# BRENDAN F. MILLER

Post-doctoral research fellow developing computational pipelines for analysis of single-cell and spatial-omics data. Molecular biologist with strong background in clinical diagnostics and cancer biology.

## CURRENT POSITION

Supervisor - Dr. Jean Fan

#### Post-Doctoral Fellow in Computational Biology Johns Hopkins University Department of Biomedical Engineering Second Se

Baltimore, MD

- · Development of open-source computational pipelines and statistical software to characterize and visualize cell type spatial organizational patterns in tissues.
- · Directly analyzed and extracted meaningful cell type spatial relationships from leadingedge technologies such as Visium, MERSCOPE, Slide-Seq, DBiT-Seq.
- Annotated cell types and quantified their spatial co-localization changes across immune tissues using CODEX highly multiplexed spatial protein expression data.
- Applied convolutional neural networks to segment cells in H&E images to increase the resolution of Visium datasets.
- Developed statistical software packages in <u>R and Python</u>. Performed extensive highthroughput analyses with a high-performance Linux cluster.
- Characterizing spatial gene expression heterogeneity in spatially resolved single-cell transcriptomic data with nonuniform cellular densities | 6 Genome Res 2021
- Reference-free cell type deconvolution of multi-cellular pixel-resolution spatially resolved transcriptomics data | *S* Nat Commun 2022

### EDUCATION

#### Ph.D., Molecular Biology

Johns Hopkins University National Institutes of Health Graduate Partnership Program Advisor - Dr. Laura Elnitski

- Dissertation: 🔗 Investigating Blood-based Biomarkers and Patterns of DNA Methylation in Tumors
- Optimized single molecule detection assay to quantify rare fragments of methylated cellfree DNA in patient plasma. Developed computational machine learning algorithms leveraging heterogeneous methylation patterns to optimize liquid biopsy cancer diagnostics.
- Developed pipeline to process cell-free DNA from hundreds of patient plasma samples. Samples were analyzed using <u>ddPCR and qPCR</u>.
- · Bisulfite sequencing analysis of extracted cell-free DNA to detect rare methylated DNA variants.
- · Assessing ZNF154 methylation in patient plasma as a multicancer marker in liquid biopsies from colon, liver, ovarian and pancreatic cancer patients | *Sci Reports 2021*
- Leveraging locus-specific epigenetic heterogeneity to improve the performance of bloodbased DNA methylation biomarkers | *O* Clin Epigenetics 2020
- The emergence of pan-cancer CIMP and its elusive interpretation | *Biomolecules 2016*

