

Randal Halfmann, Ph.D.

Stowers Institute for Medical Research
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EDUCATION

Massachusetts Institute of Technology, 2004 – 2010

Ph.D., Biology

Mentor: Susan Lindquist, Ph.D.

Thesis: *Discovery and Characterization of Prions in Saccharomyces cerevisiae*

Texas A&M University, 2000-2004

B.S., Genetics, *summa cum laude*

POSITIONS HELD

Stowers Institute for Medical Research

Assistant Investigator, Aug. 2015-present

- Quantitative prion biology
- Contributions of nucleated protein phase separations to cell identity
- Metabolic divisions of labor in *S. cerevisiae* communities

University of Kansas Medical Center

Adjunct Assistant Professor, April 2016-present

Department of Molecular & Integrative Physiology

UT Southwestern Medical Center, 2011-2015

Sara and Frank McKnight Independent Postdoctoral Fellow

Department of Biochemistry

- Protein polymerization as a paradigm for gene regulation

Whitehead Institute for Biomedical Research, 2005-2010

Graduate Research Assistant

Laboratory of Susan Lindquist, Ph.D.

- Cell and evolutionary biology of prions and prion regulation in *S. cerevisiae*
- Biochemistry of amyloidogenic proteins

Texas A&M University, 2002-2004

Undergraduate Research Assistant

Laboratory of David Stelly, Ph.D.

- Plant cytogenetics
- Novel techniques for cell cycle manipulation

GRANTS RECEIVED

Basil O'Connor Starter Scholar, March of Dimes, 2017-2018

Alzheimer's Disease Center Pilot Project, KU Medical Center, 2016-2017

Endowed Scholar, UT Southwestern Medical Center, 2015 (declined)

CPRIT (Cancer Prevention Research Institute of Texas) Scholar, 2015 (declined)

NIH Director's Early Independence Award, 2011-2016
Sara and Frank McKnight Independent Postdoctoral Fellowship, 2011-2015
National Science Foundation Graduate Research Fellowship, 2004-2007

OTHER HONORS

Young Investigator Speaker, 32nd Annual Symposium of The Protein Society, 2018
EMBO/EMBL Symposium Fellowship travel grant, 2018
Sara and Frank McKnight Independent Postdoctoral Fellow, 2011-2015
Poster Competition winner, Genetics Society of America Yeast Genetics and Mol. Biology Meeting, 2010
William Asbjornsen Albert Memorial Fellowship nominee, MIT Biology Department, 2009
Sigma Genosys Award for Undergraduate Research, 2004
University Undergraduate Research Fellow, Texas A&M University, 2003-2004
Honors Thesis: *Improved cell cycle synchronization and chromosome doubling methods in cotton*.
University Scholar, Texas A&M University, 2001-2004
Lechner Honors Scholar, Texas A&M University, 2000-2004

PUBLICATIONS

(corresponding authorship; *equal authorship)

RESEARCH PAPERS

Holliday M, Witt A, Gama AR, Walters B, Arthur C, **Halfmann R**, Rohou A, and Dueber E. (2019) Structures of autoinhibited and polymerized forms of CARD9 reveal mechanisms of CARD9 and CARD11 activation. *Nature Communications* (revision under review).

Venkatesan S*, Kandola TS*, Gama AR, Box A, and **Halfmann R**. (2019) Detecting and Characterizing Protein Self-Assembly *in vivo* by Flow Cytometry. *Journal of Visualized Experiments* (in press).

Khan T*, Kandola TS*, Wu J*, Ketter E*, Venkatesan S*, Lange JL, Gama AR, Box A, Unruh JR, Cook M, and **Halfmann R**. (2018) Quantifying nucleation *in vivo* reveals the physical basis of prion-like phase behavior. *Molecular Cell* 7(1), 155-168.

Zhang XF, Sun R, Guo Q, Zhang S, Meulia T, **Halfmann R**, Li D, Qu F. (2017) A self-perpetuating repressive state of a viral replication protein blocks superinfection by the same virus. *PLoS Pathogens* 13(3): e1006253

Close DW, Don Paul C, Langan PS, Wilce MC, Traore DA, **Halfmann R**, Rocha R, Waldo GS, Payne RJ, Rucker JB, and Prescott M. (2015) TGP, an extremely stable, non-aggregating fluorescent protein created by structure-guided surface engineering. *Proteins: Structure, Function, and Bioinformatics* 83(7), 1225-1237.

Cai X, Chen J, Xu H, Liu S, Jiang Q, **Halfmann R**, and Chen ZJ. (2014) Prion-like polymerization underlies signal transduction in antiviral immune defense and inflammasome activation. *Cell* 156(6), 1207-1222.

Holmes DL, Lancaster AK, Lindquist S, and **Halfmann R**. (2013) Heritable remodeling of yeast multicellularity by an environmentally responsive prion. *Cell* 153(1), 153-165.

