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: White, Simon

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

POSITION TITLE: Assistant 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
University of Hertfordshire, Hatfield, Hertfordshire	BS	07/2005	Applied Biology
University of Leeds, Leeds, West Yorkshire	MS	07/2006	Biosciences
University of Leeds, Leeds, West Yorkshire	PHD	01/2011	Bionanotechnology

A. Personal Statement

I am well placed to pursue the work laid out in this application. I have extensive experience working with different bacteriophages (various actinobacteriophages, see Podgorski et al. 2020, and M13 and MS2 bacteriophages). I have the experience with cryo-electron microscopy needed for success and have six structures deposited in the electron microscopy databank, and I am currently collaborating with others at the University of Connecticut on cryo-electron microscopy data. In the past year I have built de novo models using actinobacteriophage cryoEM maps (all sub 3 angstrom resolution) for seven bacteriophage (to be deposited). I have the experience needed with cryoSPARC and with Phenix for model building.

I am currently in my fourth year at the University of Connecticut as an assistant Professor. I currently supervise five graduate students (three PhD and two masters) and mentored thirteen undergraduate students (five of whom are still in my lab). We have monthly lab meetings where they present their work in a friendly and supportive environment. These lab meetings are an important tool for trouble shooting problems they may have and developing new avenues of research. They are an excellent team and we are well placed complete the stated aims.

1. Luque A, Benler S, Lee D, Brown C, White S. The Missing Tailed Phages: Prediction of Small Capsid Candidates. Microorganisms. 2020 December 08; 8(12):1944-. Available from: https://www.mdpi.com/2076-2607/8/12/1944 DOI: 10.3390/microorganisms8121944
2. Podgorski J, Calabrese J, Alexandrescu L, Jacobs-Sera D, Pope W, Hatfull G, White S. Structures of Three Actinobacteriophage Capsids: Roles of Symmetry and Accessory Proteins. Viruses. 2020 March 08; 12(3):294. Available from: https://www.mdpi.com/1999-4915/12/3/294/htm DOI: 10.3390/v12030294
3. Shakeel S, Dykeman EC, White SJ, Ora A, Cockburn JJB, Butcher SJ, Stockley PG, Twarock R. Genomic RNA folding mediates assembly of human parechovirus. Nat Commun. 2017 Feb 23;8(1):5. PubMed Central PMCID: PMC5431903.
4. White SJ, Johnson S, Szymonik M, Wardingley RA, Pye D, Davies AG, Wälti C, Stockley PG. Directed surface attachment of nanomaterials via coiled-coil-driven self-assembly. Nanotechnology. 2012 Dec 14;23(49):495304. PubMed Central PMCID: PMC4785676.

B. Positions and Honors

Positions and Employment

2017 - Assistant Professor, UNIVERSITY OF CONNECTICUT
2010 - 2017 Post doctoral research assistant, UNIVERSITY OF LEEDS

Other Experience and Professional Memberships

2018 - Member, American Society for Virology

Honors

2016	Best Poster Award at FASEB: Virus Structure and Assembly, FASEB
2016	Best Poster Award at the Astbury Conversation Symposium, University of Leeds
2016	The Dean's Vacation Research Scholarship, University of Leeds
2015	Award for Outstanding Contribution (Oral Presentation) at the XXIV Biennial Conference on Phage/Virus Assembly, Phage and Virus Assembly
2006	Award for Best Result in Year Group, University of Leeds
2005	Award for Best Result in Year Group, University of Hertfordshire

C. Contribution to Science

1. I was a PDRA at Leeds University for 5 years, working with Professor Peter Stockley, investigating the assembly mechanisms of positive sense-single stranded RNA viruses. My PDRA work has been instrumental in the discovery, characterisation and validation of a completely unsuspected aspect of the assembly mechanisms in this class of RNA viruses. It appears that they all use an evolutionarily conserved mechanism to ensure survival of the virion in the challenging environment of the infected cell. Our recent discovery of this mechanism in a picornavirus forces a re-examination of decades of research that showed that they did not exist in this family of viruses. These discoveries lead naturally to potential real world applications, including the development of novel antiviral therapies and the creation of artificial and completely safe viral vaccines.