#### B.S., Biochemistry | Pharmacology minor

University of Vermont

#### Burlington, VT

Bioconductor git/GitHub PyPI

#### Scientific Communication

High impact publications Invited conference speaker



CONTACT

➡ bmill3r@gmail.com

in brendan-f-miller Google Scholar

EXPERTISE

Assay optimization

**Cancer diagnostics** 

droplet digital PCR

**Bisulfite sequencing** 

Cell type deconvolution

Machine learning models Single-cell multi-omics

Spatial transcriptomics

Software/Coding

R/RStudio

Computing

Data Visualization

ggplot2

markdown

matplotlib R Shiny

Version Control

Bash scripting

jupyter notebook

Linux High-Performance

Python

**Epigenetics and chromatin** 

Gene expression variability

**Differential Gene Expression** 

Gene set enrichment analysis

**DNA Methylation** 

Cell-free DNA

Data Analysis

Biology

Ohttps://github.com/bmill3r

https://bmill3r.github.io/

Current 2020

> 2020 2014

2012

2008

**Q** Baltimore, MD

|          | T | AWARDS AND HONORS  |               |  |  |
|----------|---|--|---------------|--|--|
| 2022     | • | Johns Hopkins Whiting School of Engineering Excellence in Research Trainee Awar<br>Johns Hopkins University  | <b>d</b><br>D |  |  |
|          |   | • "Reference-free cell-type deconvolution of multi-cellular pixel resolution spatially resolved transcriptomics data"  |               |  |  |
| 2020     | • | ${ {oldsymbol {\mathscr O}}}$ National Human Genome Research Institute Intramural Research Award   |               |  |  |
|          |   | National Institutes of Health Question Address State Address Addre | D             |  |  |
|          |   | • Project: "Detection of Methylated Cancer Biomarkers in Cell-free DNA"  |               |  |  |
| 2020     | • |  |               |  |  |
|          |   | National Institutes of Health Question Bethesda, M   | D             |  |  |
|          |   | • Abstract: "A Methylation Density Binary Classifier for Predicting and Optimizing the Performance of Methylation Biomarkers in Clinical Samples"  |               |  |  |
| 2019     | • | ${\cal O}$ National Institutes of Health Graduate Student Research Award   |               |  |  |
|          |   | National Institutes of Health <b>Q</b> Bethesda, M   | D             |  |  |
|          |   | <ul> <li>15th Annual NIH Graduate Student Research Symposium</li> <li>Section: Pharmacology and. Clinical and Translational Science</li> </ul>   |               |  |  |
| 2017     | • |  |               |  |  |
|          |   | National Institutes of Health Question Address State Address Addre | D             |  |  |
|          |   | • Abstract: "Digital Droplet PCR Liquid Biopsy Assay for Detecting Circulating Tumor DNA in Patient Plasma"  |               |  |  |
| 2013     | • | National Institutes of Health Post-Baccalaureate Outstanding Poster Award  |               |  |  |
|          |   | National Institutes of Health  | D             |  |  |
| 2012     | • | National Institutes of Health Post-Baccalaureate Training Award  |               |  |  |
|          |   | National Institutes of Health Q Bethesda, M  | D             |  |  |
| 2012     | • | John Thanassi Research Award for Outstanding Achievements in Biochemistry<br>University of Vermont Q Burlington, V   | /T            |  |  |
| 2000     | • | Geography Bee Winner   |               |  |  |
|          |   | East Kingston Elementary School  | Н             |  |  |
|          |   | • Winner of the 5th grade Geography Bee at the Elementary School level   |               |  |  |
|          | Д | RESEARCH EXPERIENCE  |               |  |  |
| 2020     | • | Graduate Research Fellow   |               |  |  |
| <br>2014 |   | Translational and Functional Genomics Branch <b>Q</b> Bethesda, M  | D             |  |  |
|          |   | • Advisor: Dr. Laura Elnitski  |               |  |  |
|          |   | <ul> <li>Project 1: "Detection of Methylated Cancer Biomarkers in Cell-free DNA"</li> <li>Project 2: "Elucidation of Molecular Commonalities in CpG Island Methylator Phenotype<br/>Tumors Across Cancer-types"</li> </ul>   |               |  |  |

