BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Victoria L. Robinson

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

POSITION TITLE: Associate Professor, Associate Depart. Head for Graduate Research and Education

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
Trinity College, Hartford CT	BS	05/1988	Biochemistry
Villanova University, Villanova PA	MS	05/1992	Chemistry
University of Iowa, Iowa City IA	PHD	12/1997	Biochemistry/Structural Biology
HHMI/UMDNJ-RWJMS, Piscataway NJ	Post-Doc	08/2004	Structural Biology/ Microbiology

A. Personal Statement

The goal of the research in my laboratory is to understand the relationship between events triggered from the onset of stress and cellular survival. We are particularly focused on how protein biogenesis, an inherently taxing process, is regulated to conserve resources and to support adaption to adverse environmental factors ensuring homeostasis. We have many years of experience deciphering the structural and biochemical properties of proteins. Although, considered a protein structure laboratory (protein crystallography and cryoEM) laboratory, there is a wide range of experience in my group utilizing biophysical techniques, such as fluorescence spectroscopy, ITC, MST, small angle scattering (SAXS), CD, as well as numerous biochemical assays to examine enzymatic properties of proteins and their interactions with various cellular partners. Current projects are centered around studying the interaction between the ribosome and two unusual GTPases. The first is BipA, a GTPase required for regulating physiologic responses in prokaryotes upon the onset of adverse growth conditions. My lab has been investigating this protein for a number of years and through some recent cryo-EM, biochemical and in vivo studies, has developed a model as to how it contributes to stress adaptation in bacteria by controlling the flow of information via second messanger to regulate ribosomal events.

Our second project it to investigate the homolog of this protein we recently discovered in *Toxoplamsa gondii,* TgBipA. The parasites that cause malaria and toxoplasmosis contain a unique four-membraned non-photosynthetic plastid organelle, termed the apicoplast, which produces essential metabolites that the parasite cannot scavenge from the host. Knockout of TgBipA in *T. gondii* causes loss of apicoplast morphology and more significantly, the parasites do not form plaques confirming its essential role in growth. We are utilizing many techniques to understand how biochemical properties of these two proteins contribute to their cellular function. Structural studies, computational modeling, macromolecular interactions assessed by biochemical and biophysical and done routinely in my group.

For several years**,** my career was disrupted due to extreme elder care responsibilities. My research program is again well established and over the past two years, has grown to include four Ph.D. students.

Ongoing Research Support

NIH R21 Robinson (PI) 12/01/25 to 11/30/2027
Role of Alternate Ribosome Binding in Pathogenesis
Not yet Awarded, score received: 10
An effort to merge structural models, solution biophysics experiments, biochemical data and comparative microbiology as a platform to examine how several chemical disrupt the cellular function of BipA and may ultimately serve as leads for new therapeutics.

UConn Academic Themes Award Robinson, PI; Campellone Co-I 01/30/24 to 6/30/25
UConn Office of Vice President for Research (OVPR)
Anti-Infectives for Enterohemorrhagic Escherichia coli, a Global Diarrhea-Causing Pathogen without Effective Treatments
We are validating BipA, an essential protein in *Toxoplasma gondii*, as a target for anti-parasitic therapeutics.

UConn Research Excellence Award Heaslip, Robinson (Co-Is) 06/15/23 to 09/31/25
UConn Office of Vice President for Research (OVPR)
Development of new anti-parasitic drugs targeting *Toxoplasma gondii*
We are validating BipA, an essential protein in *Toxoplasma gondii*, as a target for anti-parasitic therapeutics.

Atomwise AIMS and subsequent AIMS Prime Award Robinson (PI) 12/1/18 - present
Virtual Screening for Inhibitors of the Bacterial Translation Factor BipA
Working with scientist at Atomwise to utilize virtual screening and docking with their proprietary AtomNet software to identify small molecules which modulate the biochemical activities of BipA.

Completed Research Support

Department of Defense Robinson (co-I) 1/22/20 to 12/31/2024
Cytoplasmic Suppression of Inflammatory Signaling
Define the intrinsic disorder of tNIP1 protein and its role in regulating A20 partnering, ubiquitin-binding and inflammatory pathways in cultured cells.

UConn Academic Themes Award Robinson, PI; Campellone Co-I 01/30/24 to 6/30/25
UConn Office of Vice President for Research (OVPR)
Anti-Infectives for Enterohemorrhagic Escherichia coli, a Global Diarrhea-Causing Pathogen without Effective Treatments
We are validating BipA, an essential protein in *Toxoplasma gondii*, as a target for anti-parasitic therapeutics.

