

William M. Holmes, Ph.D.

215 Sidney E. Frank Hall for Life Sciences

185 Meeting St.

Providence, Rhode Island 02912

William_holmes@brown.edu

Education

Ph.D. **Brown University**, Providence, RI
Molecular Biology, Cellular Biology, and Biochemistry, 2012

B.S. **Le Moyne College**, Syracuse, NY
Biological Sciences, Minor in Chemistry, 2004

Teaching Experience

Lecturer in Biology: Medical Sciences, Section of Biology Education
Secondary appointment: Molecular Biology, Cell Biology, and Biochemistry.
Brown University, Providence, RI (9/1/2022 – present)

Courses Offered

Associate Professor, Tenured: Rhode Island College, Providence, RI (7/2019-6/2022)

Assistant Professor: Rhode Island College, Providence, RI (1/2015 – 7/2019)

- Bio100: Fundamentals of Biology (Non-major's)
- Bio111: **Introductory Biology I** (Major's)
- Bio241: Research Colloquium
- Bio320: **Cellular and Molecular Biology**
- Bio420: **Biochemistry: Proteins and Nucleic Acids**
- Bio421: **Biochemistry of Energy and Metabolism**
- Bio460: Senior Seminar in Biology
- Bio491: **Research in Biology (Independent Study)**

Postdoctoral Teaching Fellow: College of the Holy Cross, Worcester, MA (2013 – 2015)

- Bio161: **Introduction to Cellular and Molecular Biology**, Fall 2013, Fall 2014
- Bio114: Biological Principles: Neurodegeneration and Disease, Spring 2014
- Bio301: **Biochemistry I**, Fall 2014

Technical Advisor: Project ARISE, Brown University, 2006-2009

- Project Arise is a professional development program for high school teachers designed to engage teachers and students to take an inquiry-based approach to learning about science.
- Collaborated with teachers and education professors to develop unit plans using an inquiry-based approach to learning.

Instructor: Summer@Brown, Brown University, 2009-2011.

Course: From Mad Cow Disease to Alzheimer's: Biological Basis of Disease

Graduate Tutor: Advanced Cellular Biology, Brown University, 2011

- Discussed papers assigned for the course.
- Explained research methods and discussed authors' conclusions.

Teaching Assistant: Introduction to Biochemistry (BIOL 0280), Brown University, 2008

Textbook Publications

Introductory Biology I Laboratory: Basic Principles of Cellular and Molecular Biology, Fifth Edition

William Holmes and Dorsey Weber, Rhode Island College

Publisher: AcademX Publishing Services

ISBN: 978-1-68284-516-5

*Developed and published three previous editions

Mentoring and Student Research

Biology Departmental Honors Thesis Mentees, Rhode Island College

Abigail Fluerima: "Expression and Purification of N-terminally Acetylated microtubule binding protein Tau" 4/2021

Alijah Griffith: "The purification and characterization of N-terminally acetylated Ssa1 from *Saccharomyces cerevisiae*" 4/2020

Jessica Anderson: "Building an *in vivo* model of Tau aggregation in *Saccharomyces cerevisiae*" 4/2019

Matthew Schiavo: "Characterizing growth and stress response to acetate during glucose starvation in *Saccharomyces cerevisiae*" 4/2019

Anna Lally: "Determining the effects of N-terminal acetylation on the microtubule associated protein tau" 4/2018

Jeremy Boutin: "Hsp70 Ssa1 Chaperone Activity with and without N-terminal Acetylation in *Saccharomyces cerevisiae* [PSI⁺] cells" 4/2017

Research Students

- Sara Palombo
- Katelyn Pichette
- Miguel Martinez Guzman (B.S. 2022)
- Megan McGregor (B.S. 2022)
- Floralba Parra
- Abigail Fleurima (B.S. 2021)
- Fantashia-Tene Lopes (B.S. 2020)
- Alijah Griffith (B.S. 2020)
- Jessica Anderson (B.S. 2019)
- Mathew Schiavo (B.S. 2019)
- Meagan Mycroft (C.G.S 2019)
- Brittney Bebeau (B.S 2018)

