

David I. Greenstein

Professor

Department of Genetics, Cell Biology, and Development

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Education

- 1979–1983 University of Pennsylvania
BA *magna cum laude*, majors in Chemistry and Biochemistry with distinction in Biochemistry, 1983
- 1983–1989 The Rockefeller University
PhD, Laboratory of Genetics, 1989
PhD thesis: “DNA-Protein Interactions in f1 DNA Replication,” Dr. Kensuke Horiuchi, Thesis Advisor
Dr. Norton Zinder, Head of Laboratory (deceased, 2012)
- 1989–1994 Postdoctoral Research Fellow
Harvard Medical School, Dept. of Genetics, and Massachusetts General Hospital, Dept. of Molecular Biology, Dr. Gary Ruvkun, Postdoctoral Advisor

Academic Appointments and Positions

- 2022–2023 Interim Dean
College of Biological Sciences, University of Minnesota
- 2018–2022 Associate Dean for Research
College of Biological Sciences, University of Minnesota
- 2007–2010 Associate Department Head for Teaching
Department of Genetics, Cell Biology, and Development,
College of Biological Sciences, University of Minnesota
- 2006 to present Professor
Department of Genetics, Cell Biology and Development,
University of Minnesota
- 2000–2006 Associate Professor
Department of Cell & Developmental Biology, Vanderbilt
University School of Medicine
- 2000–2006 Director of Graduate Studies
Department of Cell & Developmental Biology, Vanderbilt
University School of Medicine

- 1994–2000 Assistant Professor of Cell Biology,
Vanderbilt University School of Medicine
- 1981–1983 Undergraduate Research Assistant,
Purification of ¹⁵N-labeled amino acids for NMR studies,
Laboratory of Stanley J. Opella, PhD,
University of Pennsylvania, Department of Chemistry

Honors and Awards

American Cancer Society Junior Faculty Research Award, 1996–1999
American Cancer Society Research Scholar Award, 1996–1999
Joe C. Davis Foundation, Vice-Chancellor's Faculty Scholar Award, 1994–1996
NIH Postdoctoral Research Fellowship, 1990–1993
American Cancer Society Postdoctoral Fellowship (declined)
NIH Training Grant in Cancer and Viruses, 1986–1989
National Science Foundation Graduate Fellowship, 1983–1986
Hiram S. Lukens Memorial Scholarship Award in Chemistry, University of Pennsylvania, 1982
American Chemical Society Undergraduate Award, 1982
Benjamin Franklin Scholar, University of Pennsylvania, 1979–1983
Valedictorian, New Trier High School West, 1979

Major Research Interests

Control of germline development in *Caenorhabditis elegans*. Research focuses on the control of oocyte meiotic maturation, the oocyte-to-embryo transition, cell biology/ultrastructure of the *C. elegans* gonad, translational regulation in the germline, control of germline stem cells, and soma–germline interactions. In addition to these longstanding projects, newer initiatives seek to model human diseases using the *C. elegans* germline system, including early onset DYT1 dystonia and myelodysplastic syndromes associated with spliceosomal defects.

Career Summary

I was one of the last graduate students to join Norton Zinder's lab at The Rockefeller University where I worked under the mentorship and guidance of Ken Horiuchi on DNA replication of the bacteriophage f1. At Rockefeller, I received a firm grounding in genetics but also was introduced to a cornerstone of modern biology—the importance of using an array of cutting-edge approaches to solve important biological problems. A key lesson learned from Norton was the importance of contributing outside the lab through service to the field (peer review, public policy, outreach, and administration). This has remained a core value throughout my career. When I arrived in Gary Ruvkun's lab as one of the first postdocs, Gary encouraged me to develop my own project—exploring the fascinating developmental biology of oocytes and the beginnings of embryonic development in *C. elegans* has remained my intellectual focus and my life's work since then. Beginning at Vanderbilt University School of Medicine in 1994 as an Assistant Professor, my laboratory has been at the leading edge of the *C. elegans* germline research field. In 2006, I moved my laboratory to the University of Minnesota, which has a strong *C. elegans* research community and an excellent Developmental Biology Center. My other interests are in education, scientific administration,