   The work to identify packaging signals in human pathogens (human parechovirus, hepatitis B and C) had a major collaborative association with Prof. Reidun Twarock at the University of York (Department of Mathematics, Centre for Complex Systems Analysis). It features in high impact papers, which have been published in Nature Communications (Shakeel, Dykeman and White [joint first authors], et al.) and Nature Microbiology (Patel and White [joint first authors], et al.). It was an important corner-stone of a patent on a novel anti-viral strategy (jointly held by the Universities of York, Leeds and Helsinki, US20160326529), for which I am a co-inventor, and a Wellcome Trust Joint Senior Investigator Grant to Profs. Stockley and Twarock as well as a grant from the Medical Research Council for which I was named post-doc. The Nature Communications paper received widespread media coverage and resulted in 32 news articles, including articles in CNN and ABC. Likewise, the Nature Microbiology paper resulted in 7 news articles, a “Behind the paper” article in Nature Microbiology, a specific article in Nature Reviews Microbiology discussing the work (York, A. (2017). Viral Infection: Packing to Leave. Nature Reviews Microbiology. 15: 450-451) and three cryo-electron microscopy structures (in which I did the reconstructions) deposited in the electron microscopy data bank (EMDB-3714, EMDB-3715 and EMDB-3716).

   My other work on packaging signals has focused on one of the model systems for viral assembly: the bacteriophage MS2. Working with Prof. Reidun Twarock (York University) and Prof. Cheng Kao (Indiana University), I was part of the team that identified the 60 coat protein:RNA contacts in MS2, the first time that all of the packaging signals have been identified within a virus (see Direct Evidence for Packaging Signal-Mediated Assembly of Bacteriophage in JMB). Our work was the focus of a review by Peter Prevelige (Follow the Yellow Brick Road: A paradigm Shift in Virus Assembly, 2016, Journal of Molecular Biology, 428: 416-418) which highlights the importance of my work. The entire field of (+)ssRNA viruses must now revisit existing mechanisms of assembly in the light of our work and I expect many groups to start exploring packing signals in other (+)ssRNA viruses.

   a. Patel N, White SJ, Thompson RF, Bingham R, Weiß EU, Maskell DP, Zlotnick A, Dykeman E, Tuma R, Twarock R, Ranson NA, Stockley PG. HBV RNA pre-genome encodes specific motifs that mediate interactions with the viral core protein that promote nucleocapsid assembly. Nat Microbiol. 2017 Jun 19;2:17098. PubMed Central PMCID: PMC5495169.

b. Shakeel S, Dykeman EC, White SJ, Ora A, Cockburn JJB, Butcher SJ, Stockley PG, Twarock R. Genomic RNA folding mediates assembly of human parechovirus. Nat Commun. 2017 Feb 23;8(1):5. PubMed Central PMCID: PMC5431903.

c. Stewart H, Bingham RJ, White SJ, Dykeman EC, Zothner C, Tuplin AK, Stockley PG, Twarock R, Harris M. Identification of novel RNA secondary structures within the hepatitis C virus genome reveals a cooperative involvement in genome packaging. Sci Rep. 2016 Mar 14;6:22952. PubMed Central PMCID: PMC4789732.

d. Rolfsson Ó, Middleton S, Manfield IW, White SJ, Fan B, Vaughan R, Ranson NA, Dykeman E, Twarock R, Ford J, Kao CC, Stockley PG. Direct Evidence for Packaging Signal-Mediated Assembly of Bacteriophage MS2. J Mol Biol. 2016 Jan 29;428(2 Pt B):431-48. PubMed Central PMCID: PMC4751978.

2. I have made contributions to the field of bio-nanoscience, exploring bio-templated device construction in collaboration with Profs. Giles Davies and Christoph Wälti at the University of Leeds and Dr. Steve Johnson at the University of York. This utilized the M13 bacteriophage displaying coiled-coil motifs to specifically assemble the phage particle between two electrodes. This work culminated in the publication in the high impact journal of Angewandte Chemie studying the structure and assembly of coiled-coils on a 2-D surface. I showed that the assembly of coiled-coils on a surface results in molecular crowding and results in the properties of the coiled-coil changing, i.e. the pH at which they assemble/disassemble is radically changed when crowded onto a 2D surface, as compared to solution. This work has important implications for various 2-D surface techniques, e.g. surface plasmon resonance, and bio-nano diagnostic devices. It has been cited 9 times. The work is continuing using the B23 (circular dichroism) beamline at the diamond light source to study the control of coiled-coil interactions using voltage controlled electrodes with the aim of making a switchable surface for the capture and release of various biological molecules, e.g. specific cell types in cell sorting applications.

   a. White SJ, Johnson SD, Sellick MA, Bronowska A, Stockley PG, Wälti C. The influence of two-dimensional organization on peptide conformation. Angew Chem Int Ed Engl. 2015 Jan 12;54(3):974-8. PubMed Central PMCID: PMC4506555.

   b. White SJ, Johnson S, Szymonik M, Wardingley RA, Pye D, Davies AG, Wälti C, Stockley PG. Directed surface attachment of nanomaterials via coiled-coil-driven self-assembly. Nanotechnology. 2012 Dec 14;23(49):495304. PubMed Central PMCID: PMC4785676.

   c. White SJ, Morton DW, Cheah BC, Bronowska A, Davies AG, Stockley PG, Wälti C, Johnson S. On-surface assembly of coiled-coil heterodimers. Langmuir. 2012 Oct 2;28(39):13877-82. PubMed Central PMCID: PMC4820041.

