiments. In collaboration with Rajesh Ramachandran in the Department of Physiology and Biophysics at CWRU, we have shown that cardiolipin (CL) directly interacts with Drp1 to regulate its function (Stepanyants et al., 2015). Moreover, my group identified conformational changes in Drp1 helical polymers bound to CL lipid templates that explain the augmented activity of these complexes (Francy et

al., 2017). We also developed a novel lipid-tethering assay to examine Drp1 interactions with critical partner proteins at the surface of the membrane (Clinton et al., 2016; Clinton & Mears, 2017). One partner, called mitochondrial fission factor (Mff), was found to enhance Drp1 polymerization and activity by acting as a scaffold upon which a functional fission complex could assemble. This effect was modulated, in part, by CL and the multimeric states of both Mff and Drp1. In more recent studies, we have found that the VD of Drp1 regulates Drp1 self-assembly and interactions with Mff, and this co-complex can impart contractile strain on lipid bilayers (Clinton et al., *resubmitted*). Importantly; we were able to use cellular studies to validate our findings with isolated protein complexes. This multi-faceted approach is essential for comparing key sequence differences that modify the core protein machinery to perform distinct roles in different eukaryotic cells. For rigor and transparency, we have continually validated our approaches and shared resources with other groups to expand our understanding of the role of DSPs in mitochondrial dynamics.

a. Francy CA, Clinton RW, Fröhlich C, Murphy C, Mears JA. (2017) Cryo-EM Studies of Drp1 Reveal Cardiolipin Interactions that Activate the Helical Oligomer. *Sci. Rep.*, 7(1):10744. PMCID: PMC5587723.

a. Clinton RW, Mears JA. (2017) Using Scaffold Liposomes to Reconstitute Lipid-proximal Protein-protein Interactions In Vitro. *J. Vis. Exp.*, 119: e54971. PMCID: PMC5409191.

b. Clinton RW, Francy CA, Ramachandran R, Qi X, Mears JA. (2016) Dynamin-related Protein 1 Oligomerization in Solution Impairs Functional Interactions with Membrane-anchored Mitochondrial Fission Factor. *J. Biol. Chem.*, 291(1):478-92. PMCID: PMC4697186.

c. Stepanyants N, Macdonald PJ, Francy CA, Mears JA, Qi X, Ramachandran R. (2015) Cardiolipin's propensity for phase transition and its reorganization by dynamin-related protein 1 form a basis for mitochondrial membrane fission. *Mol. Biol. Cell.*, 26(17):3104-16. PMCID: PMC4551322.

3. In addition to protein and lipid partners, we have characterized functional differences in Drp1 due to alternative splicing (MacDonald et al., 2014 and 2016; Lu et al, 2018), post-translational modifications (Akinbiyi et al., 2022), and sequence mutations (i.e. naturally occurring patient mutations and artificial mutants) (Montecinos-Franjola et al., 2020; Clinton et al., 2020; Bauer et al., *in preparation*). These modifications “tune” the activity of Drp1 through both homogeneous and heterogeneous inter-molecular protein interactions. In this way, the assembly of the core fission machinery can be disrupted or enhanced to promote changes in mitochondrial ultrastructure as a response to cellular cues. To examine the impact of these morphological changes, we have established core protocols using high-resolution oxygen respirometry along with traditional electron transport assays to correlate changes in mitochondrial structure and physiology (Akinbiyi et al., 2022; Robertson et al., 2022 [*preprint*]).

   a. Akinbiyi EO, Abramowitz LK, Bauer BL, Stoll M, Hoppel CL, Hsiao CP, Hanover JA, and Mears JA. (2021) Blocked O-GlcNAc cycling alters mitochondrial morphology, function, and mass. *Sci. Rep.*, 11: 22106. PMCID: PMC8586252

   b. Montecinos-Franjola F, Bauer BL, Mears JA, and Ramachandran R. (2020) GFP fluorescence tagging alters dynamin-related protein 1 oligomerization dynamics and favors protein crowding-mediated mitochondrial fission. *Sci. Rep.*, 10: 14777. PMCID: PMC7479153

   c. Lu B, Kennedy B, Clinton RW, Wang E, McHugh D, Stepanyants N, Macdonald PJ, Mears JA, Qi X, and Ramachandran R. (2018) Steric interference from intrinsically disordered polypeptide regions controls dynamin-related protein 1 self-assembly during mitochondrial fission. *Sci. Rep.*, 8: 10879. PMCID: PMC6051998

   d. Macdonald PJ, Francy CA, Stepanyants N, Lehman L, Baglio A, Mears JA, Qi X, Ramachandran R. (2016) Distinct Splice Variants of Dynamin-related Protein 1 Differentially Utilize Mitochondrial Fission Factor as an Effector of Cooperative GTPase Activity. *J. Biol. Chem.*, 291: 493-507. PMCID: PMC4697187