- Anna Lally (B.S 2018)
- Jeremy Boutin (B.S 2017)
- Philip Ashkar (B.S. 2017, C.G.S 2018)
- Kate Solecito (B.S. 2016)

Undergraduate Student Advising

- Advised 20-25 undergraduate students each year
- Responsible for a broad range of advisees in Biology, Health Sciences, and Medical Imaging
- Aided students as they prepare for pre-professional careers (medical school, dental school, and physician's assistant programs)

Invited Research Talks and Guest Lectures

Invited Seminar: From Ales to Alzheimer's: How Yeast is Utilized in Current Biomedical Research, February 2016

- Science Café Woo, hosted by University of Massachusetts Medical School

Panelist: Paths to a Career in Undergraduate Teaching, University of Massachusetts Medical School, May 2014

- Hosted by: Ellen Fynan, Ph.D, Professor of Biology at Worcester State University

Guest Lecturer: Virology, College of the Holy Cross, Worcester, MA, Fall 2013

- Lecture Title "Pathology and biochemical nature of prion proteins."
- Course instructor: Ann Sheehy, Ph.D.

Guest Lecturer: Introduction to Microbiology, Assumption College, Worcester, MA, 2012/2013

- Lecture Title: "History and pathology of prion proteins."
- Course instructor: Aisling Dugan, Ph.D.

Invited Seminar: *Loss of N-Terminal Acetylation Promotes Protein Misfolding Stress and Alters Prion Propagation in vivo*, Assumption College, Worcester, MA, 2013

Guest Lecturer: Virology, Salve Regina University, Newport, RI, 2012

- Lecture Title: "History and pathology of prion proteins."
- Course instructor: Aaron Derdowski, Ph.D.

Guest Lecturer: Introduction to Biochemistry, Wheaton College, Norton, MA, 2010

- Lecture Title: "Protein structure and function."
- Course instructor: Barbara Brenessel, Ph.D.

Professional Development in Teaching

Workshop, Hewlett-Mellon Faculty Workshop, College of the Holy Cross, Worcester, MA, 2014.

- Curriculum development for introductory biology courses with a focus on community development and student retention.

Workshop, Designing Scientific Teaching Tools for Biochemistry and Molecular Biology Education, Simmons College, Boston, MA, 2014.

- ASBMB sponsored and NSF-funded workshop to develop new teaching methods centering on the foundational concepts of biochemistry and molecular biology.

Professional Development Seminar, Sheridan Center for Learning, Brown University, 2010.

- Seven seminar sessions to articulate a teaching philosophy and develop a teaching portfolio

Teaching Seminar, Sheridan Center for Learning, Brown University, 2008.

- Five lecture sessions and five workshop sessions on developing a reflective teaching practice, teaching to different learning styles, and gauging student learning through feedback
-

Research Experience

Associate Professor of Biology (Tenured), Rhode Island College (7/2019 – 6/2022)

Assistant Professor of Biology, Rhode Island College (1/2015 – 7/2019)

- Understand the effects of N-terminal acetylation on protein folding and chaperone activity, as it relates to cellular toxicity and neurodegenerative diseases.

Postdoctoral Teaching Fellow, The College of the Holy Cross

2013 – 2015

Advisor: Robert Bellin, Ph.D.

- Exploring the methods by which mammalian cells interact with the extracellular environment by utilizing different growth surfaces and determining the role of syndecan proteins, which are integral membrane proteins that interact with the extracellular matrix.

Postdoctoral Research Associate, The University of Massachusetts Medical School

2012 – 2013

Advisor: Mary Munson, Ph.D.

- Probed structural characteristics of the exocyst complex, a multisubunit protein complex responsible for exocytic vesicle trafficking, using combined proteomic, biochemical, and cell biological approaches.

