

Siddhartha G. Jena

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My research program aims to understand the mechanisms underlying genomic resilience to environmental stress, and use this understanding to engineer resilience into cells for broad therapeutic and industrial purposes. I draw from a strong background in mathematics and physics, and combine cell biological approaches with high-throughput screening, genomics, quantitative imaging, and computational protein design.

Education

Princeton University

July 2021

PhD, Molecular Biology and Biophysics

Thesis: Signaling Dynamics Shape Gene Regulation Across Scales (advisor: Jared Toettcher)

Harvard University

May 2016

AB, Chemistry and Physics (honors), joint with Mathematics, minor in Molecular and Cell Biology

Thesis: Molecular Dynamics Simulation of the Effect of Cholesterol on AQP1-Mediated Water Transport (advisor: Martin Karplus)

Research Experience

Harvard University

August 2021-Present

Postdoctoral Fellow, Department of Stem Cell and Regenerative Biology/Broad Institute

Advisor: Jason Buenrostro

Topic: High-throughput approaches for understanding and engineering chromatin function

- Developed high-throughput screening and imaging methods for evaluating the effect of engineered histones on global chromatin structure
- Employed a range of computational and experimental genomics and screening approaches, as well as expansion and high-resolution quantitative microscopy
- Leveraged deep learning and computational protein design to construct novel histone proteins for cellular engineering

Princeton University

February 2017-July 2021

Graduate Research Assistant, Department of Molecular Biology

Mentor: Jared Toettcher

Topic: Dynamic signaling-mediated cellular communication and gene regulation

- Used live-cell and fixed cell imaging to profile gene expression downstream of Erk signaling
- Built computational models to infer Erk-mediated cellular communication between keratinocytes
- Mapped enhancer grammar to developmental gene regulation in the fly embryo
- Gained expertise in cellular optogenetics, live cell microscopy, RNA-FISH, cell culture, *Drosophila* biology, and statistical modeling

Harvard University

August 2013-May 2016

Undergraduate Research Assistant, Department of Chemistry/MGH Department of Molecular Biology

Mentors: Martin Karplus, Jack Szostak

Topic: Biophysics of cellular membranes and membrane-associated proteins

- Developed molecular dynamics methods to study the effect of cholesterol content on the behavior of membrane proteins
- Identified residues in the water transporter AQP1 that are sensitive to membrane cholesterol content
- Developed imaging methods to characterize the sensitivity of hybrid membranes to cation concentration

Awards and Fellowships

2019-2021 NIH NIAMS F31 Fellowship, “Cracking the signaling code: how ERK activity dynamics coordinate gene expression and differentiation in keratinocytes”

2017 Francis Boyer Fellowship in the Life Sciences, Princeton University

2016 Honors in Chemistry and Physics Major, Harvard University Physics Department

2014 Origins of Life Initiative Summer Research Fellowship, Harvard University

2013, 2015 Fellowship, Harvard College Undergraduate Research Program

Mentorship

2022 Wilson Gomarga, Harvard BBS Rotation Student

2022 Ena Oreskovic, Harvard BBS Rotation Student

2022 Michael Quezada, Harvard/MIT MD-PhD Rotation Student

2021–2022 Amalia Driller-Colangelo, Harvard BBS Graduate Student

2020–2021 Pranav Avadhanam, (middle school student)

2020 Teoman Toprak, (high school student)

2019–2021 Catherine Yu, Undergraduate (Current: Research Assistant, NYU)

2019–2021 Served as Residential Graduate Student, Butler College, Princeton University

2018 Brittany Williams, University of Arizona Undergraduate (Current: PhD student at University of Washington)

2018 LeeRoy Borders (Rutgers University Undergraduate). Mentored through the Prison Teaching Initiative summer program

2017–2019 Kirit Limperis, Undergraduate (Current: PhD student, Columbia)

2017–2019 Danielle Isakov, Undergraduate (Current: MD-PhD student, Tri-I program)

Service

Harvard Stem Cell and Regenerative Biology Department Retreat Planning Committee, 2025: helped plan a cost-effective, educational and community-building retreat with other department members amidst funding uncertainties.

Residential Graduate Student, Butler College, Princeton University (2019–2021): In this role, I was a source of advice for undergraduates, held monthly open mic nights and study breaks, and organized trips to NYC and Philadelphia.

Harvard University Art Museums Student Board Member (2014–2016): In this role, I helped reopen the art museums to students and the public, advised on curatorial decisions, and organized community outreach with both the Harvard community and neighboring elementary, middle, and high schools.

Harvard College Undergraduate Representative Board for the Sciences (2014–2016): In this role, I advised faculty on curriculum decisions, outreach, and community building for undergrads in the sciences.

Teaching

Spring 2019 Section TA, MOL 375: Genetics, Princeton University

Spring 2018 Lab TA, MOL 101: From DNA to Human Complexity, Princeton University

Spring 2016 Course TA/Grader, Physics 15b: Electricity and Magnetism, Harvard University

Spring 2015 Course TA/Grader, Physics 15b: Electricity and Magnetism, Harvard University

Scientific Publications

1. **Jena S.G.**, Nagaraja S, Earl A.S., Driller-Colangelo A.R., Quezada M.A., Oreskovic E., Horlbeck M.A., Zhang R., Gomarga W., Buenrostro J.D. Engineered histones reshape chromatin in human cells. *bioRxiv* 2025 (*submitted*)

2. Lu Y.R., Cameron J.C., Hu. Y., ..., **Jena S.G.**, ..., Ksander B.R., Weissman J.S. Reprogramming Factors Activate a Non-Canonical Oxidative Resilience Pathway That Can Rejuvenate RPEs and Restore Vision *bioRxiv* 2025. (in revision at *Cell*)

3. Shang Y., Cho W.J., ..., **Jena S.G.**, ..., Qi X., Jena B.P. Mechanism of clinically relevant neurosecretory and metabolic impairment in Alzheimers and identification of engineered nanotherapy. *bioRxiv* 2025.