Wang G, Wang X, Yu H, Wei S, Williams N, Holmes DL, **Halfmann R**, Naidoo J, Wang L, Li L, Chen S, Harran P, Lei X, Wang X. (2013) Small-molecule activation of the TRAIL receptor DR5 in human cancer cells. *Nature Chemical Biology* 9, 84-89.

Halfmann R*, Wright J*, Alberti S, Lindquist S, Rexach M. (2012). Prion formation by a yeast GLFG nucleoporin. *Prion* 6(4).

Halfmann R*, Jarosz DF*, Jones SK, Chang A, Lancaster AK, Lindquist S. (2012). Prions are a common mechanism for phenotypic inheritance in wild yeasts. *Nature* 482(7385), 363-8.

Halfmann R*, Alberti S*, Krishnan R, Lyle N, Pappu R, Lindquist S. (2011). Opposing effects of glutamine and asparagine govern prion formation by intrinsically disordered proteins. *Molecular Cell* 43(1), 72-84.

O'Donnell CW, Waldispühl J, Lis M, **Halfmann R**, Devadas S, Lindquist S, Berger B. (2011). A method for probing the mutational landscape of amyloid structure. *Bioinformatics* 27(13):i34-42

Alberti S*, **Halfmann R***, King O, Kapila A, and Lindquist S. (2009). S. A systematic survey identifies prions and illuminates sequence features of prionogenic proteins. *Cell* 137, 146-58.

Halfmann R and Lindquist S. (2008). Screening for Amyloid Aggregation by Semi-Denaturing Detergent-Agarose Gel Electrophoresis. *Journal of Visualized Experiments* 17.

Douglas P, Treusch S, Ren H, **Halfmann R**, Duennwald M, Lindquist S, and Cyr D. (2008). Chaperone-dependent amyloid assembly protects cells from prion toxicity. *Proc. Natl. Acad. Sci. USA* 105, 7206-7211.

Halfmann R, Stelly DM, and Young DH. (2007). Towards Improved Cell Cycle Synchronization and Chromosome Preparation Methods in Cotton. *Journal of Cotton Science* 11:60–67.

REVIEWS AND PERSPECTIVES

Halfmann R. (2016). A glass menagerie of low complexity sequences. *Current Opinion in Structural Biology* 38, 9–16.

Halfmann R, Lindquist S. (2010). Epigenetics in the extreme: Prions and the inheritance of environmentally acquired traits. *Science* 330(6004), 629-32.

Alberti S, **Halfmann R**, and Lindquist S. (2010). Biochemical, cell biological and genetic assays to analyze amyloid and prion aggregation in yeast. For: *Guide to Yeast Genetics: Functional Genomics, Proteomics, and Other Systems Analysis, 2nd Ed. Methods in Enzymology* 470, 709-731.

Halfmann R, Alberti S, Lindquist S. (2010). Prions, protein homeostasis, and phenotypic diversity. *Trends in Cell Biology* 20, 125-33.

INVITED LECTURES

Cell Fate Determination by Prions. KU Cancer Center Cancer Biology Retreat. Olathe, KS. 8 June 2018

Deconstructing nucleation barriers in living cells. Workshop on The Physical Basis of Cellular Memory and Adaptation. Bellairs Research Institute of McGill University, Barbados. 14 April 2018

Rapid discovery and quantification of prion-like behavior in proteins. Genetics and Genomics (G2) Seminar Series. Texas A&M University. 5 March 2018

Deconstructing nucleation barriers to reveal the physical basis of prion behavior. Jones Seminars on Science, Technology, and Society. Dartmouth College. 9 Feb. 2018

Rapid, Quantitative Discovery of Prion-like Protein Activity. Neurology Seminar Series. University of Massachusetts Medical School. 28 Nov. 2017

Mapping the Quinary Protein Folding Landscape. Biochemistry and Molecular Biophysics Seminar Series. Kansas State University. 31 Aug. 2017

Discovery and Biological Characterization of Prion-like Switches. Neurology Grand Rounds. University of Kansas Medical Center. 4 Aug. 2017

Protein-based Self-Perpetuating Changes in Gene Expression. ASBMB Special Symposium: Evolution and Core Processes in Gene Expression. Stowers Institute, Kansas City, MO. 14 July 2017

Nucleation Barriers Govern Protein Function and Dysfunction. Susan Lindquist Legacy Symposium. Whitehead Institute, Cambridge, MA. 8 July 2017

Nucleation Landscapes Govern Protein Function and Dysfunction. FASEB Protein Aggregation in Health and Disease Conference. Steamboat Springs, CO. 12 June 2017

Prions Propagate Innate Immune Signaling. Science Friday Talks. Kansas City University of Medicine and Biosciences. 5 May 2017

Biological Consequences of Nucleation-Limited Protein Phase Behavior. Workshop on The Physical Basis of Cellular Memory and Adaptation. Bellairs Research Institute of McGill University, Barbados. 20 April 2017

Prions Propagate Innate Immune Signaling. Microbiology, Molecular Genetics & Immunology Seminar Series. University of Kansas Medical Center. 26 Jan. 2017

