James T. Neal, Ph.D.

Co-Director, T2D Systems Genomics & Merkin Institute Fellow
Investigator, Novo Nordisk Foundation Center for Genomic Mechanisms of Disease
Broad Institute of MIT and Harvard
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Neal lab website: www.neallab.org

Education

Stanford University School of Medicine, Stanford, CA:
Postdoctoral fellowship completed April 2017, Advisor: Calvin Kuo
University of Oregon, Eugene, OR:
Ph.D. in Molecular Biology completed December 2011, Advisor: Karen Guillemin
University of Washington, Seattle, WA:
B.S. in Biochemistry completed June 2004

Major Honors and Fellowships

2023	Named Investigator, NNF Center for Genomic Mechanisms of Disease
2021	NIH Director's New Innovator Award
2019	Named Merkin Institute Fellow, Broad Institute of MIT & Harvard
2016-2017	Stanford Cancer Institute postdoctoral fellowship, Stanford University
2013-2016	American Cancer Society postdoctoral fellowship, Stanford University
2012	Dean's Fellowship Award, Stanford University
2011	CHRO Young Investigator Award
2010	Cancer Federation Scholarship
2009	NIH T32 Training in Molecular Biology and Biophysics, University of Oregon
2007-2009	Keck Foundation Fellowship, University of Oregon
2005-2007	NIH T32 Graduate Training in Genetics, University of Oregon

Major Research Grants

2021-2026 **NIH DP2 GM146252:** "*Optical Functional Genomics*". Role: Principal Investigator.

2019-2021 **Mark Foundation ASPIRE Award**: "*Catalyzing Precision Medicine Through Prospective, High-Throughput Characterization of Cancer Variants*". Role: Co-Principal Investigator (with Bill Hahn).

Additional Research Grants

2023-2026 **NIH R01 HL164811:** "High-throughput cellular genetics to connect noncoding variants to coronary artery disease genes" Role: Co-Investigator (PI: Rajat Gupta)

2022- **Microsoft:** "*Microsoft Research Award - Machine learning methods for high-throughput microscopy*". Role: Principal Investigator.

2021- **Bristol-Myers Squibb**: "*Deep Mutational Scanning of Therapeutic Targets*". Role: Principal Investigator.

2019- **Calico:** "*PERISCOPE*". Role: Principal Investigator.

2019-2021 **Broad Institute**: "*Pooled Screening of Rare Disease Variants*". Role: Co-Investigator (PI: Anne Carpenter).

2019-2021 **Broad Institute:** "*Base editing as a tool for massively parallel variant phenotyping*". Role: Principal Investigator.

2019-2021 **Broad Institute:** "*Pooled image-based profiling for massively parallel cellular phenotyping*". Role: Co-Principal Investigator (with Anne Carpenter and Paul Blainey).

Research Experience/Positions

Co-Director, T2D Systems Genomics
March 2022 - Present
Metabolism Program, Broad Institute of MIT and Harvard
- Massively parallel functional genomics
- Single-cell technology development for scRNA-seq and pooled optical screening
- Novel ex vivo models for oncology and metabolic disease
- Lead systematic efforts to translate metabolic disease-associated genomic variants through gene regulatory, protein, and cellular networks into actionable preventative and therapeutic hypotheses

Senior Group Leader
July 2019 - March 2022
Cancer Program, Broad Institute of MIT and Harvard
- Massively parallel functional genomics
- Single-cell technology development for scRNA-seq and pooled optical screening
- Novel ex vivo models for immuno-oncology

Research Scientist II
May 2017 - July 2019
Cancer Program, Broad Institute of MIT and Harvard
- Massively parallel functional genomics
- Single-cell profiling with scRNA-seq and pooled optical screening

Postdoctoral Scholar
December 2011 - April 2017
Stanford School of Medicine, Hematology Division
- Developed novel 3D culture systems to study tumor biology/immunology
- Functional genomics in colorectal cancer

Graduate Research Fellow
August 2005 - December 2011
University of Oregon, Institute of Molecular Biology
- Investigated the molecular mechanisms of the Helicobacter virulence factor CagA in transgenic zebrafish and Drosophila models
- Studied bacterial regulation of cell proliferation in the developing zebrafish intestine

Clinical Laboratory Technician II
January 2004 - June 2005
University of Washington, Department of Laboratory Medicine
- Investigated the molecular mechanisms of Purkinje cell loss and cerebellar degeneration in the mouse pcd5J mutant

