

CURRICULUM VITAE: **CHRISTOPHER L. BAKER, PH.D.**

The Jackson Laboratory
600 Main St
Bar Harbor, ME 04609
christopher.baker@jax.org
Work (207) 288-6365
Cell (207) 812-8797

EDUCATION

- 2004-2010 Ph.D. Department of Genetics, Dartmouth Medical School, Hanover, NH
Molecular and Cellular Biology Program
- 2001-2004 B.S., *Summa Cum Laude*, College of Agriculture and Life Sciences, University of Vermont,

PROFESSIONAL EXPERIENCE

- 2019 Resident Supervisor, The Jackson Laboratory's Summer Student Program
- 2017-present Assistant Professor, Sackler School of Graduate Biomedical Sciences, Department of Medicine, Tufts School of Medicine, Boston, MA
- 2016-present Faculty, Graduate School of Biomedical Sciences and Engineering, The University of Maine, Orono, ME
- 2016-present Assistant Professor, The Jackson Laboratory, Bar Harbor, ME
- 2015-2016 Associate Research Scientist, The Jackson Laboratory, Bar Harbor, ME
- 2010-2015 Postdoctoral Fellow, The Jackson Laboratory, Bar Harbor, ME

PUBLICATIONS


Google citation indices: <https://scholar.google.com/citations?user=DpPqyOUAAAAJ&hl=en>

1. Byers C, Spruce C, Fortin H, Czechanski A, Munger SC, Reinholdt RG, Skelly DA, **Baker CL**. Genetic control of pluripotency epigenome determines differentiation bias in mouse embryonic stem cells. *BioRxiv*. Posted Jan 16, 2021. <https://doi.org/10.1101/2021.01.15.426861>. *Under review*
2. Kelliher CM, Lambregts R, Xiang Q, **Baker CL**, Loros JJ, Dunlap JC. **2020**. PRD-2 directly regulates casein kinase I and counteracts nonsense mediated decay in the *Neurospora* circadian clock. *eLife*, 9:e64007 doi: 10.7554/eLife.64007
3. Skelly DA, Czechanski A, Byers C, Aydin S, Spruce C, Olivier C, Choi K, Gatti DM, Raghupathy NM, Keele GR, Stanton A, Vincent M, Dion S, Greenstein I, Pankratz M, Porter DK, Martin W, O'Conner C, Qin W, Harrill AH, Choi T, Churchill GA*, Munger SC*, **Baker CL***, Reinholdt RG*. **2020**. Mapping the effects of genetic variation on chromatin state and gene expression reveals loci that control ground state pluripotency. *Cell Stem Cell*, 27(3):459-469. ***corresponding authors**

Preview: D'Antonio M, D-Antonio-Chronowska A, Frazer KA. Revealing Instability: Genetic variation underlies variability in mESC pluripotency. *Cell Stem Cell*, 27(3): 347-349.

4. Ortmann D, Brown S, Czechanski A, Aydin S, Muraro D, Huang Y, Tomaz RA, Osnato A, Canu G, Wesley BT, Skelly DA, Stegle O, Choi T, Churchill G, **Baker CL**, Munger SC, Reinholdt LG, Vallier L. **2020**. Naïve pluripotent stem cells exhibit phenotypic variability that is driven by genetic variation. *Cell Stem Cell*, 27(3):470-481.
5. Lau K, Mason EA, Kie J, De Souza DP, Kloehn J, Tull D, McConville MJ, Keniry A, Beck T, Blewitt ME, Ritchie ME, Naik SH, Zalcenstein D, Korn O, Su S, Romero IG, Spruce C, **Baker CL**, McGarr TC, Wells CA, Pera MF. **2020**. Unique properties of a subset of human pluripotent stem cells with high capacity for self-renewal. *Nat Commun.*, 11(1):2420. doi: 10.1038/s41467-020-16214-8.
6. Spruce C, Dlamini S, Ananda G, Bronkema N, Tian H, Paigen K, Carter GW, **Baker CL**. **2020**. HELLS and PRDM9 form a pioneer complex to open chromatin at meiotic recombination hotspots. *Genes Dev.*, 34: 398-412. doi:10.1101/gad.333542.119

