BIOGRAPHICAL SKETCH

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NAME: **Christine M. Dunham**

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

POSITION TITLE: Associate Professor of Biochemistry

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Barnard College, Columbia University, New York, NY	B.A.	05/1997	Chemistry
University of California, Santa Cruz, CA	Ph.D.	06/2003	Structural Biology
MRC Laboratory of Molecular Biology, Cambridge, England	Postdoc	04/2008	Structural Biology

A. Personal Statement

My recent research centers on understanding how stress alters translation, the mechanism of ribosome dysregulation, and the roles of toxin-antitoxin pairs in inhibiting protein synthesis to alter bacterial physiology.My role in this BAG proposal is to solve structures of stalled ribosomes bound to a novel rescue factor and drugs, to solve a structure of a ribosome undergoing mRNA frameshifting and how translation factors can influence such a state, and to solve structures of the ribosome undergoing modification in response to aminoglycoside exposure (Sub Project 2).

As a graduate student in Prof. William G. Scott's lab at the University of California, Santa Cruz, I used time-resolved X-ray crystallography to understand the mechanism of an RNA enzyme involved in the rolling circle replication cycle (**a**). As an American Cancer Society Postdoctoral Fellow in Dr. Venki Ramakrishnan's lab at the MRC Laboratory of Molecular Biology, I again tackled questions of RNA function but, this time, in the context of the bacterial ribosome. Using X-ray crystallography, I solved the first high resolution structure of a bacterial ribosome containing tRNA and mRNA ligands (**b**) that provided the ability to ask important biological questions of how elongation factors function (section 1, **a-d**). In my own lab, we study the molecular basis of ribosome regulation and dysregulation using biochemical, X-ray crystallographic and, more recently, single particle cryo electron microscopy (cryoEM) approaches. We have recently determined the molecular basis for tRNA-mediated ribosomal frameshifting (**c**) and using cryo-electron microscopy (cryo-EM), we have determined how structured mRNAs control translation important for mRNA frame maintenance and co-translational folding (**d**).

a. **Dunham CM**, Murray JB, and Scott WG. (2003) A Helical Twist-Induced Conformational Switch Activates Cleavage in the Hammerhead Ribozyme. *Journal of Molecular Biology* **332**(2):327-36. PMID: 12948485.
b. Selmer M*, **Dunham CM***, Murphy IV FV, Weixlbaumer A, Petry S, Kelley AC, Weir J, and Ramakrishnan V. (2006) Structure of the 70S Ribosome Complexed with mRNA and tRNA. *Science* 313(5795):1935-42. PMID: 16959973. *These authors contributed equally.
c. Hong S*, Sunita S*, Dunkle JA, Maehigashi T and **Dunham CM**. (2018) Mechanism of +1 tRNA-mediated frameshifting. *Proc Natl Acad Sci* 115(44):11226-31. PMCID: PMC6217423. *These authors contributed equally.
d. Zhang Y*, Hong S*, Ruangprasert A, Skiniotis Y and **Dunham CM**. (2018) Alternative modes of E-site tRNA binding in the presence of structured mRNAs at the mRNA entrance channel. *Structure.* 26(3):437-445. PMCID: PMC5842130. *These authors contributed equally.

B. Positions and Honors

Positions and Employment

1994-1995 NSF Summer Undergraduate Research Fellow, Albany Medical College, Albany, New York. Advisor: Professor Peter Weber.
1996 NSF Summer Undergraduate Research Fellow, University of Texas Medical Branch at Galveston. Advisor: Professor Bennett Van Houten.
2004 Medical Research Council Career Development Fellow, MRC Laboratory of Molecular Biology, Cambridge, UK. Advisor: Group Leader Venki Ramakrishnan.

2004-2008	American Cancer Society Postdoctoral Fellow, MRC Laboratory of Molecular Biology, Cambridge, UK. Advisor: Group Leader Venki Ramakrishnan.
2008-2016	Assistant Professor, Department of Biochemistry, Emory University School of Medicine, Atlanta, Georgia.
2017-present	Associate Professor, Department of Biochemistry, Emory University School of Medicine, Atlanta, Georgia.