Doctoral Candidate, Brown University

2006 - 2012

Advisor: Tricia Serio, Ph.D.

Thesis: *Mechanistic Insight into the Modulation of Prion Propagation by Co-Translationally Acting Protein Maturation Factors*

- Determined the role of co-translational protein maturation in protein misfolding and the subsequent effects on prion propagation in *Saccharomyces cerevisiae*.
- Demonstrated the novel hypothesis that co-translational acetylation of a protein's N-terminus alters its thermodynamic stability *in vivo* and this protein misfolding stress destabilizes prion aggregates functionally decoupling the presence of aggregates with their cellular phenotype.

Research Assistant, Brown University

2004 - 2006

Advisor: Gerwald Jogl, Ph.D.

- Studied the structure of inositol kinases using x-ray crystallography.
- Determined the structure of the enzyme inositol phosphate multikinase (IPMK).

- Determined the mechanism of how IPMK acts on different inositol substrates, leading to functional analysis of IPMK and determining which amino acids at its catalytic core were important for activity.

Undergraduate Researcher, Le Moyne College

2003 - 2004

Advisor: Joseph Mullins, Ph.D.

- Synthesized a naturally occurring small molecule, Chiricanine A, using a novel series of chemical reactions.

Peer Reviewed Publications

*Italics denotes undergraduate student authors

Griffith, A.A., Holmes, W., Fine Tuning: Effects of Post-Translational Modification on Hsp70 Chaperones. **Int. J Mol Sci.** 20(17). pii: E4207. doi: 10.3390/ijms20174207 (2019).

Griffith, A.A., Boutin, J., Holmes, W., A highly efficient one-step purification of the Hsp70 chaperone Ssa1. **Protein Expression and Purification** 152:56-63. doi: 10.1016/j.pep.2018.07.006 (2018).

Holmes, W., Mannakee, B., Gutenkunst, R., and Serio, TR Loss of amino-terminal acetylation suppresses a prion phenotype by modulating global protein folding. **Nature Communications** (2014).

Holmes, W., Klaips, C., and Serio, TR; Defining the Limits: Protein Aggregation and Toxicity *In Vivo*. **Critical Reviews in Biochemistry and Molecular Biology** (2014).

Holmes, W and Jogl G; Crystal structure of inositol phosphate multikinase 2 and implications for substrate specificity. **J. Biol. Chem.** **281**, 38109-38116 (2006).

Funding and Awards

RI-INBRE 2019-2022 Collaborative Research Grant, \$300,000

- Title: Effects of N-Terminal Acetylation on the Structure and Aggregation of Tau
- Funding for three undergraduate summer fellows, equipment, and laboratory supplies
- **Collaborator:** Nicholas Fawzi, Ph.D. (Brown University)

Rhode Island Foundation Medical Research Grant, \$12,000

- Title: Understanding the Effects of Metabolism on Protein Folding and Aggregation
- Funding for student stipend (part-time) and laboratory supplies

RI-INBRE 2016-2019 Early Career Development Grant, \$300,000

- Title: Effects of N-Terminal Acetylation on Chaperone Function and Protein Aggregation
- Funding for three undergraduate summer fellows, equipment, and laboratory supplies
- **Mentor:** Gerwald Jogl, Ph.D. (Brown University)

RI-INBRE 2015 Summer Undergraduate Research Grant, \$25,000

- Funding for supplies and stipends for three undergraduate researchers

College of the Holy Cross Competitive Student Summer Research Fellowships

- Received funding for two undergraduate research students for the summer of 2014

College of the Holy Cross Committee on Faculty Scholarship Research and Publication Award, 2014

- Proposal title: Developing Novel Methodologies to Recapitulate the *In Vitro* Tissue Microenvironment in Cell Culture

John G. Peterson Pre-doctoral Fellow, 2012

- Awarded annually to one Brown University graduate student in the biological sciences to support the final year of their dissertation.