mentoring, and promoting diversity in the field of genetics. I have contributed to these areas through my involvement with the Genetics Society of America and my institutional responsibilities. I served as Secretary of the society and have been on the editorial board of *GENETICS* since 2006. With several GSA colleagues, I established The *GENETICS* Peer Review Training Program to enhance the training and professional development of early career scientists—this program is still running strong and has been extended to *G3*. At my institution, I served as the Interim Dean of the College of Biological Sciences and the Associate Dean for Research.

Professional Service Activities (selected)

Genetic Society of America

GSA Peer Review Training Program, 2016–2022

GENETICS Editor-In-Chief Search Committee (Chair), 2020

GSA Secretary, 2016–2018

GSA Nominating Committee, 2016–2019

GSA Awards Committee, 2016–2018

GSA Publications Committee, 2016–2018

GENETICS Editorial board member: Senior Editor, Molecular Genetics of Development Section, 2016–present. Associate Editor, 2006–2016

C. elegans Community

Scientific Advisory Board, WormAtlas, 2018–present

The International *C. elegans* Board (US/Central/South Regional Representative), 2016–2020

Co-editor for *WormBook*, Germline section, 2014–2016

Co-organizer, Seventeenth International *C. elegans* Meeting (Los Angeles, 2009)

Review for Funding Agencies (selected)

NIH DEV1 Study Section, 2015–2019

Israel Cancer Research Fund, 2010–2012

NIH CMIR Study Section, 2007–2011

American Cancer Society DDC Review Panel, 2005–2009

Funding (active)

“The *C. elegans* Germline: A Test Tube for Cell and Developmental Biology.” National Institutes of Health (R35GM144029-01), 2022–2027. Role: PI.

“The Minnesota IRACDA Program.” National Institutes of Health (K12GM119955-06), 2020–2027. Role: PI/PD.

“An Interdisciplinary Training Program to Transform Graduate Education in Genetics and Genomics.” National Institutes of Health (T32 GM140936-02), 2021–2026. Role: PI/PD.

Patents

“Compositions and Methods of Nematode Control,” US Patent 6,863,881.

Publications

Tolkin T, Mohammad A, Starich TA, Nguyen KCQ, Hall DH, Schedl T, Hubbard EJA, Greenstein D. Innexin function dictates the spatial relationship between distal somatic cells in the *Caenorhabditis elegans* gonad without impacting the germline stem cell pool. *Elife*. 2022 Sep 13;11:e74955. doi: 10.7554/eLife.74955. PMID: 36098634; PMCID: PMC9473689.

Spike CA, Tsukamoto T, Greenstein D. Ubiquitin ligases and a processive proteasome facilitate protein clearance during the oocyte-to-embryo transition in *Caenorhabditis elegans*. *Genetics*. 2022 May 5;221(1):iyac051. doi: 10.1093/genetics/iyac051. PMID: 35377419; PMCID: PMC9071522.

Das D, Seemann J, Greenstein D, Schedl T, Arur S. Reevaluation of the role of LIP-1 as an ERK/MPK-1 dual specificity phosphatase in the *C. elegans* germline. *Proc Natl Acad Sci U S A*. 2022 Jan 18;119(3):e2113649119. doi: 10.1073/pnas.2113649119. PMID: 35022236; PMCID: PMC8784128.

Starich T, Greenstein D. A limited and diverse set of suppressor mutations restore function to INX-8 mutant hemichannels in the *Caenorhabditis elegans* somatic gonad. *Biomolecules*. 2020 Dec 10;10(12):1655. doi: 10.3390/biom10121655. PMID: 33321846; PMCID: PMC7763923.