Undergraduate Research Assistant
January 2002 - January 2004
University of Washington, Department of Laboratory Medicine
- Conducted a yeast two-hybrid screen to identify novel interactors of the human ataxin-7 protein
- Assisted with cloning, maintenance of cell lines, and mouse colony genotyping

Research Publications and Preprints

Dietlein F, Wang AB, Fagre C, Tang A, Besselink N, Cuppen E, Li C, Sunyaev SR, **Neal JT***, Van Allen EM*. Genome-wide analysis of somatic noncoding mutation patterns in cancer. ***Science***. 2022 Apr 8;376(6589):eabg5601. doi: 10.1126/science.abg5601. PMID: 35389777.
*co-senior author

Ursu O*, **Neal JT***, Shea E, Thakore PI, Jerby-Arnon L, Nguyen L, Dionne D, Diaz C, Bauman J, Mosaad MM, Fagre C, Giacomelli AO, Ly SH, Rozenblatt-Rosen O, Hahn WC, Aguirre AJ, Berger AH, Regev A, Boehm JS. Massively parallel phenotyping of variants in cancer with Perturb-seq reveals a shift in the spectrum of cell states induced by somatic mutations. ***Nature Biotechnology***. 2021. https://doi.org/10.1038/s41587-021-01160-7
*equal contribution

Hanna RE, Hegde M, Fagre CR, DeWeirdt PC, Sangree AK, Szegletes Z, Griffith A, Feeley MN, Sanson KR, Baidi Y, Koblan LW, Liu DR, **Neal JT**, Doench JG. Massively parallel assessment of human variants with base editor screens. ***Cell***. 2021 Feb 18;184(4):1064-1080.e20. doi: 10.1016/j.cell.2021.01.012. PMID: 33606977.

Horn H, Fagre C, Gupta A, Tsafou K, Fornelos N, **Neal JT***, Lage K*. Using protein interaction networks to identify cancer dependencies from tumor genome data. ***bioRxiv***. 2020 Aug 28. doi: https://doi.org/10.1101/2020.08.27.270520
*co-senior author

Neal JT*, Li X*, Zhu J, Giangarra V, Grzeskowiak CL, Ju J, Liu IH, Chiou SH, Salahudeen AA, Smith AR, Deutsch BC, Liao L, Zemek AJ, Zhao F, Karlsson K, Schultz LM, Metzner TJ, Nadauld LD, Tseng YY, Alkhairy S, Oh C, Keskula P, Mendoza-Villanueva D, De La Vega FM,

Kunz PL, Liao JC, Leppert JT, Sunwoo JB, Sabatti C, Boehm JS, Hahn WC, Zheng GXY, Davis MM, Kuo CJ. Organoid Modeling of the Tumor Immune Microenvironment. ***Cell***. 2018 Dec 13;175(7):1972-1988.e16. doi: 10.1016/j.cell.2018.11.021. PMID: 30550791.
*equal contribution

Neal JT, Kuo CJ. Organoids as models for neoplastic transformation. ***Ann Rev Path***. 2016 May 23;11:199-220.

Li X, Nadauld L, Ootani A, Corney DC, Pai R, Gevaert O, Cantrell MA, Rack PG, **Neal JT**, Chan CW, Yeung T, Gong X, Yuan J, Wilhelmy J, Robine S, Attardi LD, Plevritis SK, Hung KE, Chen CZ, Ji HP, Kuo CJ. Oncogenic transformation of diverse gastrointestinal tissues in primary organoid culture. ***Nature Medicine.*** 2014 May 25. doi: 10.1038/nm.3585.

Neal JT, Peterson TS, Kent ML, Guillemin K. *H. pylori* Virulence Factor CagA Increases Intestinal Cell Proliferation by Wnt Pathway Activation in a Transgenic Zebrafish Model. ***Disease Models and Mechanisms***. 2013 May;6(3):802-10.

Rosenbluh J, Nijhawan D, Cox AG, Li X, **Neal JT**, Schafer EJ, Zack TI, Wang X, Tsherniak A, Schinzel AC, Shao DD, Schumacher SE, Weir BA, Vazquez F, Cowley GS, Root DE, Mesirov JP, Beroukhim R, Kuo CJ, Goessling W, Hahn WC. β-Catenin-driven cancers require a YAP1 transcriptional complex for survival and tumorigenesis. ***Cell***. 2012 Dec 21;151(7):1457-73.