| 2014              | • | Graduate Research Fellow       ♥ Baltimore, MD         Research Rotation       ♥ Baltimore, MD         Carnegie Instituion of Washington       Department of Embryology         • Advisor: Dr. Alex Bortvin       •         • Project: "Quantitation of transposable element abundance in RNA-seq data"         • Comparison and benchmarking of multiple bioinformatic pipelines for taxonomic classification and quantification of DNA transposable elements in biological samples.         • Preprocessing, alignment, and filtering of NGS RNA-seq reads followed by quantitation of genomic feature overlaps using combination of bowtie, bedtools, and custom Python scripts |
|-------------------|---|--|
| 2014<br> <br>2012 | • | Post-Baccalaureate Research Fellow         Genomic Structure and Function Section         • Advisor: Dr. Anthony Furano         • Project: "Factors that Determine Strand Selection During Repair of T/G Mismatches"   |
| 2012<br> <br>2011 | • | Undergraduate Researcher<br>Department of Pharmacology • University of Vermont<br>• Advisor: Dr. Wolfgang Dostmann<br>• Project: "Purification and Long-term Storage of Toxoplasma gondii PKGII Protein"   |
| 2011              | • | Undergraduate Researcher<br>Department of Biochemistry Ouriversity of Vermont<br>• Advisor: Dr. Anne B. Mason<br>• Project: "Identification of Key Residues of Human Transferrin and Transferrin Receptor"   |
| 2007              | • | Research Assistant       University of Massachusetts, Lowell, MA         Department of Biological Sciences       University of Massachusetts, Lowell, MA         • Advisor: Dr. Brian Bettencourt       Project: "Variation inn Hsp70 Expression During Natural Thermal Stress Drives Differential Suppression of poly-Q Toxicity"   |
|                   |   | TEACHING EXPERIENCE  |
| 2016<br> <br>2015 | • | Lecturer - Research Tools for Studying Disease<br>National Institutes of Health♥ Bethesda, MD• Developed syllabus, overall course structure, and administered grades for "Proteins I" and<br>"Computational Biology" lectures  |
| 2015              | • | Teaching Assistant - General Biology         Johns Hopkins University         • Managed laboratory section, which included experimental setup, development of instructional lectures, and adminstration of assignments and exams   |
| 2014<br> <br>2012 | • | Program Leader         Health Education Outreach Program         • Taught topics in medicine and healthcare to underpriviledged and underrepresented communities   |
| 2012<br> <br>2010 | • | Tutor - General Chemistry and Organic Chemistry         University of Vermont         • Established and oversaw individual and group tutoring sessions   |

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| 2022   | •   | High School Summer Student   | Baltimore MD                                    |
|--|---|--|---|
|  |   | Johns Hopkins University   | ▼ Dattinore, MD                                 |
|  |   | <ul> <li>Efficient Detection of Gene Expression Patterns in Large Spatia<br/>Transcriptomics Datasets with Pseudospot Aggregation</li> <li>Mayling Chen</li> </ul> | ally Resolved Single-Cell                       |
| 2022   | •   | Undergraduate Research Assistant   |   |
| <br>2021   |   | Johns Hopkins University   | Saltimore, MD                                   |
| 2021   |   | <ul> <li>STdeconvolve Computational Performance Benchmarking</li> <li>Feiyang</li> </ul>   |   |
|  |   | INVITED SPEAKER  |   |
| • Reference-free cell-type deconvolutior resolved transcriptomics data |   | Reference-free cell-type deconvolution of multi-cellular pixe<br>resolved transcriptomics data   | el resolution spatially                         |
|  |   | NYU Langone Single Cell Club   | <b>Q</b> Virtual                                |
| 2022   | •   | Reference-free cell-type deconvolution of multi-cellular pixe<br>resolved transcriptomics data   | el resolution spatially                         |
|  |   | ${\cal O}$ Bioengineering Solutions for Biology and Medicine   | <b>Q</b> Munich, Germany                        |
| 2022   | •   | Reference-free cell-type deconvolution of multi-cellular pixe<br>resolved transcriptomics data   | el resolution spatially                         |
|  |   | ${oldsymbol \mathscr O}$ CNS Research Showcase at Indiana University   | <b>Q</b> Virtual                                |
| 2021   | •   | Reference-free cell-type deconvolution of multi-cellular pixe<br>resolved transcriptomics data   | el resolution spatially                         |
|  |   | ${oldsymbol \mathscr O}$ University of Sydney Bioinformatics Seminar Series  | <b>Q</b> Virtual                                |
| 2019   | •   | A methylation density binary classifier for predicting and op<br>of methylation biomarkers in clinical samples   | timizing the performance                        |
|  |   | Circulating Nucleic Acids/Liquid Biopsy Interest Group   | <b>Q</b> Virtual                                |
| 2018   | •   | Advancement in ovarian carcinoma detection using circula patient plasma samples  | ting cell-free DNA from                         |
|  |   | National Human Genome Research Institute Symposium   | <b>Q</b> Bethesda, MD                           |
| 2018   | •   | Detecting DNA methylation patterns in patient plasma to in   | prove cancer diagnostics                        |
|  |   | NIEHS Inflammation Faculty Workshop  | Research Triangle Park, NC                      |
| 2018   | •   | Detecting DNA methylation patterns in patient plasma to in<br>3rd Annual Liquid Biopsy Summit  | prove cancer diagnostics<br>♥ San Francisco, CA |
|  | Ŀ   | SELECTED POSTER PRESENTATIONS  |   |
| 2020   | • A methylation density binary classifier for predicting and optimizing the |  | timizing the performance                        |
|  |   | Advances in Genome Biology and Technology  | <b>Q</b> Marco Island, FL                       |
| 2017   | •   | Detecting DNA methylation in blood for cancer diagnostics  | -   |
|  |   | Next Generation Diagnostics Summit   | • Washington, DC                                |
| 2017   | •   | Detecting DNA methylation in blood for cancer diagnostics  | ♥ Heidelberg, Germanv                           |
|  |   | Lindo chi omaan and chigeneucs meeting   | <u> </u>  |