4. My foundation for cryo-EM training started as a postdoctoral fellow in the lab of Dr. Jenny Hinshaw at the NIH. The key reason that I chose to pursue my postdoctoral studies with Jenny was the opportunity to learn and implement biochemical and structural methods that matched the computational training I received during

my graduate training (*see below*). This multi-faceted approach was used to examine the process of dynamin-mediated vesicle release during endocytosis. Dynamin is a force-generating enzyme that constricts membranes upon GTP hydrolysis. By combining cryo-EM and x-ray structures, I was able to generate pseudo-atomic models for dynamin-mediated membrane constriction that, for the first time, illustrated conformational changes in dynamin assemblies that promote membrane constriction (Mears et al., 2007). Later, I determined an improved structure of dynamin using cryo-EM that identified novel protein motions that propagate within the oligomer to generate contractile force during membrane scission (Chappie et al., 2011). These results identified the conserved mechanochemical core of dynamin and have broad-reaching implications for the entire family of DSPs. These experiences and the expertise acquired made me uniquely qualified to address the functional roles of DSPs in regulating organelle morphology in my own lab.

a. Chappie JS, Mears JA, Fang S, Leonard M, Schmid SL, Milligan RA, Hinshaw JE, Dyda F. (2011) A pseudoatomic model of the dynamin polymer identifies a hydrolysis-dependent powerstroke. *Cell*, 147(1):209-22. PMCID: PMC3185303.
b. Mears JA, Hinshaw JE. (2008) Visualization of dynamins. *Methods Cell Biol.*, 88:237-56. PMCID: PMC2692555.
c. Mears JA, Ray P, Hinshaw JE. (2007) A corkscrew model for dynamin constriction. *Structure*, 15(10):1190-202. PMCID: PMC2211526.

5. I began my structural biology training in the lab of Dr. Stephen Harvey, where I examined the spatial relationships of highly conserved functional domains in evolutionarily diverse ribosomes. By combining data from various experimental disciplines, I developed detailed models that described the key structural elements of protein translation (Mears et al, 2002). I focused on mitochondrial ribosomes, as their rRNAs are drastically reduced when compared with bacterial rRNAs. This reduction is compensated for by an increase in protein content, and I could model these changes to map evolutionary changes within an essential cellular machinery (Mears et al, 2006). I continue to use this training in my lab to address structural changes in important cellular machines with a particular focus on mitochondrial protein complexes (Sha et al., 2021; Ducich et al., 2022).

a. Ducich NH, Cioffi G, Jin B, Barnholtz-Sloan JS, Mears JA, and Bedoyan JK. (2022) Solvent accessibility of E1α and E1β residues with known missense variations causing pyruvate dehydrogenase complex (PDC) deficiency: Impact on PDC-E1 structure and function. *J. Inherit. Metab. Dis.* Online ahead of print. PMID: 35038180
b. Sha Z, Montano MM, Rochon K, Mears JA, Deredge D, Wintrode P, Szweda L, Mikita N and Lee I. (2021) A Structure and Function Relationship Study to Identify the Impact of the R721G Mutation in The Human Mitochondrial Lon Protease. *Arch Biochem Biophys*. 710:108983. PMID: 34228963
c. Mears JA, Sharma MR, Gutell RR, McCook AS, Richardson PE, Caulfield TR, Agrawal RK, Harvey SC. (2006) A structural model for the large subunit of the mammalian mitochondrial ribosome. *J. Mol. Biol.*, 358(1):193-212. PMCID: PMC3495566.
d. Mears JA, Cannone JJ, Stagg SM, Gutell RR, Agrawal RK, Harvey SC. (2002) Modeling a minimal ribosome based on comparative sequence analysis. *J. Mol. Biol.*, 321(2):215-34. PubMed PMID: 12144780.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/jason.mears.1/bibliography/public/

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: Rochon, Kristy J.