Reid DW*, Muyskens JB*, **Neal JT***, Gaddini GW, Cho LY, Wandler AM, Botham CM, Guillemin K. Identification of genetic modifiers of CagA-induced epithelial disruption in Drosophila. ***Front Cell Infect Microbiol***. 2012;2:24.
*equal contribution

Cheesman SE, **Neal JT**, Mittge E, Seredick BM, Guillemin K. Epithelial cell proliferation in the developing zebrafish intestine is regulated by the Wnt pathway and microbial signaling via Myd88. ***Proc. Natl. Acad. Sci. U.S.A*** 2011 Mar;108

Chakrabarti L, **Neal JT**, Miles M, Martinez RA, Smith AC, Sopher BL, La Spada AR. The Purkinje cell degeneration 5J mutation is a single amino acid insertion that destabilizes Nna1 protein. ***Mammalian Genome***. 2006 Feb;17(2):103-10.

Other Publications

Neal JT, Boehm JS, Hahn WC. From Variants to Functions - New Strategies for the Interpretation of Cancer Genomes. Guest Editorial. NIH Office of Cancer Genomics e-Newsletter. 2019 Mar.

Neal JT, Cantrell MA, Kuo CJ. Functional Validation of Novel Cancer Driver Loci Using Three-Dimensional Organoid Cultures. Guest Editorial. NIH Office of Cancer Genomics e-Newsletter. 2014 Jul.

Neal JT. Two-Body Blessing. Nature. 2013 Sep 5;501:127.

Neal JT. Mentoring: More than just a pair of hands. Naturejobs Blog. 2013 Aug 29.

Patents/applications

Jesse Boehm, Niklas Rindtorff, **James T. Neal**, Aviad Tsherniak, Mushriq Muhib Al-Jazrawe, inventors; Broad Institute of MIT & Harvard, assignee. Living Biosensors. U.S. Non-Provisional Patent Application No. 17/113,790. 2020.

Aviv Regev, Pratiksha Thakore, John Doench, **James T. Neal**, Jesse Boehm, Oana Ursu, inventors; Broad Institute of MIT & Harvard, assignee. Methods and compositions for multiplexing single cell and single nuclei sequencing. U.S. Provisional Patent Application No. 62/813,674. 2019.

James T. Neal, Calvin Jay Kuo, inventors; Stanford University, assignee. Methods to preserve tumor-stromal interactions in culture and therapeutic predictive applications thereof. United States Patent No. 11,180,735. 2021.

Invited Lectures

Novo Nordisk Foundation Center Variant-to-Function Symposium, Cambridge, MA, March 2023
TargetCancer Foundation Think Tank on Advancing Gastroesophageal Cancer Research, Boston, MA, November 2019
Science for All Seasons, Cambridge, MA, February 2019
German Academic International Network Meeting, San Francisco, CA, August 2015
Colon Cancer Family Registry Meeting, Honolulu, HI, June 2015
NCI Cancer Target Discovery and Development Network Meeting, Rockville, MD, April 2014
Bay Area Postdoctoral Symposium, San Francisco, CA, March 2014
16th International Workshop on Campylobacter, Helicobacter, and Related Organisms, Vancouver, BC, August 2011
West Coast Helicobacter pylori Symposium, Davis, CA, April 2010

Teaching

Bio422/522 - Protein Toxins in Cell Biology, 2010 - 2011
University of Oregon, Guest Lecturer
Bio309 - Biology of Tropical Diseases: Africa, 2006
University of Oregon, Graduate Teaching Assistant
Bio252 - Biochemistry and Cell Physiology, 2005
University of Oregon, Graduate Teaching Assistant
Bio358 – Investigations in Medical Physiology, 2005
University of Oregon, Graduate Teaching Assistant

Institutional Service

Broad Institute Scientific Retreat, Co-Chair, 2021-
Broad Institute Scientific Retreat, Committee Member and Subcommittee co-chair, 2018-
SPARC Grant Review Committee, Member, 2020-
BroadIgnite Committee, Member, 2020-