| 2013 | • | Factors that determine strand selection during repair of T/G mismatches   |
|------|---|---|
|      | • | 13th Annual Postbac Poster Day 🛛 🗣 Bethesda, MD   |
|      | Ø | PREPRINT PUBLICATIONS   |
| 2015 | • | Building genomic analysis pipelines in a hackathon setting with bioinformatician teams: DNA-Seq, Epigenomics, Metagenomics, and RNA-Seq   |
|      |   | 🔗 bioRxiv 018085  |
|      |   | <ul> <li>Ben Busby, Allissa Dillman, Claire L. Simpson, Ian Fingerman, Sijung Yun, David M.<br/>Kristensen, Lisa Federer, Naisha Shah, Matthew C. LaFave, Laura Jimenez-Barron, Manjusha<br/>Pande, Wen Luo, Brendan Miller, Cem Mayden, Dhruva Chandramohan, Kipper Fletez-<br/>Brant, Paul W. Bible, Sergej Nowoshilow, Alfred Chan, Eric JC Galvez, Jeremy Chignell, Joseph<br/>N. Paulson, Manoj Kandpal, Suhyeon Yoon, Esther Asaki, Abhinav Nellore, Adam Stine,<br/>Robert Sanders, Jesse Becker, Matt Lesko, Mordechai Abzug, Eugene Yaschenko</li> </ul> |
|      |   | SELECTED PUBLICATIONS   |
| 022  | • | Reference-free celltype deconvolution of multi-cellular pixel-resolution spatially resolved transcriptomics data<br>Nat Commun 13, 2339 (2022)  |
|      |   | <ul> <li>Brendan F. Miller, Feiyang Huang, Lyla Atta, Arpan Sahoo, Jean Fan</li> <li>Software:  STdeconvolve</li> </ul>   |
| 021  | • | Characterizing spatial gene expression heterogeneity in spatially resolved single-cell transcriptomics data with nonuniform cellular densities  |
|      |   | <b>Ø</b> Genome Res. 2021. 31: 1843-1855  |
|      |   | <ul> <li>Brendan F. Miller, Dhananjay Bambah-Mukku, Catherine Dulac, Xiaowei Zhuang, Jean Fan</li> <li>Software: <i>O</i> MERINGUE</li> </ul>   |
| .021 | • | Assessing ZNF154 methylation in patient plasma as a multicancer marker in liquid biopsies from colon, liver, ovarian and pancreatic cancer patients   |
|      |   | <b>Ø</b> Sci Rep 11, 221 (2021)   |
|      |   | • Brendan F. Miller, Hanna M. Petrykowska, Laura Elnitski   |
| 020  | • | Leveraging locus-specific epigenetic heterogeneity to improve the performance of<br>blood-based DNA methylation biomarkers  |
|      |   | 🔗 Clin Epigenet 12, 154 (2020)  |
|      |   | <ul> <li>Brendan F. Miller, Thomas R. Pisanic II, Gennady Margolin, Hanna M. Petrykowska, Pornpat<br/>Athamanolap, Akosua Osei-Tutu, Tza-Huei Wang, Christina Annunziata, Laura Elnitski</li> <li>Software: Software: Software: Software</li> </ul>   |
| 019  | • | Identification of human silencers by correlating cross-tissue epigenetic profiles and gene expression   |
|      |   | 🔗 Genome Research. 2019 March; 29(3):1-11   |
|      |   | • Di Huang, Hanna M. Petrykowska, <b>Brendan F. Miller</b> , Laura Elnitski, Ivan Ovcharenko  |
| 018  | • | Transient reduction of DNA methylation at the onset of meiosis in male mice   |
|      |   | 🔗 Epigenetics and Chromatin. 2018 April; 11:15  |
|      |   | • Valeriya Gaysinskaya, <b>Brendan F. Miller</b> , Godfried W. van der Heijden, Kasper D. Hansen,<br>Alex Bortvin   |
| 016  | • | The emergence of pan-cancer CIMP and its elusive interpretation   |
|      |   | 𝔗 Biomolecules. 2016 Nov; 6(4):45   |
|      |   | • Brendan F. Miller, Francisco Sanchez-Vega, Laura Elnitski   |
|      |   |   |