Molecular and Cell Biology and Biochemistry Research Training Grant, 2007-2008

- T32 GM007601, Brown University

Le Moyne College Independent Study Award, 2004

- Synthesis of the small molecule Chiricanine A
Award provides support for research materials and travel to academic conferences.

Undergraduate Research Student Talks

Underline denotes undergraduate presenter

Haddad, S., Stanton, M., **Holmes, W.**, Parrillo, A., Lambert, C., and Bellin, R.; *The Effect of Surface Growth Conditions on the Induction of Apoptosis by Human Fibroblasts*. Northeast Undergraduate Research and Development Symposium, University of New England, Biddeford, ME, 2014.

Poster Presentations

underline denotes undergraduate presenter

Anderson, J., **Holmes, W.**, Expression of Tau in *Saccharomyces cerevisiae* to Determine Effects of N-Terminal Acetylation, RI-INBRE SURF Conference, University of Rhode Island, 7/2018.

Griffith, AA., **Holmes, W.**, An Effective One-step Purification of the Hsp70 class chaperone Ssa1. RI- INBRE SURF Conference, University of Rhode Island, 7/2018.

Fleurima, A., Lally, A., **Holmes, W.**, The Effects of N-Terminal Acetylation on the Protein Tau. RI- INBRE SURF Conference, University of Rhode Island, 7/2018.

Anderson, J., **Holmes, W.**, Expression of Tau in *Saccharomyces cerevisiae* to Determine Effects of N-Terminal Acetylation, Protein Society Annual Meeting, Boston, Ma, 7/2018.

Griffith, AA., **Holmes, W.**, An Effective One-step Purification of the Hsp70 class chaperone Ssa1., Protein Society Annual Meeting, Boston, Ma, 7/2018.

Lally, A., **Holmes, W.**, Expression of Tau in *Saccharomyces cerevisiae* to Determine Effects of N-Terminal Acetylation, Protein Society Annual Meeting, Boston, Ma, 7/2018.

Holmes, W., Lally, A., Griffith, AA., Anderson, J., Determining the effects of N-terminal acetylation on protein homeostasis. RI NIH IDeA Symposium, Brown University, 6/8/2018

Lally, A., **Holmes, W.** Determining the Effects of N-terminal Acetylation on the Microtubule-associated Protein Tau. Association of Biochemistry and Molecular Biology (ASBMB) Annual Meeting, San Diego, Ca, 4/2018.

Lally, A., **Holmes, W.** Determining the Effects of N-terminal Acetylation on the Microtubule-associated Protein Tau. RI- INBRE SURF Conference, University of Rhode Island, 7/2017.

Anderson, J., **Holmes, W.** Expression of Tau in *Saccharomyces cerevisiae* to Determine Effects of N-Terminal Acetylation, RI-INBRE SURF Conference, University of Rhode Island, 7/2017.

Griffith, AA., **Holmes, W.** An Effective One-step Purification of Ssa1 in *Saccharomyces cerevisiae*. RI- INBRE SURF Conference, University of Rhode Island, 7/2017.

Lally, A., **Holmes, W.** Determining the Effects of N-terminal Acetylation on the Microtubule-associated Protein Tau. RI Alzheimer's Association Meeting. 4/2017

****A. Lally won best Basic Science Poster Award**

Anderson, J., **Holmes, W.** Expression of Tau in *saccharomyces cerevisiae* to Determine the Effects of N-terminal Acetylation. RI Alzheimer's Association Meeting. 4/2017

Boutin, J., **Holmes, W.** Protein A Tagging of Hsp70 Ssa1 in *Saccharomyces cerevisiae*, RI-INBRE SURF Conference, University of Rhode Island, 7/2016.

Anderson, J., **Holmes, W.** Expression of Tau in *Saccharomyces cerevisiae* to Determine Effects of N-Terminal Acetylation, RI-INBRE SURF Conference, University of Rhode Island, 7/2016.