Other Experience, Service and Professional Memberships

2001-present	RNA Society (since 2005), American Crystallographic Association (since 2001), Biochemical Society UK (2004-2007), American Society for Microbiology (ASM; since 2008), and The American Society for Biochemistry and Molecular Biology (ASBMB; since 2011).
2008-present	Temporary grant reviewer/study section: NSF, Genes and Genome Systems (two times); NIH K99 Pathways to Independence Awards study section (once); NIH Macromolecular Structure and Function C (MSFC) grant study section (once); American Heart Association, Basic Cell Protein and Crystallography grant study section (three times); NSF, Division of Molecular and Cellular Biosciences, Gene Expression study section (three times); NSF Division of Molecular and Cellular Biosciences, Gene Expression study section, CAREER award fellowships (once); NIH ZRG1 Biological Chemistry and Macromolecular Physics (P01; one time); NIH Molecular Genetics A (MGA) grant study section (three times); American Cancer Society, RNA Mechanisms of Cancer grant study section (once); NSF Graduate Student Research Fellowship predoctoral study section, Division of Molecular and Cellular Biosciences (once); Swiss National Science Foundation grant reviewer (once).
2008-present	Manuscript reviewer: *Nature, Science, PNAS, Cell, Molecular Cell, Nucleic Acids Research*, *Structure*, *J. Biol. Chem., Biochemistry*, *Biophysical Journal, Molecular Microbiology, Nature Structure & Molecular Biology*, *Journal of Bacteriology*, *Journal of American Chemistry Society*, *RNA*, *PLoS Genetics, Scientific Reports, Nature Chemical Biology, PLoS ONE.*
2009	Session chair, “Ribosome Regulation: Assembly, Modification and Function”, ASM conference, Philadelphia, PA.
2011	Conference organizing committee, Suddath symposium on the Ribosome, Institute for Bioengineering & Bioscience, Georgia Tech, Atlanta, GA.
2012	Session chair, “Supramolecular Assemblies”, American Crystallographic Association conference, Honolulu, HI.
2013	Pew Charitable Trusts 2014 Conference organization committee, Chile.
2015	2016 Conference Organizing committee, ASBMB, San Diego, CA.
2015	Session chair, “Translation and sRNA function”, Molecular Genetics of Bacteria and Phages Meeting, Madison, WI.
2016	Session chair, “Words from the Beamline”, SER-CAT Annual Meeting, Emory University, Atlanta, GA.
2016	Session chair, “Building Molecular Machinery”, American Society for Biochemistry and Molecular Biology, San Diego, CA.
2016	Faculty mentor, GRC Microbial Stress Responses, Mt Holyoke, MA.
2018 - 2022	NIH Permanent Study Section Member, Molecular Genetics A
2018 - present	Editorial Board Member, *Molecular Microbiology*
2018 - present	Editorial Board Member, *Journal of Biological Chemistry*
2019	Session chair, “Structure of toxin-antitoxins”, EMBO toxin-antitoxin conference, Windsor, UK.
2020	Session chair, “Ribosomes”, CSHL Translational Control Meeting.

Awards/Honors

1999 - 2003	NSF-GAANN Graduate Research Fellowship
2003	Best Poster Prize, Gordon Research Conference on Nucleic Acids (Ph.D.)
2010 - 2015	NSF Early Career Development (CAREER) Award
2011 - 2015	Pew Scholar in the Biomedical Sciences
2016 - 2021	Burroughs Wellcome Investigator in the Pathogenesis of Infectious Diseases
2017	American Crystallographic Association Etter Early Career Awardee
2018	American Society of Biochemistry and Molecular Biology (ASBMB) Young Investigator
2018	Cozzarelli Prize, National Academy of Sciences, Best Biological Sciences paper in *PNAS*

C. Contribution to Science

Link to a more complete list of publications (currently 33 research papers and 4 reviews/book chapters): http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/45371674/?sort=date&direction=ascending

Since I was a postdoctoral fellow in Dr. Venki Ramakrishnan's lab, I have focused my research on understanding the molecular basis of protein synthesis (**Contribution 1**). These structural insights changed the way we could mechanistically dissect translation to understand function and dysregulation. We next studied how the ribosome prevented non-canonical mechanisms of gene expression including mRNA frameshifting (**Contribution 2**)**.** We discovered how tRNA modifications control the mRNA frame and how their absence causes allosteric dysregulation of the ribosome. Our interests in protein synthesis led us to study bacterial toxins that control translation to limit growth and cause tolerance to antibiotics (**Contribution 3**). Related to inhibition of translation, toxin biology is control by toxin suppression by antitoxins, transcriptional autorepression to limit expression, and activation by controlled proteolysis of antitoxins (**Contribution 4**). Lastly, we augment our studies with interdisciplinary collaborations to understand the regulation of protein synthesis with other research groups including the Fredrick, Conn and Skiniotis labs (**Contribution 5**).