START Preliminary Proof-of-Concept Fund Robinson (PI) 12/31/19 to 12/31/22
UConn Office of Vice President for Research (OVPR)
Structure Based Virtual Screening to Uncover Inhibitors of BipA
These funds are to continue our work characterizing small molecule inhibitors of BipA as potential antimicrobials.

START Preliminary Proof-of-Concept Fund Heaslip, Robinson (Co-PIs) 5/31/21 to 06/30/22
UConn Office of Vice President for Research (OVPR)
Development of new anti-parasitic drugs targeting *Toxoplasma gondii*
We are validating BipA, an essential protein in Toxoplasma gondii, as a target for anti-parasitic therapeutics.

UConn Research Excellence Program Award Robinson, Benson (co-PIs) 7/1/18 to 6/30/22
Harmonizing Physiology with Structural Biology Approaches to Define the Roles of the BipA in Translation
The goal of this research is to define the biochemical features of BipA that support its role in stress adaptation.

B. Positions, Scientific Appointments, and Honors

Positions and Employment:

2024-present Director, UConn MCB Biophysical Core Facility
2022-present Associate Dept. Head, Graduate Research and Education, MCB Dept., UConn Storrs.
2017-present Director, UConn Professional Master's Program in Applied Biochemistry and Cell Biology
2010-present Associate Professor, Dept. of Molecular and Cell Biology, University of Connecticut, Storrs
2004-2010 Assistant Professor, Dept. of Molecular and Cell Biology, University of Connecticut, Storrs
1999-2004 Post-doctoral Associate, HHMI/ UMDNJ-RWJMS
1998 Post-doctoral Fellow, SmithKline Beecham Pharmaceuticals, King of Prussia, PA
1992-1997 Graduate Research Assistant, University of Iowa
1990-1992 Assistant Scientist, Rhone-Poulenc Rorer Biotechnology, Inc., King of Prussia, PA
1988-1990 Research Assistant, Rhone-Poulenc Rorer Biotechnology, Inc., King of Prussia, PA

Honors and Awards:

2009 Faculty Early Career Development Award, National Science Foundation
2006 American Heart Association (AHA) Scientist Development Grant
2001 Research Achievement Award, UMDNJ-RWJMS
1994-1997 Predoctoral Fellowship, Univ. of Iowa Center for Biocatalysis and Bioprocessing
1994 American Heart Association (AHA) Predoctoral Fellowship (declined)

Other Experience and Professional Memberships:

2021-present Associate Editor, Molecular Recognition, Frontiers in Molecular Biosciences
2019-present NSF Panel Participant
2020-2022 Member, Medicinal Chemistry Faculty Search, UConn School of Pharmacy
2020-present UConn MCB/STEM Workplace Navigator
2017-present Member, Graduate School Hearing and Conflict Mediation Advisory Committees
2017-2018 Member, Biophysical Core Director Search Committee
2016-2017 Member, MCB Tenure Track Search Committee
2015-2021 Review Editor, Molecular Recognition, Frontiers in Molecular Biosciences
2015-2022 Member, Graduate Faculty Council
2012-present Director, UConn Partnership for Excellence in Structure Biology
2011-2017 Co-head, Protein X-ray Crystallography Facility, University of Connecticut
2011-2016 Structural Biology, Biochemistry and Biophysics Graduate Program Chair
2010-2018 Member, Dept. Promotion, Tenure and Review Committee; Chaired, 2016-18, 2020-22
2010-present Member, American Heart Assoc. Basic Cell - Protein & Crystallography Peer Review Committee
2010-2014 Ombudsperson, Department of Physics, University of Connecticut
2007-2016 NSF Peer Reviewer, ad hoc
2005-present Member, Institute for Material Sciences, Univ. of Connecticut, Storrs, CT