| 2014     | • | Repair of naturally occurring mispairs can induce mutations in flanking DNA   |
|----------|---|---|
|          |   | 𝔗 eLife 2014;3:e02001   |
|          |   | • Jia Chen, <b>Brendan F. Miller</b> , Anthony V. Furano  |
| 2012     | • | Structure-based Mutagenesis Reveals Critical Residues in the Transferrin Receptor<br>Participating in the Mechanism of pH-induced Release of Iron from Human Serum<br>Transferrin   |
|          |   | 🔗 Biochemistry. 2012 Feb; 51(10):2113-21  |
|          |   | • Ashley N. Steere, N. Dennis Chasteen, <b>Brendan F. Miller</b> , Valerie C. Smith, Ross T. A. MacGillivray, Anne B. Mason   |
| 2012     | • | Ionic Residues of Human Serum Transferrin that Affect Binding to the Transferrin<br>Receptor and Iron Release from the Complex  |
|          |   | 𝔗 Biochemistry. 2012 Dec; 51(2):686-94  |
|          |   | • Ashley N. Steere, <b>Brendan F. Miller</b> , Samantha E. Roberts, Shaina L. Byrne, N. Dennis<br>Chasteen, Valerie C. Smith, Ross T. A. MacGillivray, Anne B. Mason.   |
|          | G | SOFTWARE  |
| 2021     | • | STdeconvolve  |
|          |   |   |
|          |   | • Unsupervised machine learning approach to deconvolve multi-cellular pixel resolution<br>spatial transcriptomics datasets in order to recover the putative transcriptomic profiles of<br>cell-types and their proportional representation within spatially resolved pixels without<br>reliance on external single-cell transcriptomics references. |
| 2021     | • | MERINGUE  |
|          |   |   |
|          |   | • MERINGUE characterizes spatial gene expression heterogeneity in spatially resolved single-<br>cell transcriptomics data with non-uniform cellular densities.  |
| 2020     | • | EpiClass  |
|          |   | https://pypi.org/project/EpiClass/  |
|          |   | <ul> <li>Optimizing and predicting performance of DNA methylation biomarkers using sequence<br/>methylation density information.</li> </ul>   |
|          | 5 | SERVICE   |
| Current  | • | The Liquid Biopsies (LB) Scientific Interest Group (SIG)  |
| <br>2019 |   | Research Webinar Committee Co-Leader  |
| 2013     |   | • The aims of the Liquid Biopsies Interest Group are to: (1) foster scientific exchange; (2) communication of research (3); working towards establishing standard practices for circulating nucleic acids studies; (4) sharing and optimization of techniques.  |
| 2021     | • | Journal Reviewer - Nature Protocols   |
|          |   | Prioritization of cell-types responsive to biological perturbations in single-cell data with Augur. Nat Protoc 16, 3836-3873 (2021)   |
| 2019     | • | Journal Reviewer - Epigenomics  |
|          |   |   |