Article highlighted in: Alavattam KG, Abe H, Namekawa SH. Pioneering meiotic recombination. 2020. *Genes Dev.*, 34:395-397.
7. Mihola O, Pratto F, Brick K, Linhartova E, Flachs P, **Baker CL**, Sedlacek R, Paigen K, Petkov PM, Camerini-Otero D, Trachtulec Z. **2019**. Histone methyltransferase PRDM9 is partially dispensable for meiosis in male mice. *Genome Research*, doi:10.1101/gr.244426.118
8. **Baker CL***, Walker M, Arat S, Ananda G, Petkova P, Powers N, Tian H, Spruce C, Ji B, Rausch D, Choi K, Petkov PM, Carter GW, Paigen K*. **2019**. Tissue-specific *trans* regulation of the mouse epigenome. *Genetics*, <https://doi.org/10.1534/genetics.118.301697>. *corresponding authors
9. **Baker CL** and Pera MF. **2018**. Capturing Totipotent Stem Cells. *Cell Stem Cell*, 22(1):25-34.
10. Powers NR, Parvanov ED, **Baker CL**, Walker M, Petkov PM, Paigen K. **2016**. The meiotic recombination activator PRDM9 trimethylates both H3K36 and H3K4 at recombination hotspots in vivo. *PLoS Genetics*, 12(6):e1006146. doi:10.1371/journal.pgen.1006146
11. Narasimhan V, Hunt K*, Mason D*, **Baker CL***, *et al.* [35 authors]. **2016**. Health and population effects of rare gene knockouts in adult humans with related parents. *Science*, 352(6284):474-7. doi: 10.1126/science.aac8624 *equal contribution
12. **Baker CL**, Petkova P, Walker M, Flachs P, Mihola O, Trachtulec Z, Petkov PM, Paigen K. **2015**. Multimer formation explains allelic suppression at PRDM9 hotspots. *PLoS Genetics*, 11(9): e1005512. doi:10.1371/journal.pgen.1005512
13. Walker M, Billings T, **Baker CL**, Powers N, Tian H, Saxl RL, Choi K, Hibbs MA, Carter GW, Handel MA, Paigen K, Petkov PM. **2015**. Affinity-seq detects genome-wide PRDM9 binding sites and reveals the impact of prior chromatin modifications on mammalian recombination hotspot usage. *Epigenetics & Chromatin*, 8:31: doi: 10.1186/s13072-015-0024-6
14. Sun F, Fujiwara Y, Reinholdt R, Hu, J, Saxl RL, **Baker CL**, Petkov PM, Paigen K, Handel MA. **2015**. Nuclear localization of PRDM9 and its role in meiotic chromatin modifications and homologous synapsis. *Chromosoma*: 1-19.
15. **Baker CL**, Kajita S, Walker M, Saxl RL, Raghupathy N, Choi K, Petkov PM, Paigen K. **2015**. PRDM9 drives evolutionary erosion of hotspots through haplotype-specific initiation of meiotic recombination. *PLoS Genetics*, 11(1): e1004916. doi:10.1371/journal.pgen.1004916
16. Larrondo LF, Olivares-Yanez C, **Baker CL**, Loros JL, Dunlap JC. **2015**. Decoupling circadian clock protein turnover from circadian period determination. *Science*, 347(6221):1257277.