Huelgas-Morales G, Sanders M, Mekonnen G, Tsukamoto T, Greenstein D. Decreased mechanotransduction prevents nuclear collapse in a *Caenorhabditis elegans* laminopathy. *Proc Natl Acad Sci U S A*. 2020 Dec 8;117(49):31301-31308. doi: 10.1073/pnas.2015050117. Epub 2020 Nov 23. PMID: 33229589; PMCID: PMC7733798.

Tsukamoto T, Gearhart MD, Kim S, Mekonnen G, Spike CA, Greenstein D. Insights into the involvement of spliceosomal mutations in myelodysplastic disorders from Analysis of SACY-1/DDX41 in *Caenorhabditis elegans*. *Genetics*. 2020 Apr;214(4):869-893. doi: 10.1534/genetics.119.302973. Epub 2020 Feb 14. PMID: 32060018; PMCID: PMC7153925.

Huelgas-Morales G, Greenstein D. Control of oocyte meiotic maturation in *C. elegans*. *Semin Cell Dev Biol*. 2018 Dec;84:90-99. doi: 10.1016/j.semcdb.2017.12.005. Epub 2017 Dec 26. PMID: 29242146; PMCID: PMC6019635.

Spike CA, Huelgas-Morales G, Tsukamoto T, Greenstein D. Multiple mechanisms inactivate the LIN-41 RNA-binding protein to ensure a robust oocyte-to-embryo transition in *Caenorhabditis elegans*. *Genetics*. 2018 Nov;210(3):1011-1037. doi: 10.1534/genetics.118.301421. Epub 2018 Sep 11. PMID: 30206186; PMCID: PMC6218228.

Huelgas Morales G, Greenstein D. *C. elegans* germline cell death, live! *PLoS Genet*. 2018 Jul 19;14(7):e1007425. doi: 10.1371/journal.pgen.1007425. PMID: 30024884; PMCID: PMC6053124.

Huelgas-Morales G, Greenstein D. Control of oocyte meiotic maturation in *C. elegans*. *Semin Cell Dev Biol*. 2018 Dec;84:90-99. doi: 10.1016/j.semcd.2017.12.005. Epub 2017 Dec 26. PMID: 29242146; PMCID: PMC6019635.

Tsukamoto T, Gearhart MD, Spike CA, Huelgas-Morales G, Mews M, Boag PR, Beilharz TH, Greenstein D. LIN-41 and OMA ribonucleoprotein complexes mediate a translational repression-to-activation switch controlling oocyte meiotic maturation and the oocyte-to-embryo transition in *Caenorhabditis elegans*. *Genetics*. 2017 Aug;206(4):2007-2039. doi: 10.1534/genetics.117.203174. Epub 2017 Jun 1. PMID: 28576864; PMCID: PMC5560804.

Huelgas-Morales G, Silva-García CG, Salinas LS, Greenstein D, Navarro RE. The stress granule RNA-binding protein TIAR-1 protects female germ cells from heat shock in *Caenorhabditis elegans*. *G3 (Bethesda)*. 2016 Apr 7;6(4):1031-47. doi: 10.1534/g3.115.026815. PMID: 26865701; PMCID: PMC4825639.

Voronina E, Greenstein D. Germ cell fate determination in *C. elegans*. John Wiley & Sons, Ltd, Chichester; *eLS* 2016. DOI: 10.1002/9780470015902.a0001501.pub2

Spike CA, Coetzee D, Eichten C, Wang X, Hansen D, Greenstein D. The TRIM-NHL protein LIN-41 and the OMA RNA-binding proteins antagonistically control the prophase-to-metaphase transition and growth of *Caenorhabditis elegans* oocytes. *Genetics*. 2014 Dec;198(4):1535-58. doi: 10.1534/genetics.114.168831. Epub 2014 Sep 26. PMID: 25261698; PMCID: PMC4256770.