eRA COMMONS USER NAME (credential, e.g., agency login): K_ROCHON1

POSITION TITLE: PhD Candidate

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 MM/YYYY	FIELD OF STUDY
Central State University	BS	08/2015	05/2017	Biology
Central State University	BS	08/2015	05/2017	Chemistry
Case Western Reserve University	PhD	8/2017	Present	Pharmacology

A. Personal Statement

My immediate goal is to resolve the native structure of dynamin-related protein 1 (Drp1) in a pre-assembled state and in assembled, helical polymers on lipid templates that mimic the outer mitochondrial membrane (OMM). These structures will characterize the conformational changes that drive assembly of larger oligomers necessary for mitochondrial fission and will elucidate key regulatory regions of the protein that may be future therapeutic targets. My long-term research interests are focus on therapeutics and translational research in mitochondrial diseases. My academic background in both biology and chemistry has provided a strong foundation and my current field of study in Pharmacology will provide me with the background needed to achieve these goals. Additionally, I have a strong background in leadership and planning skills gained through active duty service as an officer in the United States Air Force. When I returned to school in 2014, my goal was to focus on research. Through my undergraduate experiences and the opportunities to explore different research areas in CWRU's school of medicine, I have refined that passion. Within the PhD program at CWRU, I was not content to look at translation research from the perspective of one discipline while choosing my lab. I made a conscious effort to explored research laboratories in pathology, physiology and biophysics, pharmacology, and neuroscience. Through these four research rotations I was exposed to unique perspectives needed for a wholistic approached to translational research. Additionally, I discovered a talent and passion for microscopy imaging and analysis. I joined Jason Mears' lab officially in January 2018 where I am using cryo-EM, confocal microscopy and molecular dynamic simulations to study mitochondrial dynamics.

In the same way my research can contribute to new paradigms, I'm interested in using my experiences to encourage and mentor minority students to increase diversity in biomedical research. A diversity of thought and life experiences are critical for the advancement of innovation and discovery. To that end, I have professional objectives focused on mentoring a

diverse group of the next generation scientists. Having attended a Historically Black College (HBCU), I have seen how important it is for minority students to have mentors that can encourage their academic progress by not just talking about what's possible, but showing them how to set and achieve their goals. I would like to return to Central State to reach out to the students in the natural sciences program to tell them about graduate school and help them with their strategies as they approach graduation. I'm also interested in establishing a connection with my tribe, the Menominee Nation. Through a partnership with their Tribal Education Department, outreach to the youth on the reservation could expose the next generation to biomedical science programs and careers.

B. Positions and Honors

Positions and Employment

2004 - 2008 Public Affairs Officer/Program Manager, United States Air Force
2008 - 2013 Data Analytics and Strategy Development, Dayton Development Coalition
2013 - 2017 Grant Writer
2015 - 2017 Technology Validation and Prototyping, InfiniPure

Other Experience and Professional Memberships

2000 - 2002 President, Phi Theta Kappa Honor Society, Beta Beta Psi Chapter
2015 - 2017 Member, American Chemical Society
2017 - Present Member, Tri Beta Honor Society
2019 - Present Member, Microscopy Society of America

Honors & Awards

2002 Leadership Award, Air Force Reserve Officer Training Corps (AFROTC)
2003 USAA Spirit Award, AFROTC
2004 Distinguished Graduate, AFROTC
2004 Cadet of the Year, AFROTC
2005 National Defense Service Medal
2005 Global War on Terrorism Service Medal
2015 - 2017 Scholarship, DoD-STEM
2016 Patterson Award, American Chemical Society
2017 - 2018 Fellowship, The Paul Berg and Harland Wood Distinguished Graduate Fellowship
2018-2020 NIH diversity supplement, PA-18-586
2019 1st Place Poster Award, Microscopy and Microanalysis 2019 Conference
2019 Greenfield Travel Award, Best Departmental Journal Club Presentation
2019 Best Oral Presentation, CWRU Pharmacology Research Symposium
2020 CWRU Pharmacology Department Commendation for Outstanding Research, Scholarship, and Service
2021 CWRU Pharmacology Department Commendation for Outstanding Research, Scholarship, and Service
2021 Best Poster Presentation, CWRU Pharmacology Research Symposium