17. Bubier JA, Jay JJ, **Baker CL**, Bergeson SE, Ohno H, Metten P, Crabbe JC, Chesler EJ. **2014**. Identification of a QTL in *Mus musculus* for alcohol preference, withdrawal, and Ap3m2 expression using integrative functional genomics and precision genetics. *Genetics*, 197(4):1377-93.
 18. **Baker CL**, Walker M, Kajita S, Petkov PM, Paigen K. **2014**. PRDM9 binding organizes hotspot nucleosomes and limits Holliday junction migration. *Genome Research*, 24(5):724-732.
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19. Billings T, Parvanov ED, **Baker CL**, Walker M, Paigen K, Petkov PM. **2013**. DNA binding specificities of the long zing finger recombination protein PRDM9. *Genome Biology*, 14:R35
 20. **Baker CL**, Loros JJ, and Dunlap JC. **2012**. The circadian clock *Neurospora crassa*. *FEMS Microbiology Reviews*, 36(1):95-110.
 21. **Baker CL** and Dunlap JC. **2009**. Circadian Rhythms: Phosphorylating the CLOCK. *Cell Cycle*, 9(2):231-2.
 22. Mehra A, **Baker CL**, Loros JJ, and Dunlap JC. **2009**. Post translational modifications in circadian rhythms. *TiBS*, 34(10):483-90.
 23. Mehra A, Shi M, **Baker CL**, Colot HV, Loros JJ, Dunlap JC. **2009**. CK2 and temperature compensation in *Neurospora*. *Sleep and Biological Rhythms*, 7(3)162-171.
 24. **Baker CL**, Kettenbach AN, Loros JJ, Gerber SA, and Dunlap JC. **2009**. Quantitative proteomics reveals a dynamic interactome and phase-specific phosphorylation in the *Neurospora* circadian clock. *Molecular Cell*, 34(3):354-63.
 25. Mehra A, Shi M, **Baker CL**, Colot HV, Loros JJ, and Dunlap JC. **2009**. A role for Casein Kinase 2 in the mechanism underlying circadian temperature compensation. *Cell*, 137(4):749-60.
 26. Larrondo LF, Colot HV, **Baker CL**, Loros JJ, and Dunlap, JC. **2009**. Fungal Functional Genomics: Tunable Knockout-Knockin-expression and tagging strategies. *Eukaryotic Cell*, 8(5)800-4.
 27. Loros JJ, Dunlap JC, Larrondo LF, Shi M, Belden WJ, Gooch VD, Chen CH, **Baker CL**, Mehra A, Colot HV, Schwerdtfeger C, Lambreghts R, Collopy PD, Gamsby JJ, Hong CI. **2007**. Circadian output, input, and intracellular oscillators: insights into the circadian systems of single cells. *Cold Spring Harb Symp Quant Biol*, 72:201-14.
 28. Dunlap JC, Loros JJ, Colot HV, Mehra A, Belden WJ, Shi M, Hong CI, Larrondo LF, **Baker CL**, Chen-Hui C, Schwerdtfeger C, Collopy PD, Gamsby JJ, Lambreghts R. **2007**. A circadian clock in *Neurospora*: How genes and proteins cooperate to produce a sustained, entrainable, and compensated biological oscillator with a period of about a day. *Cold Spring Harb Symp Quant Biol*, 72:57-68.
 29. Pogueiro AM, Liu Q, **Baker CL**, Dunlap JC, Loros JJ. **2006**. The *Neurospora* checkpoint kinase 2: a regulatory link between the circadian and cell cycles. *Science*, 313(5787):644-9.

FUNDING

R35GM133724-01 Effort: 51%

National Institute of General Medical Sciences, NIH

Cellular Systems Genetic Approaches to Understanding Regulatory Variation

In this proposal we will quickly and efficiently define the pathways and mechanisms that modulate regulatory variation and function during early mammalian development by leveraging natural variation intrinsic in a unique mouse embryonic stem cell system.

Role: PI

07/01/2019 - 06/30/2024

Annual Direct Costs: \$250,000

Total Direct Costs: \$1,250,000

JAX-DIF-FY20-CLB-Neurogenetics (Baker, Chesler) Effort: N/A 01/31/2020 - 01/30/2021
The Jackson Laboratory Director's Innovation Fund
Investigating Epigenomic Mechanisms underlying the Neurogenetics of Addiction Total Direct Costs: \$133,672
The major goals of this study are to determine the effect of genetic background and sex on chromatin accessibility at cis-regulatory elements in the striatum, a critical brain structure implicated in multiple substance abuse disorders; to identify role of genetic background on proportion of cell-types in the striatum; and to integrate expression and behavior QTL from models of addiction with variation in chromatin accessibility.
Role: PI

R24OD030037 (Reinholdt, Baker, Munger) Effort: 15% 02/26/21 – 01/31/2025
Office of the Director, National Institutes of Health Annual Direct Costs: \$495,000
Total Direct Costs: \$1,917,165

Genetically Diverse Mouse Embryonic Stem Cells: A Platform for Cellular Systems Genetics
The objective of this application is to generate a thoroughly-validated panel of genetically diverse mouse embryonic stem cells (mESC) that will enable widespread adoption of cellular systems genetics.