*These authors contributed equally. #Co-corresponding authors.

1. Protein synthesis is carried out by the ribosome and is one of the most conserved biological processes. As a postdoctoral fellow in 2009 Chemistry Nobel Laureate Venki Ramakrishnan's lab, I solved the first high-resolution structure of the entire bacterial ribosome (**a**). This work continues to impact the field and has been cited >900 times. Although this methodology helped push the field forward, the most significant biological achievement has been the mechanistic insights such structures have revealed, including how translation factors facilitate termination and recycling (**b**), how GTPase elongation factors modulate activity (**c**), and how bacterial toxins target the ribosome during the stringent response (**d**).
   a. Selmer M*, **Dunham CM***, Murphy IV FV, Weixlbaumer A, Petry S, Kelley AC, Weir J, and Ramakrishnan V. (2006) Structure of the 70S Ribosome Complexed with mRNA and tRNA. *Science* 313(5795):1935-42. PMID: 16959973.
   b. Weixlbaumer A, Petry S*, **Dunham CM***, Selmer M*, Kelley AC and Ramakrishnan V. (2007) Crystal structure of the ribosome recycling factor bound to the ribosome. *Nat Struct Mol Biol* 14(8):733-7. PMID: 17660830.
   c. Gao Y-G, Selmer M, **Dunham CM**, Weixlbaumer A, Kelley AC, Ramakrishnan V. (2009) The Structure of the Ribosome with Elongation Factor G Trapped in the Posttranslocational State. *Science* 326(5953):694-99. PMCID: PMC3763468.
   d. Neubauer C*, Gao Y-G*, Andersen KR*, **Dunham CM**, Kelley AC, Hentschel J, Gerdes K, Ramakrishnan V and Brodersen DE. (2009) The structural basis for mRNA recognition and cleavage by the ribosome-dependent endonuclease RelE. *Cell* 139(6):1084-1095. PMCID: PMC2807027.

2. Ribosomal frameshifting is a key regulatory mechanism to control gene expression whereby the noncanonical reading of the genetic code facilitates expression of different protein products. Frameshift-prone tRNAs and mRNAs that contain complex tertiary structures to physically block unwinding by the ribosome during elongation are two major causes for the change in the mRNA reading frame. As a postdoctoral fellow in Venki Ramakrishnan's lab, I solved the first x-ray crystal structure of a frameshift suppressor tRNA bound to the 30S decoding center (**a**). These studies provided an alternative model for how tRNAs facilitate a change in the reading frame. In my own lab, I have extended these initial observations by solving a number of different frameshift-prone tRNAs bound to the 70S ribosome that have defined how additional tRNA nucleotides and modifications in the anticodon loop regulate the mRNA reading frame (**b,c**). Further, we discovered how tRNA modifications maintain the mRNA frame and how dysregulation results in the ribosome losing its grip on the mRNA (**d**).
   a. Maehigashi T*, Dunkle JA*, *Miles SJ* and **Dunham CM**. (2014) Structural insights into +1 frameshifting promoted by expanded or modification-deficient anticodon stem-loops. *Proc Natl Acad Sci* 111(35):12740-5. PMCID: PMC4156745.
   b. Fagan CE, Maehigashi T, Dunkle JA, *Miles SJ* and **Dunham CM**. (2014) Structural insights into translational recoding by suppressor $tRNA^{SufJ}$. *RNA* 12:1944-55. PMCID: PMC4238358.
   c. Hong S*, Sunita S*, Dunkle JA, Maehigashi T and **Dunham CM**. (2018) Mechanism of +1 tRNA-mediated frameshifting. *Proc Natl Acad Sci* 115(44):11226-31. PMCID: PMC6217423.
      Commentary by JF Atkins. Culmination of a half-century quest reveals insight into mutant tRNA-mediated frameshifting after tRNA departure from the decoding site. *Proc Natl Acad Sci* 115(44):11221-23. PMCID in progress.

d. Nguyen HA, Hoffer ED and **Dunham CM**. (2019) Importance of tRNA anticodon loop modification and a conserved, noncanonical anticodon stem pairing in $tRNA^{Pro}_{CGG}$ for decoding. 294(14):5281-91. PMCID: PMC6462517. *Selected as the Editor's Pick, an honor bestowed on the top 2% of JBC papers.*