C. Contributions to Science

1. The Role of Bacterial GTPases in Translation and Stress: My interest in bacterial GTPases began during my time at UMDNJ where I solved the first structure of a GTPase with multiple G-domains, a bacterial protein EngA (Der). This work continued at UConn where my group determined the ribosome binding properties of the translation factor BipA. We had the novel finding that BipA forms two distinct biologically relevant complexes with the ribosome, 70S:BipA and 30S:BipA. This is the only bacterial protein known to have two distinct ribosome binding modes. The formation of these species is dependent upon the guanine nucleotide pool in the cell, specifically GTP and ppGpp, an alarmone responsible for adaptation to altered growth conditions in bacterial cells. We have submitted an article describing the requirement of BipA for adaptation to and re-stablishing homeostasis after the onset of various stress (Bova, R.A., Benson, D.R. and Robinson, V.L. Physiological Role of BipA in *Escherichia coli* MG1655 During Stress Adaptation, under revision at *Appl. Environ. Microbiol.*). Our data suggests that BipA acts as an intermediary between the ribosome and the cellular environment and that its structural and regulatory properties influence how the ribosome responds to current cellular conditions. We have another under review utilized solution biophysics, mutagenesis and biochemistry to identify a specificity determinant for ppGpp binding to BipA. Our initial work stimulated numerous investigations into how ppGpp

might regulate the biochemical and biophysical properties of various GTPases to synchronize adaptive responses to translational events.

a. Robinson, V.L., Hwang, J., Fox., E., Inouye., M. and Stock, A.M. (2002) Domain arrangement of Der, A Switch Protein Containing Two GTPase Domains. *Structure* **10**:1649-58.
b. deLivron, M.A. and Robinson, V.L. (2008) *Salmonella enterica* Typhimurium BipA Exhibits Two Distinct Ribosome Binding Modes. *J. Bacteriol.* **190**:5944-52.
c. deLivron, M.A., Makanji, H.S., Lane, M.C. and Robinson, V.L. (2009) A Novel Domain In Translational GTPase BipA Mediates Interaction with the 70S Ribosome and Influences GTP Hydrolysis. *Biochemistry* **48**:10533-41.

2. Drug Design for DHFR and other antibiotics inhibit Ribosomal Processes. We have had a large role supporting structure-based design strategies with several collaborators at UConn as well as the development of antimicrobials drug development projects within my own group. We have been working with Dr. Dennis Wright's group to design new antifolate chemotype that is able to maintain potency against trimethoprim (TMP)-resistant dihydrofolate reductase (DHFR) enzymes. In addition, we have supported ongoing work from Dr. Mark Peczuh group (Chemistry, UConn) to develop novel classes of glycosylated small molecules to target the 70S ribosome in gram negative bacteria. And finally, we have been validating and screening small molecule libraries for their influence on the biochemical and cellular properties of BipA. Its involvement in rapidly shifting the cellular physiology of bacteria to promote an adaptive response by facilitating the formation of new translational complexes may make it a good antimicrobial target.

a. AI is a viable alternative to high throughput screening: a 318-target study *Sci Rep* **14**, 7526 (2024). https://doi.org/10.1038/s41598-024-54655-z.
b. Krucinska, J., Lombardo, M.N., Erlandsen, H., Hazeen, A., Duay, S.S., Pattis, J.G., Robinson, V.L., May, E.R. and Wright, D.L. (2019) "Functional and structural basis of *E. coli* enolase inhibition by SF2312: a mimic of the carbanion intermediate." *Sci Rep.* 9(1):17106. PMCID: PMC6863902.
c. Mayo, C.B., Erlandsen, H., Mouser, D.J., Feinstein, A.G., Robinson, V.L., May, E.R. and Cole. J.L. (2019) "Structural Basis of Protein Kinase R Autophosphorylation." *Biochemistry*. 58(27):2967-77. PMCID: PMC6615999
d. Krucinska, J., Falcone. E, Erlandsen, H., Hazeen, A., Lombardo, M.N., Estrada, A., Robinson, V.L., Anderson, A.C. and Wright, D.L. (2019) Structural and Functional Studies of Bacterial Enolase, a Potential Target against Gram-Negative Pathogens. *Biochem.* **58**:1188-97. PMCID: PMC6511404.
e. Cannone, Z., Shaqra, A.M., Lorenc, C., Henowitz, L., Keshipeddy, S., Robinson, V.L., Zweifach, A., Wright, D. and Peczuh, M.W. (2019) Post-Glycosylation Diversification (PGD): An approach for Assembling Collections of Glycosylated Small Molecules. *ACS Comb. Sci.* 21:192-7. PMCID: 30607941