Spike CA, Coetzee D, Nishi Y, Guven-Ozkan T, Oldenbroek M, Yamamoto I, Lin R, Greenstein D. Translational control of the oogenic program by components of OMA ribonucleoprotein particles in *Caenorhabditis elegans*. *Genetics*. 2014 Dec;198(4):1513-33. doi: 10.1534/genetics.114.168823. Epub 2014 Sep 26. PMID: 25261697; PMCID: PMC4256769.

Starich TA, Hall DH, Greenstein D. Two classes of gap junction channels mediate soma-germline interactions essential for germline proliferation and gametogenesis in *Caenorhabditis elegans*. *Genetics*. 2014 Nov;198(3):1127-53. doi: 10.1534/genetics.114.168815. Epub 2014 Sep 6. PMID: 25195067; PMCID: PMC4224157.

Oldenbroek M, Robertson SM, Guven-Ozkan T, Spike C, Greenstein D, Lin R. Regulation of maternal Wnt mRNA translation in *C. elegans* embryos. *Development*. 2013 Nov;140(22):4614-23. doi: 10.1242/dev.096313. Epub 2013 Oct 16. PMID: 24131629; PMCID: PMC3817945.

Kim S, Spike C, Greenstein D. Control of oocyte growth and meiotic maturation in *Caenorhabditis elegans*. *Adv Exp Med Biol*. 2013;757:277-320. doi: 10.1007/978-1-4614-4015-4_10. PMID: 22872481; PMCID: PMC3819423.

Kim S, Govindan JA, Tu ZJ, Greenstein D. SACY-1 DEAD-Box helicase links the somatic control of oocyte meiotic maturation to the sperm-to-oocyte switch and gamete maintenance

- in *Caenorhabditis elegans*. *Genetics*. 2012 Nov;192(3):905-28. doi: 10.1534/genetics.112.143271. Epub 2012 Aug 10. PMID: 22887816; PMCID: PMC3522166.
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- Yamamoto I, Kosinski ME, Greenstein D. Start me up: cell signaling and the journey from oocyte to embryo in *C. elegans*. *Dev Dyn*. 2006 Mar;235(3):571-85. doi: 10.1002/dvdy.20662. PMID: 16372336.

Greenstein D, Lee LA. Oocyte-to-embryo transition: kinase cabal plots regime change. *Curr Biol*. 2006 Feb 7;16(3):R93-5. doi: 10.1016/j.cub.2006.01.028. PMID: 16461272.

Kosinski M, McDonald K, Schwartz J, Yamamoto I, Greenstein D. *C. elegans* sperm bud vesicles to deliver a meiotic maturation signal to distant oocytes. *Development*. 2005 Aug;132(15):3357-69. doi: 10.1242/dev.01916. Epub 2005 Jun 23. PMID: 15975936.

Greenstein D. Control of oocyte meiotic maturation and fertilization. *WormBook*. 2005 Dec 28:1-12. doi: 10.1895/wormbook.1.53.1. PMID: 18050412; PMCID: PMC4781623.

Hubbard EJ, Greenstein D. Introduction to the germ line. *WormBook*. 2005 Sep 1:1-4. doi: 10.1895/wormbook.1.18.1. PMID: 18050415; PMCID: PMC4781435.

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Miller MA, Ruest PJ, Kosinski M, Hanks SK, Greenstein D. An Eph receptor sperm-sensing control mechanism for oocyte meiotic maturation in *Caenorhabditis elegans*. *Genes Dev*. 2003 Jan 15;17(2):187-200. doi: 10.1101/gad.1028303. PMID: 12533508; PMCID: PMC195972.

Miller MA, Nguyen VQ, Lee MH, Kosinski M, Schedl T, Caprioli RM, Greenstein D. A sperm cytoskeletal protein that signals oocyte meiotic maturation and ovulation. *Science*. 2001 Mar 16;291(5511):2144-7. doi: 10.1126/science.1057586. Erratum in: *Science* 2001 Apr 27;292(5517):639. Erratum in: *Science* 2001 Apr 6;292(5514):53. PMID: 11251118.