3. Bacteria quickly adapt to changing environmental conditions by altering their gene expression to facilitate survival. My laboratory has investigated the roles that toxin-antitoxin pairs play in this transition. A majority of toxins inhibit protein synthesis and my laboratory has been focused on the largest class of translational inhibitors, ribosome-dependent toxins. These toxins recognize and cleave mRNA bound to the ribosome. We identified the *E. coli* YafQ toxin features required for ribosome binding and mRNA catalysis that distinguishes these specialized RNases from general microbial RNases (**a**). In contrast to the prevailing view that bacterial toxins are global translational inhibitors, we demonstrated that the ribosome-dependent HigB toxin only cleaves specific mRNA transcripts which suggests a more specialized role in the regulation of protein synthesis (**b**). Further, we identified the small ribosomal 30S subunit as a HigB toxin target suggesting that toxins recognize the initiation phase of translation (**c**) and demonstrated which HigB residues are critical for mRNA cleavage (**d**). Our results have provided significant insights into the molecular mechanism of toxin-mediated regulation of gene expression during stress and suggest that each toxin may be tuned to a specific stress.
   a. Maehigashi T*, Ruangprasert A*, Miles SJ and **Dunham CM**. (2015) Molecular basis of ribosome regulation and mRNA hydrolysis by the *E. coli* YafQ toxin. *Nucleic Acids Res* 43(16):8002-12. PMCID: PMC4652777.
   b. Schureck MA, Dunkle JA, Maehigashi T, Miles SJ and **Dunham CM**. (2015) Defining the mRNA recognition signature of a bacterial protein toxin. *Proc Natl Acad Sci* 112(45):13862-7. PMCID: PMC4653167.
   c. Schureck MA, Maehigashi T, Miles SJ, Marquez J and **Dunham CM**. (2016) mRNA bound to the 30S subunit is a HigB endonuclease substrate. *RNA* 22(8):1261-70. PMCID: PMC4931118.
   d. Schureck MA, Repack A, Miles SJ, Marquez J and **Dunham CM** (2016) Mechanism of endonuclease cleavage by the HigB toxin. *Nucleic Acids Res* 44(16):7944-53. PMCID: PMC5027501.

4. To address what are the critical molecular interactions between antitoxin and toxin that inhibit toxin activity, we solved X-ray crystal structures of two toxin-antitoxin family members regulated by diverse stresses: *P. vulgaris* HigBA complex (**a**) and *E. coli* DinJ-YafQ complex (**b**). To understand *Mycobacterium tuberculosis* toxins involved in ribosome inhibition, we studied the structure and function of the MazF-mt6 toxin where we identified determinants for the evolutionary degeneracy of the MazF toxin family (**c**). Lastly, we identified how the *E. coli* DinJ antitoxin undergoes selectively proteolysis by Lon protease during stress to release the YafQ toxin (**d**).
   a. Schureck MA, Maehigashi T, Miles SJ, Marquez J, Ei Cho S, Erdman R and **Dunham CM**. (2014) Structure of the *P. vulgaris* HigB-$(HigA)_2$-HigB toxin-antitoxin complex. *J Biol Chem* 289(2):1060-70. PMCID: PMC3887174.
   b. Ruangprasert A*, Maehigashi T*, Miles SJ, Giridharan N, Liu JX and **Dunham CM**. (2014) Mechanisms of toxin inhibition and transcriptional repression by *E. coli* DinJ-YafQ. *J Biol Chem* 289(30):20559-69. PMCID: PMC4110269.
   c. Hoffer EA, Miles SJ and **Dunham CM**. (2017) The structure and function of *Mycobacterium tuberculosis* MazF-mt6 provides insights into conserved features of MazF endonucleases. *J Biol Chem* 292(19):7718-26. PMCID: PMC5427253. (cover image)
   d. Ruangprasert A, Maehigashi T, Miles SJ and **Dunham CM**. (2017) Importance of the *E. coli* DinJ antitoxin carboxy terminus for toxin suppression and regulated proteolysis. *Mol Micro* 104(1):65-77. PMID: 28164393.