C. Contribution to Science

1. **Undergraduate Research:** My undergraduate research experience included three diverse projects: At Central State University, I completed two semesters of Chemistry research on the synthesis process and the evaluation of anti-biological activity for sulfanilamide azo-dyes. As the lead student researcher on the project, I developed the process for synthesis, determined the functional group series that would be used, conducted IR and NMR analysis of the compounds, and coordinated the research plan for future semester's research as new students join the project. In my dual major, I also conducted an additional research project for Biology, focused on the feasibility of establishing bioreactors in rural India. The study abroad assessed the required amount of biomass needed to power small rural villages and the anticipated methane yields. Data was shared with researchers at the University of Bangalore in India. Through a ten-week summer internship at the University of Cincinnati, I was mentored by Prof. George Stan and contributed by studying computational models of biological nanomachines in mediated protein unfolding. Through my contribution, I obtained novel results on the impact of crowding on Clp-mediated protein unfolding. This internship culminated in an invitation for a poster presentation and abstract publication at the 2016 Annual Biomedical Research Conference for Minority Students (ABRCMS).
    a. Rochon K, Javidialesaadi A, Stan G. Effect of Crowding of Tandem Substrates in Protein Unfolding and Translocation Mediated by Clp Biological Nanomachines. Annual Biomedical Research Conference for Minority Students; 2016 November, Tampa, FL. (abstract and poster presentation)

2. **Graduate Research**: My research rotations at CWRU allowed for the exploration of a variety of neurodegenerative disorders in the context of different research questions. First, I worked in Dr. Qingzhong Kong's lab in the Pathology department where my primary goal was to find an antibody that could detect the N1 fragment of the human prion protein (PrP). I completed a series of experiments which evaluated four antibodies, identifying one with the potential for further testing and experimentation. In Dr. Rajesh Ramachandran's lab in the Physiology and Biophysics department I successfully transfected three variants of Drp1 for characterization. One variant expressed high levels of GTPase activity, which was unexpected and will be studied further in the lab. This variant was also carried over into the pharmacology rotation. Finally, in Dr. Bruce Trapp's lab in Neuroscience at the Cleveland Clinic I studied the mechanisms of neuronal degeneration in Multiple Sclerosis (MS) and documented novel evidence of cases in which neurodegeneration occurred absent of demyelination. Additionally, I was able to characterize the location of axonal swelling in MRI regions of interest. The results will be further characterized and images I obtained are planned to appear in a future publication. Since joining Jason Mears lab, I have resolved a sub-20 Å structure of both wild type Drp1 (WT) and a Drp1 mutant which yields an assembly defective dimer. When compared to the crystal structure, our EM structures demonstrate a shift in conformation of the GTPase domains. These results suggest that the GTPase domain may be in an inhibited state that shields the stalk from forming intermolecular contact. Additionally, I have resolved mid-resolution structures of the Drp1 tetramer, and Drp1 polymers on phosphatidic acid (PA) and cardiolipin (CL) lipid templates. Initial results of the single-particle structures were presented at the 2019 Microscopy and Microanalysis Meeting where my poster won first place for graduate student presentations in the biological sciences track.
    a. Rochon, K, Bauer, B, and Means JA. Conformational changes in solution multimers of dynamin-related protein 1 (Drp1) facilitate functional assembly. 3DEM Gordon

Research Conference and Seminar, 2021 Nov, Waterville Valley, NH. (Poster Presentation)

b. Sha Z, Montano MM, Rochon K, Mears JA, Deredge D, Wintrode P, Szweda L, Mikita N, Lee I. A structure and function relationship study to identify the impact of the R721G mutation in the human mitochondrial lon protease. Arch Biochem Biophys. 2021 Oct 15;710:108983. doi: 10.1016/j.abb.2021.108983. Epub 2021 Jul 3. PMID: 34228963.
c. Rochon, K, Tornes-Blanco, A, and Mears JA. Conformational Changes in Solution Multimers of Dynamin-related Protein 1 (Drp1) Facilitate Functional Assembly. Annual Microscopy and Microanalysis Meeting, 2020 August, Virtual Meeting. (Short paper published in the meeting proceedings and platform presentation)
d. Rochon, K and Mears, JA. Determining the Solution Structure of the Drp1 and its Role in the Assembly of the Mitochondrial Fission Machinery. Annual Microscopy and Microanalysis Meeting, 2019 August, Portland, OR. (Short paper published in the meeting proceedings and poster presentation)
e. Rochon K, Javidialesaadi A, Stan G. Effect of Crowding of Tandem Substrates in Protein Unfolding and Translocation Mediated by Clp Biological Nanomachines. Annual Biomedical Research Conference for Minority

3. **Current Funding Source:** NIH National Institute of General Medical Sciences, Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research F31 GM139324-03

4. **Citizenship:** U.S. citizen.