3. Understanding Nucleo-cytoplasmic Trafficking and IDPs: We have been addressing questions regarding the molecular mechanism of action of nucleostemin, a circularly permuted GTPase that plays an important role in maintaining nucleolar integrity. NS shuttles from the nucleolus to the nucleoplasm in response to cell cycle changes and stress conditions. This trafficking depends on interactions with multiple partners that regulate critical processes such as cellular proliferation, ribosome biogenesis and DNA maintenance thereby ensuring homeostasis in eukaryotic cells. All of these activities suggest that NS acts as a GTP dependent regulatory link between developmental controls and cell cycle machinery. We have applied bioinformatics tools together with numerous biophysical techniques to begin to understand the solution properties of *Drosophila melanogaster* nucleostemin 1 (NS). Our studies indicate that NS has large regions of disorder at the termini while the core cpGTPase domain is structured (Daman, T.H. *et al.* Intrinsic Structural Disorder Revealed in the Circularly Permuted GTPase Nucleostemin, under review*)*. Combining SAXS data and molecular dynamics flexible fitting, we provide the first structural model of this family of proteins. Future goals include how the permutation of the G-domain, leading to the repositioning of the switch I region, influences the enzymatic properties of the protein. Our experience with intrinsically disordered proteins has led to a collaboration with Dr. Brian Aneskievich (UConn School of Pharmacy) to understand how the disordered regions in tNIP, a protein involved in inflammatory pathways, provide a scaffold for its interactions with A20 and ubiquitin.

a. Rosby, R., Cui, Z., Rogers, E., deLivron, M.A., Robinson, V.L. and DiMario, P.J. (2009) Knockdown of the Drosophila GTPase nucleostemin 1 impairs large ribosomal subunit biogenesis, cell growth, and midgut precursor cell maintenance. *Mol. Biol. Cell*. **20**:4424-34.
b. Shamilov, R, Robinson, V.L. and Aneskievich, B.J. (2021) Seeing Kerotinocyte Proteins Through the Looking Glass of Intrinsic Disorder. *Int. J. Mol. Sci.*, **22**:7912.

4. **Two-Component Signaling Field:** My work contributed to the understanding that response regulator proteins utilized distinct signaling mechanisms. During my post-doctoral work, I crystallized the second full length response regulator (RR) from the OmpR/PhoB family of proteins. Mutational study was then designed to examine how intermolecular contacts contributed to communication between the N- and C-terminal domains of these RRs. We also carried out a complete structural analysis addressing the dephosphorylation of CheY by its cognate phosphatase CheZ. Through multiple structures and complimentary biochemistry, we proved that CheZ associates with a "meta-active" state of CheY that is distinct from either the active or inactive form of the protein indicating a continuous flow of information between these two partners. At UConn, I collaborated with Drs. Andrei Alexandrescu and Dan Gage to solve the NMR structure of an unusual RR Sma1. This CheY like protein is missing the fourth α-helix of the consensus 455 face but instead has a dynamic loop suggesting that it has an altered recognition interface for binding to downstream effectors.

a. Stock, A.M., Robinson, V.L. and Goudreau, P.N. (2000) Two-component signal transduction. *Ann. Rev. Biochem*. **69**:183-215.
b. Robinson, V.L., Wu, T. and Stock, A.M. (2003) Structural Analysis of the interdomain interface of DrrB, An OmpR/PhoB family member from *Thermotoga maritima*. *J. Bacteriol*. **185**:4186-94.
c. Guhaniyogi, J., Robinson, V.L. and Stock, A.M. (2006) Crystal structures of beryllium fluoride-free and beryllium fluoride-bound CheY in complex with the conserved C-terminal peptide of CheZ reveal dual binding modes specific to CheY conformation. *J. Mol. Biol.* **359**:624-45.
d. Sheftic, S.R., Garcia, P.P., Robinson, V.L., Gage, D.J. and Alexandrescu, A.T. (2012) Nuclear magnetic resonance structure and dynamics of the response regulator Sma0114 from *Sinorhizobium meliloti. Biochem.* **51**:6932-41.

Complete List of Published Work in MyBibliography:
https://pubmed.ncbi.nlm.nih.gov/?term=robinson+vl&sort=pubdate

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: Tristan Evans

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

POSITION TITLE: Graduate Research Assistant/Teaching Assistant

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 Connecticut	BSc	9/1/2017	5/1/2021	Molecular and Cell Bio
University of Connecticut	PhD	9/1/2021	Ongoing	Structural Biochemistry
University of Connecticut	Cert.	8/26/2024	Ongoing	Higher Level Ed.