5. Natural collaborations with groups having overlapping interests also resulted in significant advances in our understanding of how translation is regulated. In collaboration with the Fredrick lab, we determined the structural basis for 16S ribosomal RNA *ribosome ambiguity mutations* (*ram*) mutations (**a,b**). In collaboration with the Conn lab, we determined the molecular basis for recognition of a complex RNA tertiary structure within the context of the intact 30S subunit by a pathogen-derived aminoglycoside-resistance rRNA methyltransferase. These studies were the first of a modification enzyme bound to a ribosome and helped rationalize why an intact 30S subunit was required for recognition by this family of enzymes (**c**). In collaboration with the Skiniotis lab, we solved high resolution cryo-EM structures of the ribosome translating a structured mRNA that causes frameshifting (**d**).

a. Fagan CE, Dunkle JA, Maehigashi T, Dang MN, Deveraj A, Miles SJ, Qin D, Fredrick K and **Dunham CM**. (2013) Reorganization of an intersubunit bridge induced by disparate 16S ribosomal ambiguity mutations mimics an EF-Tu-bound state. *Proc Natl Acad Sci* 110(24):9716-21. PMCID: PMC3683721.
   Commentary by PB Moore. Ribosomal ambiguity made less ambiguous. *Proc Natl Acad Sci* **110**(24):9627-8. PMCID PMC3683732.
b. Hoffer ED, Maehigashi T, Fredrick K, and **Dunham CM**. (2018) Ribosomal ambiguity (*ram)* mutations promote 30S domain closure and thereby increase miscoding. *Nucleic Acids Res, epub Nov 22.* PMCID in progress. (cover image)
c. Dunkle JA, Vinnal K, Desai PM, Zelinskaya N, Savic M, West DM, Conn GL* and **Dunham CM***. (2014) Molecular recognition and modification of the 30S ribosome by the aminoglycoside-resistance methyltransferase NpmA. *Proc Natl Acad Sci* 111(17):6275-80. PMCID: PMC4035980.
d. Zhang Y*, Hong S*, Ruangprasert A, Skiniotis G and **Dunham CM**. (2018) Alternative modes of E-site tRNA binding in the presence of structured mRNAs at the mRNA entrance channel. *Structure.* 26(3):437-445. PMCID: PMC5842130.

D. Research Support

Ongoing Research Support

R01 GM093278, NIH/NIGMS Dunham (PI) 09/01/19-08/31/23
Molecular basis of ribosomal frameshifting. This project aims to understand the molecular and biochemical basis for bacterial ribosomal frameshifting resulting from modification deficient tRNAs or complex mRNAs.

R01 AI088025, NIH/NIAID Conn, Dunham (MPI) 05/01/20- 04/30/25
*RNA modification and antibiotic resistance***.** This project investigates how ribosomal RNA methyltransferase enzymes confer resistance to aminoglycoside antibiotics.

Cystic Fibrosis Foundation New Investigator, DUNHAM19I0 Dunham (PI) 11/01/19- 10/31/21
Visualizing Co-translational Folding of CFTR. This project aims to determine the molecular basis of CFTR ∆508 folding defects on the ribosome.

Investigator in the Pathogenesis of Infectious Diseases
Burroughs Wellcome Fund Dunham (PI) 07/01/16-06/30/21
*Characterization of Pathways involved in Bacterial Persistence and Antibiotic Resistance***.** This project aims to determine the molecular mechanisms by which bacteria activate toxins in response to stress.

NSF CHE 1808711 Dunham (PI) 08/01/18-07/31/21
Expanding the genetic code: the rationale design of frameshift suppressor tRNAs in recoding. This project aims to expand the coding capacity of tRNAs using a rational, structure-based redesign.

R01 GM065183, NIH/NIGMS Ibba, Kearns, Dunham (MPI) 09/01/17- 08/31/21
Mechanisms of Translational Control. This project aims to understand the mechanism of ribosome stalling during poly-proline stretches.

R01 GM121650-01A1, NIH/NIGMS Keiler (PI) 08/01/17-07/30/21
Ribosome Rescue. This project focuses on understanding why ribosome rescue pathways inhibit bacterial growth. Role: subcontract

Carb-X (Combating Antibiotic Resistant Bacteria) Microbiotix (PI) 11/01/19-10/31/21
EF-Tu binding acylaminoheterocycles targeting MDR Neisseria Gonorrhoeae. The role of the Dunham lab is to solve high-resolution structures of EF-Tu bound to antibiotics. Role: Consortium Co-Investigator

NSF CHE 2003157 Weinert (PI) 08/01/20-07/30/23
Collaborative Research: Heme Distortion and Protein-Protein Contacts in Oxygen-Dependent Globin Coupled Sensor Signaling Project. The role of the Dunham lab is to solve high-resolution structures of globin coupled sensors. Role: subcontract