Quantitative Prion Biology. Biochemistry and Molecular Biology Guest Seminar. University of Kansas Medical Center. 16 Dec. 2016

Collective Behavior in a Unicellular Eukaryote. Conflict and Cooperation in Cellular Populations. NCBS-Instem, Bangalore, India. 16 Oct. 2016

Quantitative Prion Biology. Student-invited Biochemistry Seminar Series. University of Pennsylvania. 29 Sep. 2016

Quantitative Prion Biology. Workshop on The Physical Basis of Cellular Memory and Adaptation. Bellairs Research Institute of McGill University, Barbados. 20 April 2016

Quantitative Prion Biology. School of Biological Sciences Seminar. University of Missouri-Kansas City. 17 March 2016

Quantitative Prion Biology. Physiology Seminar Series. University of Kansas Medical Center. 14 March 2016

Functional cell fate determination by self-templated protein aggregation. KU Cancer Center Seminar Series. University of Kansas Medical Center. 2 Feb. 2016

The Social Lives of Prions. FASEB Molecular Mechanisms and Physiological Consequences of Protein Aggregation. West Palm Beach, FL. 24 June 2015.

The Social Lives of Prions. Pathology Seminar Series. Case Western Reserve University. 18 May 2015

Detection and Functional Characterization of Prion-Like Protein Self-Assembly. NIH Common Fund High-Risk High-Reward Symposium. National Institutes of Health, Bethesda, MD. 17 Dec. 2014

Prions functionally decide cell fate. Biology Seminar Series. University of Texas at Arlington. 9 Oct. 2014

Social behaviors driven by protein aggregation in budding yeast. Harvard FAS Center for Systems Biology. Cambridge, MA. 25 Sep. 2013

Prion-driven multicellularity in budding yeast. Gordon Conference on Stress Proteins in Growth, Development and Disease. Mt. Snow, VT. 10 July 2013

Prion-driven multicellularity in budding yeast. Human Genetics Seminar Series. University of Michigan Medical School. 4 Dec. 2012

Heritable remodeling of facultative multicellularity by an environmentally responsive prion. 2012 Gordon Conference on Intrinsically Disordered Proteins. Mt. Snow, VT. 11 July 2012

Environmentally regulated prion switching heritably remodels yeast social behaviors. 39th Annual Meeting of the Texas Genetics Society. San Antonio, TX. 23 March 2012

Discovery of a large repertoire of prions in yeast. Brooklyn College. Brooklyn, NY. 20 Nov. 2009

High throughput protein purification using the BioRobot 8000. Boston Automation Symposium. Cambridge, MA. 26 Sep. 2008

TEACHING AND MENTORING

Instructor, Graduate Cell Biology: 2015 – present

- One of four faculty teaching a graduate class on advanced topics in Cell Biology

Instructor, Responsible Conduct in Research: 2019 -- present

- One of three faculty delivering a lecture on Responsible authorship, publication, and peer review to SIMR scientific trainees and staff

Trainees

- Alejandro Rodriguez Gama, Stowers Institute PhD student (06/2017 – present)
- Tejbir Kandola, Open University PhD student (02/2017 – present)
- Jianzheng Wu, KU Medical Center PhD student (05/2016 – present)
- Shriram Venkatesan, Postdoc (03/2016 – present)
- Tarique Khan, Postdoc (09/2013 – 07/2017)

Contributor to *The Scientist* magazine: 01/01/2014

- Authored "[The Bright Side of Prions](#)", an article that explains current topics in prion biology to a general audience.

Guest speaker for The TWiT Netcast Network: 06/04/2010

- [Futures in Biotech 57](#): Mechanisms Of Non-Mendelian Inheritance In Evolution.

iBioSeminars: 8/2009

- Authored online educational tools (lecture notes, questions, assignments) to accompany Susan Lindquist's lecture: "[The Surprising World of Prion Biology](#)"

Mentor, Undergraduate Research Opportunities Program: MIT, 2/2008 – 12/2008

- Provided guidance and training in molecular biology for a biology undergraduate.

Teaching Assistant: The Protein Folding Problem, MIT, fall 2007

- Prepared and delivered lectures and accompanying assignments on protein folding experimental techniques to undergraduate and graduate students.

Teaching Assistant: Experimental Molecular Biology: Biotechnology III, MIT, spring 2006

- Provided guidance and technical expertise for undergraduates while they developed independent semester-long projects in a molecular biology lab.

MISCELLANEOUS

Memberships: Protein Society, Genetics Society of America, American Society for Cell Biology, American Association for Cancer Research

Ad Hoc Reviewer: NIH, Wellcome Trust, Science, PNAS, Journal of Biological Chemistry, Biophysical Journal, PLoS Genetics, Journal of Molecular Biology, PLoSOne, Prion, JoVE, FEMS Yeast Research, Proteomics, Semin Cell Dev Biol, Biology Open, Cell Reports