A. Personal Statement

I have always maintained a desire to gain and spread knowledge. As a child it began with lighthearted fun facts and as I matured it developed into a hunger to push the boundaries of science. This spark did not fully ignite until my freshman year at the University of Connecticut when I was introduced to epigenetics offhandedly by an Anthropology teaching assistant. My fascination with this topic motivated me to switch my major to Molecular and Cell Biology (MCB). The summer before my sophomore year, I joined Dr. Michael O'Neill's lab in the MCB department where my passion for research was fully developed. In 2021, I continued at UConn as a doctoral student in the MCB Ph.D. program. My scientific interests pivoted again as I became a member of Dr. Simon White's group. Dr. White utilizes biophysical methods and structural biology, mainly cryoEM, to understand how RNA viruses assemble. He is also interested in the evolution, stability and assembly of actinobacteriophage. I became involved in this bacteriophage research and solved over a dozen structures learning the nuances of cryoEM including grid prepration, data collection and processing, de novo model building and refinement. Earlier this year, Dr. White transitioned out of academia, and I joined Dr. Victoria Robinson's group. Instead of working with bacteriophages I am now studying their prey, specifically *Escherichia coli*, and how they respond to environmental stress such as nutrient deprivation. Our lab does not solely focus on structural biology but utilizes microbiology, biophysics and biochemistry to obtain a wholistic explanation of stress adaptation in microrganisms. My main project is to obtain a structural description of how the translational GTPase BipA forms a complex with two *E. coli* ribosomal species using cryoEM.

B. Positions, Scientific Appointments and Honors

2025	Jean Lucas-Lenard Special Summer Fellowship in Biochemistry
2024 – Present	Assistant Director, University Writing Center, University of Connecticut
2023 – Present	Graduate Research Assistant, Robinson Lab, MCB Department, University of Connecticut
2021 – 2023	Graduate Research Assistant, White Lab, MCB Department, University of Connecticut
2020 – 2021	Institute for Brain and Cognitive Sciences Grant Recipient
2018 – 2021	Undergraduate Research Assistant, M. O'Neill Lab, MCB Deparment, University of Connecticut

C. Contributions to Science

Undergraduate Research: From the summer of 2018 to the summer of 2021, I was part of Dr. Michael O'Neill's lab at the University of Connecticut. Dr. O'Neill's work focused on the epigenetics of *Mus musculus*. Specifically, a novel imprinted gene on the mouse X chromosome with links to autism. During my time in the lab, I identified potential protein interactions between the X chromosome gene and other proteins involved in the process known as Meiotic Sex Chromosome Inactivation (MSCI). Using gene knockdown mice, I also observed a sublethal event leading to a bias in sex of offspring, relating to the phenomenon of transgenerational epigenetic inheritance.

1. Natali Sobel Naveh, Robert J. Foley, Katelyn R. DeNegre, **Tristan C. Evans**, Anne Czechanski, Laura G. Reinholdt, Michael J. O'Neill. Deficiency of SYCP3-related XLR3 disrupts the initiation of meiotic sex chromosome inactivation in mouse spermatogenesis. **doi:** https://doi.org/10.1101/2021.03.30.437712

Graduate Research: Starting in 2021 I joined the UConn MCB graduate school and decided to switch focus to structural protein work. I was intrigued by the work of Simon White, combining cryoEM and virology to better understand bacteriophages. Before he left the university, I modeled dozens of phage proteins. We are currently finishing a paper that combines Alphafold predictions and validated EM structures of the bacteriophage major tail protein. Through this project I have 10 PDB validated structures ready to be deposited in tandem.

After Simon's departure, I transferred to the lab of Dr. Victoria Robinson, someone who I had worked closely with during my time in the White lab. My current project involves examining complex formation between the ribosome and several proteins required for the bacterial stress response, particularly those involved in protein production. From data sets collected at NCCAT, I have three different structures of the bacterial GTPase BipA in complex with the 70S ribosome at 2.1 – 2.5 Å. These three structures have given us great insight into BipA's function in microorganisms. Wet lab studies are ongoing to validate our models and a paper will be submitted Fall 2025. I have also become the point person in the UConn MCB department for grid preparation and software training. My goal is to merge my cryoEM expertise with biochemistry and microbiology to produce new insights into the bacterial stress response.

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
2021	Research in Progress	S
2021	Lab Rotations	S
2021	Intro to Research	A
2021	Faculty Research	S
2022	Virology	A
2022	Scientific Writing	A
2022	Responsible Conduct Research	S
2022	Foundations of Structural Biochem	A
2022	Structure and Dynamics of Macromolecular Machines	A
2022	Research in Progress	S
2022	Invited Seminar	S
2022	Research	A
2023	Techniques of Biophysical Chemistry	B
2023	Structure/Function of Biological Macromolecules	B