BIOGRAPHICAL SKETCH

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NAME: Pooja Srinivas

eRA COMMONS USER NAME (credential, e.g., agency login): psrini7

POSITION TITLE: Graduate Student, Molecular and Systems Pharmacology Graduate Program

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	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Berkeley, California	B.A	08/2013	05/2017	Molecular and Cell Biology
Emory University, Atlanta, GA	Ph.D.	08/2017	05/2022 (expected)	Molecular and Systems Pharmacology

A. Personal Statement

I am submitting this proposal to support my development into an independent researcher. My goal for obtaining a Ph.D. is to become an independent biomedical researcher in an academic institution, performing research that will benefit mankind, through fundamental research of important biological questions. I am currently seeking a Ph.D. degree in molecular and systems pharmacology, and conducting biochemistry and molecular biology research. I have been working to achieve this goal from my undergraduate career, performing research, and becoming interested in cellular and molecular mechanisms, and how these mechanisms can contribute to human health.

During my undergraduate, I had the opportunity to conduct research in several labs, spanning across a range of research fields. This not only gave me exposure to a wide variety of research fields, but also gave me the opportunity to explore different areas of research, and establish the type of research I enjoyed studying. I first worked at the NIH, through the Summer Internship Program, under Dr. Bin Gao at the Laboratory of Liver Diseases at the National Institute of Alcohol Abuse and Alcoholism. I gained wet-lab experience by studying the immunological responses and molecular pathogenesis of alcoholic liver diseases, focusing on how diet affects liver physiology and metabolism in binge drinkers by assessment of neutrophil and natural killer T-cell infiltration in a mouse model. I became proficient in many techniques during this 10-week experience, including mouse handling, RT-PCR, histological examination, and immunohistochemistry. This experience also fueled my interest in exploring more fields of research. I joined the lab of Dr. Fenyong Liu, a professor of infectious diseases at UC Berkeley, through the undergraduate research apprenticeship program. Here, I studied genetic factors that contribute to latency of human cytomegalovirus in a cell culture system; I learned basics of cell culture, performing transfections, and fluorescence microscopy. I later joined the lab of Dr. Lance Kriegsfeld, studying circadian control of the reproductive axis. In this lab, using mouse and hamster animal models, I studied the circadian control of hypothalamic neuron regulation on the female reproductive system. I became proficient in animal handling, including perfusions and tissue extractions, RNA extraction and q-RT-PCR, and immunohistochemistry. Though diverse in research fields, these experiences taught me a wide range of wet lab techniques applicable to research areas, and exposed me to different areas of basic scientific research. Additionally, through my computational toxicology class, I conducted a research project, a meta-analysis of sources of arsenic contamination in drinking water, correlated to increased lung cancer incidence. My project was selected by the professor to submit to the Society of Toxicology meeting, where I presented this research.

When choosing a lab to conduct my Ph.D. research, I wanted to join a lab that would challenge me to think critically about significant biological questions. I chose the laboratory of Dr. Christine Dunham, focusing on mechanisms of translation regulation in bacteria. Dr. Dunham is an accomplished structural biologist and biochemist; her mentorship and lab provides the ideal environment to complete my proposed research. My

proposed studies are looking at mechanisms of ribosome rescue, an essential bacterial process. The long-term goal of this project is to understand the molecular mechanisms of the novel rescue protein ArfT in its role in ribosome stalling rescue in *F. tularensis,* to provide a basis for structure-activity relationship analysis to develop new antibiotics against this novel target. This project involves working directly with the Keiler Lab at Penn State, and the Emory Apkarian Integrated Electron Microscopy Core, providing the opportunity for collaboration with scientists both within my school and between different institutions. My work and the lab also provides me with the ideal avenue to become a productive scientist, and many opportunities to disseminate my research at national and international conferences, publish peer-reviewed manuscripts, and mentor students. My choice of sponsor, research project, and the training I hope to receive from this fellowship will provide me a solid foundation for my future career goals to become a postdoctoral fellow, and later an academic researcher at a R-1 research institution.