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Greenstein D, Brent R. Introduction to vectors derived from filamentous phages. *Curr Protoc Mol Biol*. 2001 May;Chapter 1:Unit1.14. doi: 10.1002/0471142727.mb0114s13. PMID: 18265042.

Furuta T, Tuck S, Kirchner J, Koch B, Auty R, Kitagawa R, Rose AM, Greenstein D. EMB-30: an APC4 homologue required for metaphase-to-anaphase transitions during meiosis and mitosis in *Caenorhabditis elegans*. *Mol Biol Cell*. 2000 Apr;11(4):1401-19. doi: 10.1091/mbc.11.4.1401. PMID: 10749938; PMCID: PMC14855.

Hubbard EJ, Greenstein D. The *Caenorhabditis elegans* gonad: a test tube for cell and developmental biology. *Dev Dyn*. 2000 May;218(1):2-22. doi: 10.1002/(SICI)1097-0177(200005)218:1<2::AID-DVDY2>3.0.CO;2-W. PMID: 10822256.

Hall DH, Winfrey VP, Blaeuer G, Hoffman LH, Furuta T, Rose KL, Hobert O, Greenstein D. Ultrastructural features of the adult hermaphrodite gonad of *Caenorhabditis elegans*: relations between the germ line and soma. *Dev Biol*. 1999 Aug 1;212(1):101-23. doi: 10.1006/dbio.1999.9356. PMID: 10419689.

Zhang Y, Ferreira HB, Greenstein D, Chisholm A, Emmons SW. Regulated nuclear entry of the *C. elegans* Pax-6 transcription factor. *Mech Dev*. 1998 Nov;78(1-2):179-87. doi: 10.1016/s0925-4773(98)00171-3. PMID: 9858725.

Rose KL, Winfrey VP, Hoffman LH, Hall DH, Furuta T, Greenstein D. The POU gene *ceh-18* promotes gonadal sheath cell differentiation and function required for meiotic maturation and ovulation in *Caenorhabditis elegans*. *Dev Biol*. 1997 Dec 1;192(1):59-77. doi: 10.1006/dbio.1997.8728. PMID: 9405097.

Greenstein D, Hird S, Plasterk RH, Andachi Y, Kohara Y, Wang B, Finney M, Ruvkun G. Targeted mutations in the *Caenorhabditis elegans* POU homeo box gene *ceh-18* cause defects in oocyte cell cycle arrest, gonad migration, and epidermal differentiation. *Genes Dev*. 1994 Aug 15;8(16):1935-48. doi: 10.1101/gad.8.16.1935. PMID: 7958868.

Higashitani A, Greenstein D, Hirokawa H, Asano S, Horiuchi K. Multiple DNA conformational changes induced by an initiator protein precede the nicking reaction in a rolling circle replication origin. *J Mol Biol*. 1994 Apr 8;237(4):388-400. doi: 10.1006/jmbi.1994.1242. PMID: 8151700.

Higashitani A, Greenstein D, Horiuchi K. A single amino acid substitution reduces the superhelicity requirement of a replication initiator protein. *Nucleic Acids Res*. 1992 Jun 11;20(11):2685-91. doi: 10.1093/nar/20.11.2685. PMID: 1614854; PMCID: PMC336908.

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Greenstein D, Horiuchi K. Replication enhancer-independent mutation increases the cooperativity with which an initiator protein binds its origin. *J Mol Biol*. 1990 Jan 5;211(1):91-101. doi: 10.1016/0022-2836(90)90013-C. PMID: 2405167.

Greenstein D, Horiuchi K. Double-strand cleavage and strand joining by the replication initiator protein of filamentous phage f1. *J Biol Chem*. 1989 Jul 25;264(21):12627-32. PMID: 2663862.

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