Role: Multi-PI

COMPLETED

JAX-DIF-FY19-CB-SCM (Baker, Pera, Munger, Skelly, Reinholdt) Effort: N/A 04/19/2019 - 04/18/2020
The Jackson Laboratory Director's Innovation Fund
Genetic control of cellular heterogeneity in pluripotent stem cells Total Direct Costs: \$220,000
The goal of this proposal is to profile transcript abundance in mouse and human PSCs to delineate the regulatory networks that underlie cell heterogeneity across a panel of diverse genetic backgrounds. We will use 1) single cell (sc)RNA-Seq to capture population dynamics and developmental trajectories, and 2) FACS isolation of specific subpopulations at different stages of pluripotency using cell-surface markers followed by standard RNA-Seq.
Role: PI

JAX-DIF-FY17-CB-SCM (Baker, Churchill, Munger, Reinholdt) Effort: N/A 04/01/2017 - 10/31/2018
The Jackson Laboratory Director's Innovation Fund Annual Direct Costs: \$178,000
DO and CC RIX mESCs. An Advanced Platform for Cellular Systems Genetics Total Direct Costs: \$178,000
The goal of this proposal is to demonstrate the power of the founder strain, DO, and CC-RIX mESC lines as a platform for cellular systems genetics. To that end, we will profile the chromatin landscape and cellular proteomes of undifferentiated mESC lines comprising the eight founder strains of the DO/CC, 150 individual outbred DO lines, and 10 F1 progeny (CC-RIX) from crosses of CC strains.
Role: PI

JAX-DIF-FY17-KP (Paigen, Baker, Petkov) 03/01/2017 - 12/31/2017
The Jackson Laboratory Director's Innovation Fund Annual Direct Costs: \$43,200
Understanding the Chromatin Regulatory System Total Direct Costs: \$43,200
The goal of this project is to expand our understanding of a newly discovered system of trans-acting genes comprising a Chromatin Regulatory System (CRS) that controls the epigenetic landscape.
Role: Co-Investigator

F32GM101736-01 (Baker, PI) 2012-2014 (salary support)
National Institute of General Medical Sciences, NIH
Ruth I. Kirschstein National Research Service Award
Title: Genetic Dissection of Quantitative Control of Recombination

AWARDS AND HONORS

2016 PALM (Promoting Active Learning and Mentoring) Fellowship. [see press](#)

Christopher L Baker CV
March 2021

NSF funded fellowship to promote long-term mentorship to improve undergraduate education.

- 2014 Outstanding Oral Presentation, 28th International Mammalian Genome Conference
- 2013 Outstanding Oral Presentation, 27th International Mammalian Genome Conference
- 2012-2013 Ruth I. Kirschstein National Research Service Award
Individual postdoctoral fellowship
- 2010-2012 T32 Postdoctoral Fellowship, The Jackson Laboratory
Institutional competitive fellowship
- 2010 John W. Strohbehn Award for Excellence in Biomedical Research, Dartmouth Medical School
awarded to a single graduating Ph.D.
- 2009 Rosaline Borison Memorial Fellowship
- 2008 Society for Research on Biological Rhythms (SRBR) Excellence Award
student travel award
- 2007 Albert J. Ryan Fellow, Albert J. Ryan Foundation
- 2006-2008 National Institute for Health Pre-doctoral Training Grant, Dartmouth Medical School
- 2003 & 2004 Hughes Endeavor for Life Science Excellence Grant (HELIX), University of Vermont
competitive undergraduate research award
- 2003 Class of 1939 Scholarship, a merit based award, University of Vermont
- 2003 James E. Ludlow Endowed Scholarship Award, University of Vermont
- 2002 & 2003 Holzer Memorial Scholarship, a merit based award, University of Vermont

INVITED PRESENTATIONS

1. Cold Spring Harbor Laboratory, The Genome Access Course. November 11th, 2019.
2. Sloan Kettering Cancer Center, Manhattan, NY. November 10th, 2019.
3. Tufts University Sackler Medical School, Boston, MA. Department of Genetics Seminar. May 9th, 2018.
Natural genetic variation shapes the epigenetic landscape and patterns of inheritance.
4. Time of Our Life Symposium. July 13-14th, 2017. Hanover, NH. Genetic control of the epigenetic landscape.
5. 44th Annual Maine Biological and Medical Science Symposium. April 28-29th, 2017. Mount Desert Biological Laboratory. Non-Mendelian inheritance, meiotic drive, and genetic recombination.