B. Positions and Honors

Positions and Employment

May 2014 – Aug 2014 **Summer research Intern**, NIAAA, NIH
Supervisor: Dr. Bin Gao

Jan 2014 – May 2017 **Note-taker and Exam Scribe**, Disabled Students Program, UC Berkeley

Jan 2015 – Aug 2015 **Undergraduate Research Apprentice**, Department of Infections Diseases, UC Berkeley
Supervisor: Dr. Fenyong Liu

Jan 2016 – May 2017 **Research Assistant**, Department of Psychology, UC Berkeley
Supervisor: Dr. Lance Kriegsfeld

Aug 2018 – Present **Graduate Student Researcher**, Department of Biochemistry, Emory University
Supervisor: Dr. Christine Dunham

Academic and Professional Honors

2013 – 2017 **Honors to Date, UC Berkeley:** completion of at least 12 letter-graded units and a cumulative GPA equivalent to that required for Distinction in General Scholarship (rough equivalent to *cum laude)*
2014 – 2016 **Dean's List, UC Berkeley:** 13 or more letter-graded units, GPA in the top 10% of undergraduates
2017 **Graduated 'Distinction in General Scholarship', UC Berkeley:** *cum laude* rough equivalent
2018 – 2019 **Appointment to T32-GM008602 Pharmacological Training Grant**, Emory University
2020 – 2022 **Appointment to T32-AI106699 Anti-infectives Training Grant,** Emory University

Other Experiences

2018 Member, Association of Women in Science
2018 Member, American Society for Biochemistry and Molecular Biology
2018 Member, International Chemical Biology Society
2020 Member, RNA Society

C. Contributions to Science

1. **Meta-analysis of the geographic association of inorganic arsenic in drinking water, correlated with lung cancer and environmental contamination sources.**

With Dr. Dale Johnson, as independent research stemming from the completion of a computational toxicology class, we conducted research on sources of drinking water contaminated with inorganic arsenic, focusing on the Barnett Shale region of Texas and Oklahoma, where hydraulic fracturing as a natural gas extraction method is predominant. We correlated high levels of arsenic contamination, and genetic polymorphisms within the exposed population, to higher incidence of lung cancer in this region. We presented this data at the 2017 Society of Toxicology Meeting in Baltimore, Maryland

a. P. Srinivas, J. Tian, D.E. Johnson (2017) Geographic Association Study of Arsenic in Drinking Water, Correlating Cancer Statistics, and Sources of Contamination. *Toxicologist* 156(1) 185

2. **Circadian regulation of RFRP-3 Inhibition the hypothalamic-pituitary-gonadal axis**

With Dr. Lance Kriegsfeld, we worked on establishing the role of Arginine, Phenylalanine amide-related peptide-3 (RFRP-3), also known as gonadotropin inhibiting hormone, in regulating the time-sensitive pre-ovulatory luteinizing hormone (LH) surge. This work was conducted in Syrian hamsters, and all animal work was conducted before I joined the lab. I was responsible for sectioning brains, and establishing and optimizing an RNA extraction protocol for the different regions of the hypothalamus and pituitary, to maximize total RNA extracted and RNA integrity. I also worked on designing effective housekeeping gene primers, that did not exhibit circadian regulation in any region of interest. This work was presented at the 2016 Society for Behavioral Neuroendocrinology Conference in Montréal, Canada.

a. N. Gotlieb, C. N. Baker, P. Srinivas, V. J. Kim, L. J. Kriegsfeld. (2016) Time-dependent Sensitivity of the GnRH System to RFRP-3 Inhibition in the control of the Preovulatory LH surge. Society for Behavioral Neuroendocrinology

3. **Alternative mechanisms of ribosome rescue**

My current project in Dr. Christine Dunham's laboratory focuses on ribosome stalling rescue in the pathogenic bacterium *F. tularensis.* I will work to address the biochemical and structural basis of ribosome stalling rescue of the novel alternative release factor, ArfT.

a. P. Srinivas, Goralski, T. D. P., Keiler, K. C., Dunham, C. M. "Alternative mechanisms of ribosome stalling rescue in the Gram-negative bacterium Francisella tularensis," American Society for Biochemistry and Molecular Biology National Meeting, April 6-9, 2018 in Orlando, Fl. [Poster]

b. Z. D. Aron, A. Mehrani, E. D. Hoffer, K. L. Connolly, M. C. Torhan, J. N. Alumasa, P. Srinivas, M. Cabrera, D. Hosangadi, J. S. Barbor, S. Cardinale, S. Kwasny, M. Butler, T. Opperman, T. Bowlin, A. Jerse, S. M. Stagg, C. M. Dunham, K. C. Keiler. (2020) Ribosome rescue inhibitors cure gonorrhea using a new mechanism. [Submitted]