3. I have used SELEX to identify many novel RNA aptamers which have played an important role in the development of biosensors. The first set of aptamers was involved in the detection of the aminoglycoside antibiotics in collaboration with FERA (Food and Environment Research Agency) in the U.K. who wanted to develop a cheap and quick biosensor for the detection of aminoglycoside antibiotics in milk. Aptamers were discovered that could be used in an assay and detect the antibiotics in the nM range. The second set of RNA aptamers that I developed was for the differentiation between different conformations of amyloid precursors. I successfully identified aptamers that could achieve this.

   a. Sarell CJ, Karamanos TK, White SJ, Bunka DHJ, Kalverda AP, Thompson GS, Barker AM, Stockley PG, Radford SE. Distinguishing closely related amyloid precursors using an RNA aptamer. J Biol Chem. 2014 Sep 26;289(39):26859-26871. PubMed Central PMCID: PMC4175327.

   b. Derbyshire N, White SJ, Bunka DH, Song L, Stead S, Tarbin J, Sharman M, Zhou D, Stockley PG. Toggled RNA aptamers against aminoglycosides allowing facile detection of antibiotics using gold nanoparticle assays. Anal Chem. 2012 Aug 7;84(15):6595-602. PubMed Central PMCID: PMC3413241.

D. Scholastic Performance

Ongoing Research Support

Start-up grant, University of Connecticut
White, Simon (PI)
08/23/17-08/23/22
Department Start-up grant.
The purpose of this grant is to set up the PI's laboratory, as well as a facility for cryoEM sample preparation. To be used to fund preliminary studies needed to be competitive for extramural research support
Role: PI

1 R21 AI156838-01, NIH
White, Simon (PI)
12/01/20-11/30/22
Characterization of long-circulating phages isolated from in vivo mouse studies
Role: PI

Completed Research Support

17-EXO17_2-0063, NASA
White, Simon (PI)
04/01/18-03/31/21
Characterizing the molecular mechanisms and the limits of archaeal gene transfer using Haloferax volcanii as a model genetic system
Though archaea are largely unexplored for horizontal gene transfer mechanisms, the model archaeon Haloferax volcanii has demonstrated a cell-cell contact mediated DNA transfer mechanism involving cell fusion events that generate a 1N/2N/1N chromosome copy number cycle. This mechanism leads to the recombination of DNA, and changes their genotype and phenotype. How this mechanism functions in the genetically tractable Haloferax volcanii is still not understood and many of the features remain elusive. The following specific aims/objectives are proposed to delve deeper into the ambiguities! 1) Identify and characterize components required for cell-cell contact mediated gene exchange (mating) in Haloferax volcanii. 2) Identify and characterize components of a homoserine lactone based quorum sensing system in Haloferax volcanii. 3) Characterize the limits to HGT via mating in Hfx. volcanii.
Role: Co-Investigator

AIMS, ATOMWISE AIMS AWARD
White, Simon (PI)
05/31/18-05/31/20
EV71 2C as a drug target
The EV71 crystal structure was used to identify 72+ compounds identified with a customized small molecule virtual screen using Atomwise's AI technology. Atomwise ship these compounds to the researcher for testing in a malachite green ATPase assay.
Role: PI

Research Excellence Program, Internal funding
White, Simon (PI)
06/30/19-06/30/20
Understanding the role of non-coding RNA in the Picornavirus life-cycle

Undertake next-generation sequencing of cells infected with Picornaviruses to identify common non-coding RNAs differentially expressed during infection
Role: PI

Program in Accelerated therapeutics for healthcare trailblazer award, Internal funding
White, Simon (PI)
06/30/19-06/30/20
Screening for small molecule inhibitors against Enterovirus D68 2C helicase
Identify small molecule inhibitors that specifically inhibit the conserved 2C helicase of EVD68
Role: PI

Program in Innovative Therapeutics for Connecticut's Health (PITCH) program, Internal
White, Simon (PI)
05/01/19-04/01/20
The Picornavirus 2C as a drug target
Developing novel anti-virals against human rhinovirus and enterovirus 71.
Role: PI

Scholarship Facilitation Fund, Internal funding
White, Simon (PI)
01/02/19-01/02/20
Understanding viral evolution through structural analysis
Use cryo-EM to analyze the major capsid proteins of related bacteriophage that infect the Actinobacteria
Role: PI

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: Victoria Robinson

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
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 crystallography 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 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 bacteria upon the onset of adverse growth conditions. The second is a circularly permuted GTPase, nucleostemin, which shuttles from the nucleolus to the cytoplasm to support the maturation of the 60S ribosomal subunit.