CONFERENCE PRESENTATIONS

1. Stem Cell Biology. September 17-21st, 2019. Cold Spring Harbor, NY. Genetic variation influences ground state pluripotency in embryonic stem cells through a hierarchy of molecular phenotypes.
2. The 32nd International Mammalian Genome Conference. November 11-14th, 2018. Rio Mar, PR. A nucleosome remodeling factor is required for PRDM9-dependent meiotic recombination.
3. Mammalian Genetic and Genomics: From Molecular Mechanisms to Translational Applications. October 24-27th, 2017. EMBL Heidelberg, Germany. Genetic control of the epigenetic landscape.

4. The Allied Genetics Conference. July 13-17th, 2016. Orlando, FL. Natural genetic variation controls chromatin state in male germ cells.
5. The 28th International Mammalian Genome Conference. October 25-29th, 2014. Bar Harbor, ME. PRDM9 drives evolutionary erosion of hotspots. **Selected as outstanding presentation**
6. The 27th International Mammalian Genome Conference. September 15, 2013. Salamanca, Spain. Genome-wide analysis of PRDM9-dependent chromatin modification. **Selected as outstanding presentation**
7. The Center for Genome Dynamics Advisory Board Meeting. June 25, 2013. Bar Harbor, ME. Genome-wide analysis of PRDM9-dependent chromatin modification.

POSTER PRESENTATIONS

1. The Identity and Evolution of Cell Types. May 4-7th, 2021. Virtual. Genetic control of the pluripotency epigenome determines differentiation bias in mouse embryonic stem cells.
2. 3D Genome: Gene Regulation and Disease. March 17-21st, 2019. Banff, Alberta, Canada. PRDM9-dependent recruitment of HELLS is required for activation of meiotic recombination and fertility.
3. Population, Evolutionary and Quantitative Genetics Conference. May 13-16th, 2018. Madison, WI. Tissue-specific *trans* regulation of the chromatin landscape.
4. Chromosome Architecture and Chromosome Organization. March 23-27th, 2018. Whistler, Canada. Tissue-specific *trans* regulation of the chromatin landscape.
5. Chromatin and Epigenetics. May 3-6th, 2017. EMBL Heidelberg, Germany. Generic control of epigenetic landscape in germ cells.
6. The 29th International Mammalian Genome Conference. November 8-11th, 2015. Yokohama, Japan. Multimer formation explains allelic suppression of PRDM9 recombination hotspots.
7. The Biology of Genomes. May 5-9th, 2015. Cold Spring Harbor, NY. Poster. Multimer formation explains allelic suppression of PRDM9 recombination hotspots.
8. Gordon Research Conference: Meiosis. June 1-6th, 2014. New London, NH. PRDM9 drives evolutionary erosion of hotspots through haplotype-specific initiation of meiotic recombination.
9. Gordon Research Seminar: Meiosis. June 2-3, 2012. New London, NH. Poster presentation: PRDM9 dependent Histone H3 Lysine 4 trimethylation and DNA binding at human hotspots.
10. The 10th International Conference on Systems Biology 2009. August 30 – September 4, 2009. Stanford, CA. Quantitative proteomics investigation of the *Neurospora* circadian system.
11. Society for Research on Biological Rhythms 20th Anniversary Meeting. May 17-21, 2008. Sandestin, FL. Analysis of protein interactions in the *Neurospora crassa* circadian clock.
12. Neurospora 2008 Asilomar Meeting. March 27-30, 2008. Asilomar, CA. Characterization of the *Neurospora crassa* circadian clock interactome.
13. Albert J. Ryan Foundation Annual Meeting. May 2007. Holderness, NH. Multisite phosphorylation of a *Neurospora* circadian clock protein.

TRAINING AND MENTORSHIP

Predoctoral students

Christopher L Baker CV
March 2021

2013-2014 Shimpei Kajita (1 year exchange programs for predoctoral students from Japan)

2017-current Candice Byers, Tufts University, Genetics Program

2020-current Haley Fortin, Tufts University, Genetics Program

Rotations

2018 spring Uma Aurora, Tufts University

2019 winter Ben Clauss, Tufts University

2020 winter Haley Fortin, Tufts University

2020 spring Elli Hartig, Tufts University

Master's thesis students

2018-2021 Catrina Spruce, Molecular and Biomedical Sciences Program, University of Maine