4. Payzin-Dogru D., Blair S.J*, **Jena S.G.***, ..., Buenrostro J.D., Haas B.J., Chiu I.M., Sackton T.B., Whited J.L. Peripheral nervous system mediates body-wide stem cell activation for limb regeneration. *bioRxiv* 2024, (in press at *Cell*.)

5. Verma A.*, Yu, C.*, Bachl, S.,..., **Jena S.G.**, Marson A., Carnevale J., Van Valen D., Engelhardt B.E. Cellular behavior analysis from live-cell imaging of TCR T cell–cancer cell interactions *bioRxiv* 2024. (in revision at *Nat. Biotech.*)

6. Verma A.*, **Jena S.G.***, Isakov D.R., Aoki K., Toettcher J.E., Engelhardt B.E. A self-exciting point process to study multi-cellular spatial signaling patterns. *PNAS* 118 (32) (2021).

7. Avadhanam P.*, **Jena S.G.*** Restricted Positional Games. *arXiv*:2108.12839. 2021.

8. **Jena S.G.**, Yu C., Toettcher J.E. Dynamics and heterogeneity of Erk-induced immediate-early gene expression. *bioRxiv*, 2021, in revision.

9. Keller S.H.*, **Jena S.G.***, Yamazaki Y., Lim B. Regulation of spatiotemporal limits of developmental gene expression via enhancer grammar. *PNAS* 117 (26) 15096–15103 (2020).

10. Ravindran P.T., Wilson M.Z., **Jena S.G.**, Toettcher J.E. Engineering combinatorial and dynamic decoders using synthetic immediate-early genes. *Comms. Biol.* 2020.

11. Goglia A.G.*, Wilson M.Z.*, **Jena S.G.**, Silbert J., Basta L.P., Devenport D., Toettcher J.E. A Live-Cell Screen for Altered Erk Dynamics Reveals Principles of Proliferative Control. *Cell Syst.* 10 (3) (2020).

12. Golonka D., Fischbach P., **Jena S.G.**, Kleeberg J.R.W., Essen L., Toettcher J.E., Zurbriggen M.D., Moglich A. Deconstructing and repurposing the light-regulated interplay between Arabidopsis phytochromes and interacting factors. *Comms. Biol.* 2 (2019).
 13. Jin L.*, Kamat N.P.*, **Jena S.G.**, Szostak J.W. Fatty Acid/Phospholipid Blended Membranes: A Potential Intermediate State in Protocellular Evolution. *Small* 14.15 (2018).
 14. **Jena S.G.** (2016) A Random Graph Model of Density Thresholds in Swarming Cells. *J. Cell. Mol. Med.* 20(3): 413-421.
 15. **Jena S.G.** (2013) Involvement of potassium channel in AQP1-mediated water and gas transport in erythrocytes. *J. Biol Phys Chem* 13: 12-17.
 16. **Jena S.G.**, Lee, J-S. (2010) High Cholesterol Impairs Water and Gas Transport in Red Blood Cells and is Ameliorated by the PLA2 Inhibitor ONO-RS-082. *J. Biol Phys Chem* 10: 127-134.
- * denotes equal contribution.**

Reviews

1. **Jena S.G.***, Verma A.*, Engelhardt B.E. Answering open questions in biology using spatial genomics and structured methods.. *BMC Bioinformatics* 2024.
2. **Jena S.G.***, Goglia A.G.*, Engelhardt B.E. Towards ‘end-to-end’ analysis and understanding of biological timecourse data. *Biochem J* (2022) 479 (11): 1257–1263.
3. **Jena S.G.**, Toettcher J.E. The role of timing in biological perception and actuation. *Phys. Biol.* (2021)

Invited Talks

- 2025 Oxford Biochemistry Departmental Seminar. *Engineered histones reshape chromatin in human cells.* (Host: Tobias Warnecke)
- 2025 Harvard Stem Cell and Regenerative Biology Departmental Seminar. *Engineered histones reshape chromatin in human cells.* (Host: Kara McKinley)
- 2023 MIT Department of Chemistry. *How to compartmentalize a genome.* (Host: Bin Zhang)

Conference Presentations

- 2025 EMBO Workshop: EvoChromo: Evolutionary approaches to research in chromatin. *Engineered histones reshape chromatin in human cells.* **Oral Presentation**
- 2024 Gordon Conference on Chromatin Structure and Function. *Mapping the evolutionary design space of the core histones.* **Poster**
- 2021 American Society for Biochemistry and Molecular Biology Conference. *Dynamics and heterogeneity of Erk-induced immediate-early gene expression.* **Oral Presentation**
- 2020 Keystone Symposium on Gene Regulation. *Dynamic signaling and stochastic transcription intersect to modulate heterogeneity.* **Poster**
- 2017 American Physical Society March Meeting. *Information Propagation in Developmental Enhancers.* **Oral Presentation**
- 2016 Origins of Life Symposium, Harvard University. *Cation Stability of Blended Phospholipid/Fatty Acid Vesicles.* **Poster**

References

- Jason Buenrostro
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Harvard University/Broad Institute
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- Jared Toettcher
Associate Professor, Molecular Biology/Bioengineering
Princeton University
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- Barbara Engelhardt
Professor, Computer Science
Stanford University/Gladstone Institutes
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