We have many years of experience working with BipA and so I am particularly excited about this multi-disciplinary collaboration with Dr. Simon White (University of Connecticut) and Dr. Ganesh Anand (Pennsylvania State University) integrating biochemical and atomic level structural data with ongoing cellular studies in my lab to define the role of this protein in pathogenesis and colonization, the primary goal of this which is to validate BipA as a therapeutic target for antimicrobials with non-traditional mechanisms of action.

1. Shamilov, R., Robinson, V.L. and Aneskievich, B.J. (2021) Seeing Keratinocyte Proteins through the Looking Glass of Intrinsic Disorder. *Int. J. Mol. Sci.* 22(15):7912. PMCID: PMC8348711.
2. 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.
3. 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

4. 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.
5. 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

B. Positions and Honors

Positions and Employment:

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

Other Experience and Professional Memberships:

2021-present Associate Editor, Molecular Recognition, Frontiers in Molecular Biosciences
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 Faculty Search Committee
2015-2021 Review Editor, Molecular Recognition, Frontiers in Molecular Biosciences
2015-present 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-present Member, Dept. Promotion, Tenure and Review Committee; Chaired, 2016-18, 2020-22
2010-2020 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

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)

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 recently submitted an article describing the requirement of BipA for adaptation to and re-stablishing homeostasis after the onset of various stress (Bova, R.A., Robinson, V.L. and Benson, D.R. 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. These findings spurred 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.
d. Sullivan, S.C., deLivron, M.A., Shaqra, A.M., Erlandsen, H. and Robinson, V.L. Allosteric communication pathway links distant functional sites in the Translation Factor BipA. (under review at *J. Biol. Chem.*)

2. 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.

3. 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.

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

Ongoing Research Support

Department of Defense Robinson (co-I) 1/22/20 to 12/31/2022
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.

START Preliminary Proof-of-Concept Fund Heaslip, Robinson (Co-Is) 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.

START Preliminary Proof-of-Concept Fund Robinson (PI) 12/31/19 to 4/30/22
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.

UConn Research Excellence Program Award Robinson (PI) 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.

Atomwise AIMS and subsequent AIMS Prime Award Robinson (PI) 12/1/18; ongoing
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

START Preliminary Proof-of-Concept Fund Robinson (PI) 4/01/19 to 3/31/21
UConn Office of Vice President for Research (OVPR)
Investigating Host-Pathogen Interactions Regulated by BipA for Antimicrobial Development
Using an enterohemorrhagic *Escherichia coli* (EHEC) model system we are determining how BipA is regulating actin pedestal formation associated with host-pathogen interactions and colonization .

AG161195 Lynes (PI) 9/1/17 to 8/31/20
Connecticut Innovations
A Therapeutic Monoclonal Antibody for the Treatment of Inflammatory Bowel Disease
The goal of this project is to determine how an antibody raised against the stress response protein metallothionine (MT) influences the progression of the immune response.
Role: Co-Investigator

R21 AI104841 Wright (PI), Robinson (co-I) 06/15/2018 to 05/31/2020
Targeting Glycolytic Enzymes as an Antibacterial Strategy
The goal is to explore if nonbenzenoid aromatic tropolone natural products are exceptional candidates for developing cell-permeable enolase inhibitors and if differences at either the target or pathway level can be exploited for selective blockade of the bacterial glycolytic machinery.
Role: Co-Investigator

PITCH2 Award Robinson (PI) 04/1/19 to 12/31/20
Program for Innovative Therapeutics for Connecticut's Health (PITCH) Stage 2
Connecticut Innovations
High Throughput Screening to Identify Small Molecule Inhibitors of BipA

Support the physiochemical characterization of small molecule effectors of BipA and determine key structure-activity relationships.

PITCH Award Robinson (PI) 10/1/17 to 12/01/18
Program for Innovative Therapeutics for Connecticut's Health (PITCH)
Connecticut Innovations
Determine Potential Resistance and Small Molecule Assay Development/Inhibitor Screening
The main aim of the project is to develop and optimize a high throughput screen and secondary screening protocols to search for and validate small molecule inhibitors of BipA.