Post-baccalaureate Interns

2017-2018 Sbonga Dlamini

2021- Anna Struba

Summer student/interns

2017, 2018 Naomi Bronkema, Swarthmore College

2019 Elizabeth Raruk

2021 Alex Mora

Thesis Committee Membership

2017-2019 Eraj Khokhar, The Graduate School of Biomedical Science and Engineering, University of Maine

2018- Jessie Rochester, The Graduate School of Biomedical Science and Engineering, University of Maine

2018- Uma Aurora, Sackler School of Graduate Biomedical Sciences, Tufts University

2019- Ben Clauss, Sackler School of Graduate Biomedical Sciences, Tufts University *committee chair

Qualifying Exam Committee

2020 Tufts Qualifying Exam Advisor for all first year students

2018 Uma Aurora, Tufts University

2018 Salwa Mostafa, Tufts University

2019 Ben Clauss, Tufts University *committee chair

TEACHING EXPERIENCE

2021-2022 Course Director, Mammalian Genetics, Tufts/GSBSE/The Jackson Laboratory, Bar Harbor, ME

2018-2019 Faculty advisor for Tufts Genetics journal club. Course #: GENE-0295-101

- 2016-current Instructor, Mammalian Genetics II, Tufts/GSBSE/The Jackson Laboratory, Bar Harbor, ME
(*seminar course for first year graduate students. I teach one lecture and workshop on epigenetics and chromatin*)
- 2016 Instructor, Colby College Genomics Course, The Jackson Laboratory, Bar Harbor, ME (*two week course focusing on learning genomics, both laboratory and computational modules*)
- 2014-2017 Teaching Assistant and Instructor, Genetics I and Genetics II, The Jackson Laboratory, Bar Harbor, ME (*college level introductory genetics course for JAX employee's*)
- 2013 Instructor, Topics in Biomedical Research, College of the Atlantic, Bar Harbor, ME
- 2013 Guest Lecturer, Genomics and Bioinformatics, Middlebury College, Middlebury VT
course instructor Jeremy Ward, Ph.D.
- 2012 Instructor, Cutting Edge Techniques, The Jackson Laboratory summer student program, Bar Harbor, ME
- 2006 Teaching Assistant, Molecular Genetics of Prokaryotes and Lower Eukaryotes, Dartmouth College, Hanover, NH
- 2002 Teaching Assistant, CDAE Department course on computer applications, University of Vermont, Burlington, VT

ADDITIONAL TRAINING

- 2014 The Jackson Laboratory, Bar Harbor, ME
The Whole Scientist Course (one-week course)
- 2012 The Jackson Laboratory, Bar Harbor, ME
Short Course on Medical and Experimental Mammalian Genetics (two-week course)
- 2011 The Jackson Laboratory, Bar Harbor, ME
Short Course on Systems Genetics (one-week course)

SERVICE COMMITTEES

- 2019-current Tufts Graduate School JAX Genetics Program Admissions Committee
- 2018-current Faculty partner for Protein Purification and Production (PPP) core service at The Jackson Laboratory
- 2018-2020 Bioinformatics Training Working Group, The Jackson Laboratory. Committee to develop a plan to provide training for JAX researchers and trainees in computational and statistics skills.
- 2017-2019 Faculty retreat planning committee. Two-year term. *committee chair 2019
- 2017-2020 Research Animal Facility Advisory Committee, The Jackson Laboratory
- 2006-07 Molecular and Cellular Biology Graduate Committee, Dartmouth College
- 2003-04 Dean's Student Advisory Committee, University of Vermont

PROFESSIONAL MEMBERSHIP

American Association for the Advancement of Science

Genetic Society of America

International Mammalian Genome Society

International Society for Stem Cell Research

SCIENTIFIC COMMUNITY SERVICE

2017 University of Maine Student Symposium Judge, Cross Insurance Center, Bangor, ME

2015 Science Fair Judge, Conners Emmerson Elementary School, Bar Harbor, ME

2011 Maine State Science Fair Judge, grades 9-12, Bar Harbor, ME

2012-current Guest Speaker for science lessons at local elementary and middle schools

2009 Vermont State Science Fair Judge, grades 6-12, Norwich University, VT

2006 School-to-Career Mentor, service for high school students, NH

Ad hoc reviewer: Nature Communications, PLoS One, Philosophical Transactions B, Mammalian Genome, Genome Research, Stem Cell Reports, NPJ Regenerative Medicine