4. **Oligomeric state of binding of HigBA transcriptional repression**

My rotation project in Dr. Christine Dunham's laboratory focused on characterizing the oligomeric state of binding of the toxin-antitoxin complex HigBA to its operator. I conducted electrophoretic mobility shift assays and analytical ultracentrifugation to assess whether the toxin-antitoxin complex had functional repression of the *higBA* operon as a trimer species (HigA-HigB-HigA) or a tetramer species (HigA-$HigB_s$-HigA). *Italics denotes manuscripts in progress*

a. *M. A. Schureck, E. D. Hoffer, D. Wang, P. Srinivas, N. Onouha, S. E. Cho, J. Meisner, S. J. Miles, C. M. Dunham. (2020) "A trimer to tetramer transition regulates transcriptional regulation of the higBA toxin-antitoxin operon"*

D. Additional Information: Research Support and/or Scholastic Performance

YEAR	COURSE TITLE	GRADE
	UC BERKELEY, GPA: 3.83	
2013	General Chemistry	B+
2013	General Chemistry Lab	A
2013	Elementary Latin 1	A
2013	Calculus 1A	A-
2013	Mechanical Engineering Directed Group Study	P*
2014	General Biology	B+
2014	Chemical Structures and Reactivity 1	B+
2014	Organic Chemistry Lab 1	A
2014	Elementary Latin 2	A
2014	Ethnic Studies Supervised Group Study	P*
2014	Calculus 1B	A
2014	Chemical Structures and Reactivity 2	A

YEAR	COURSE TITLE	GRADE
2014	Organic Chemistry Lab 2	A
2014	Introductory Physics 1A	A
2014	Urban Experience	B+
2014	Southern Baroque Art	P
2014	Middle Eastern Perspectives	A
2014	Seminar on Health and Medical Issues	P*
2015	Introductory Physics 1B	B+
2015	General Psychology	A
2015	Multivariable Calculus	P
2015	Public Health Graduate Seminar	A
2015	Theater Directed Group Study	P*
2015	Neurobiology of Stress	A
2015	Biophysical Chemistry	A
2015	Structure and Interpretation of Computer Programs	P
2015	Human Anatomy	P
2015	Linear Algebra and Differential Equations	P
2016	Microbial Genomics and Genetics	A
2016	Biochemistry: Pathways, Mechanisms, and Regulation	A
2016	Human Food Practices	A
2016	Computational Toxicology	A+
2016	Inorganic Chemistry in Biological Systems	A
2016	Biological Clocks	A+
2016	General Biochemistry	B+
2016	Nutritional Function and Metabolism	P
2017	Hormones and Behavior	A+
2017	Biochemistry and Molecular Biology	A
2017	Drug Action	A
	EMORY UNIVERSITY, GPA: 4.0	
2017	Introduction to Molecular and Systems Pharmacology I	A
2017	Basic Biomedical and Biological Science	A
2017	Ethical Issues in Pharmacology	S
2017	Jones Program in Ethics Core Class	S
2017	Introductory Graduate Seminar	A
2017	Laboratory Rotations	S
2018	Introduction to Molecular and Systems Pharmacology II	A
2018	Drug Metabolism and Toxicology	A
2018	Statistical Design and Analysis of Experiments	A
2018	Graduate Seminar	A
2018	Laboratory Rotations	S
2018	Advanced Graduate Research	A
2018	Grant Writing for Molecular and Systems Pharmacology	A
2018	Advanced Graduate Research	A
2018	Jones Program in Ethics: Predicting Mental Illness	S
2018	Ethical Issues in Pharmacology	S
2018	Introductory Graduate Seminar	A
2018	Graduate School Teaching Workshop	S
2018	Teaching Assistantship	S
2019	Introduction to Pharmacology Based Pharmacokinetic Modeling	A
2019	Jones Program in Ethics: Mitigating Implicit Bias	S
2019	Jones Program in Ethics: How to Translate Academia	S
2019	Jones Program in Ethics: Leading a Diverse Group of People	S
2019	Introductory Graduate Seminar	A
2019	Advanced Graduate Research	A
2019	Advance. Graduate Research	A
2019	Advanced Graduate Seminar	S

YEAR	COURSE TITLE	GRADE
2020	Advanced Graduate Research	A
2020	Advanced Graduate Seminar	S

Courses at UC Berkeley are graded from an A+ – F- scale, with non-letter graded courses offered for Pass/Not Pass (P/NP) credit. *Courses not offered for letter grade

Courses at Emory University are graded from an A – F scale, with non-letter graded courses offered for Satisfactory/Unsatisfactory (S/U) credit. Any course taken for S/U credit does not have a letter grade option.