Lally, A., **Holmes, W.** Expressing and Purifying the Mammalian Protein Tau in *Escherichia coli* to Assess How N-Terminal Acetylation Alters Structure and Function, RI-INBRE SURF Conference, University of Rhode Island, 7/2016.

Boutin, J. & **Holmes, W.** Understanding the Effects of N-Terminal Acetylation on the Hsp70 Chaperone Ssa1. FASEB: Protein Folding in the Cell, Saxons River, VT. July 24, 2016.

Holmes, W., Sollecito, K., Ashkar, P. and Boutin, J., Understanding the effects of N-terminal acetylation on protein function and aggregation, RI NIH IDeA Symposium, Brown University, 3/17/2016

Boutin, J., **Holmes, W.** Protein A Tagging of Hsp70 Ssa1 in *Saccharomyces cerevisiae*, RI-INBRE SURF Conference, University of Rhode Island, 7/2015.

Sollecito, K., **Holmes, W.** Expressing the N-Terminal Acetylase Complex NatA in *Escherichia coli*, RI-INBRE SURF Conference, University of Rhode Island, 7/2015.

Ashkar, P., **Holmes, W.** Using *Saccharomyces cerevisiae* as a Model Organism to Study N-Terminal Acetylation of Tau, RI-INBRE SURF Conference, University of Rhode Island, 7/2015.

Holmes W., Haddad S., Connolly L., Stanton M, Lambert C, Bellin R; Utilizing Novel Methodologies to Recapitulate the In Vivo Tissue Microenvironment in Cell Culture. American Society for Cell Biology Meeting, Philadelphia, PA, 2014

Connolly L, Bellin R, and **Holmes W**; Heparan Sulfate and Sulfatase Activity: Effects of Changing Sulfatio Patterns on Tumorigenesis in Mammary Epithelia. College of the Holy Cross Summer Research Symposium, Worcester, MA, 2014

Haddad S, Stanton M, Lambert C, Bellin R, and **Holmes W**; The effects of Surface Growth Conditions on the Morphology and Cytoskeleton of Mammalian Cells. College of the Holy Cross Summer Research Symposium, Worcester, MA, 2014

Holmes W and Serio T; Loss of N-Terminal Acetylation Promotes Protein Misfolding Stress and Modulates Prion Propagation. Molecular Chaperones & Stress Responses Meeting, Cold Spring Harbor, NY, 2012.

Holmes W and Serio T; Effect of Ribosome Associated Chaperones on the Sup35 Prion. 5th International Congress in Stress Response in Biology and Medicine, Quebec City, Canada, 2011.

Holmes W and Jogl G; Crystal structure of inositol polyphosphate multikinase 2 with substrate kinetic analysis. Rhode Island Research Alliance Symposium, Providence, RI, 2007.

Jogl G and **Holmes W**; Crystal structure of inositol polyphosphate multikinase 2 with substrate kinetic analysis. American Crystallographic Association National Meeting, Salt Lake City, UT, 2007.

Service and Contributions

Service to Rhode Island College and the greater scientific community

College Council 2016-2021

- At-Large and Biology Department representative

Biology Department Committees

- Introductory Biology Steering Committee
- Faculty Search Committee (2016 and 2017 Cell Biologist searches)
- Retreat Committee
- Website Committee

National Science Foundation Graduate Research Fellowships Program (GRFP)

- Invited reviewer (2017, 2019, 2020)

Professional Society Memberships

- American Society for Biochemistry and Cell Biology (ASBMB)
- The Protein Society
- American Society for Cell Biologists (ASCB)

Computer Skills

Languages: Python, Perl, JavaScript, C/C++, HTML, ImageJ Macro scripting

Operating Systems: Linux (Fedora, Ubuntu), MacOSX, Windows

Applications: Microsoft Office, Adobe Creative Suite, Gene Construction Kit, ImageJ, MyCourses, Moodle, and Blackboard (Online Learning Management Systems)