Broad Operations Committee, Member, 2020-
Cancer Program Strategy Committee, Member, 2020-2022
Cancer Program Senior Advisory Committee, Member, 2020-2022
Cancer Program Meeting Co-organizer, 2020
Technology Engagement Team - Cancer Task Force, 2019
Variant to Function Project Steering Committee, Member, 2018-2019

Other Professional Service

Scientific alliance membership
International Common Disease Alliance, Cellular Programs Working Group Member, 2021-
Atlas of Variant Effects Alliance, Co-Founder & Executive Committee Member, 2020-

Administration and conference/workshop chairing
Atlas of Variant Effects Alliance Launch meeting, Co-organizer and Session Chair, Virtual, October 2020
AAMC Graduate Education and Training Group, 2014 - 2016
Stanford School of Medicine Faculty Senate Executive Committee, 2014 - 2015
Stanford School of Medicine Faculty Senate, 2014 - 2015
Stanford Provost's Postdoctoral Advisory Committee, 2014 - 2015
Stanford Postdoctoral Association, Chair, 2014 - 2015
Stanford Faculty Senate Computing Committee (C-ACIS), 2013 - 2014
Stanford Postdoctoral Association, Elected Council Member, 2013 - 2015

Journal Reviewer (ad-hoc)
Cell
JCO Precision Oncology
Nature
Nature Cancer
Nature Medicine

Professional Society Memberships

Global Alliance for Genomics and Health, 2017 - present
National Postdoctoral Association, 2014 - 2017
American Association for Cancer Research, 2013 - 2020
Society for Developmental Biology, 2009 - 2011
American Society for Microbiology, 2006 - 2008

Postdoctoral, Graduate, and Staff Research Supervised

2021-present: Meraj Ramezani, Research Scientist
2020-2022: Allison Brill, Postdoctoral Associate; subsequently patent technology specialist at Wolf Greenfield
2019-present: Alex Wang, Research Scientist
2019-present Mariam Mosaad, Senior Research Associate, subsequently PhD student at MD Anderson

2018-2021: Oana Ursu, Postdoctoral Associate (co-mentored, primary mentor: Aviv Regev), subsequently Scientist at Genentech
2018-2019: Niklas Rindtorff, Fulbright Fellow and Visiting MD/PhD Student from Heidelberg University (co-mentored with Jesse Boehm)
2017-2021: Avtar Singh, Postdoctoral Associate (co-mentored, primary mentor: Paul Blainey), subsequently Senior Scientist at Genentech

Postbaccalaureate and Undergraduate Research Supervised

2022-present: Jenlu Pagnotta, Postbaccalaureate Research Associate
2022-present: Gunjan Jetley, Postbaccalaureate Research Associate
2021-present: Arno Lim, Undergraduate Honors Researcher from Tufts University
2021-present: Eddy Leardini, Postbaccalaureate Research Associate
2021-present: Sofia Lombana Rengifo, Postbaccalaureate Research Associate
2021-present: Jason Lim, Postbaccalaureate Research Associate
2020-present: Maria Lozada, Postbaccalaureate Research Associate
2019-2021: Yossef Baidi, Postbaccalaureate Research Associate; subsequently PhD Student at Harvard University
2019-2021: Sanam Kavari, Postbaccalaureate Research Associate; subsequently MD/PhD Student at University of Pennsylvania
2019-2021: Varsha Prakash, Postbaccalaureate Research Associate; subsequently MD student at UCSD
2018-2021: Julia Bauman, Postbaccalaureate Research Associate; subsequently PhD Student at Stanford University
2018-2021: Celeste Diaz, Postbaccalaureate Research Associate; subsequently PhD Student at Stanford University
2018-2020: Christian Fagre, Postbaccalaureate Research Associate; subsequently PhD Student at Yale
2018: Katharine Courtemanche, Summer Intern from Harvard University
2017-2018: Emily Shea, Postbaccalaureate Research Associate; subsequently MD/PhD student at University of Pennsylvania
2016-2017: Lillian Liao, Undergraduate Honors Thesis; subsequently Medical Student at Columbia University
2014-2017: Iris Liu, Undergraduate Researcher; subsequently Medical Student at UCSF, then Surgical Resident at UCSF
2014-2015: William Kindschuh, Undergraduate Researcher; subsequently MD/PhD Student at Columbia University
2012-2017: Brian Deutsch, Undergraduate Honors Thesis; subsequently MD student at Mount Sinai Medical School, then Surgical Resident at Massachusetts General Hospital