Daniel M. Jordan, Ph.D.

October 2022

CONTACT INFORMATION

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he, him, his Pronouns:

EDUCATION

Ph.D. in BIOPHYSICS, Harvard Graduate School of Arts and Sci-

ences, Cambridge, MA

Dissertation: "Predicting the Effects of Missense Variation on Protein Structure, Function, and Evolution" | Advisor: Prof. Shamil

R. Sunyaev

B.A. in Physics and Philosophy, Yale College, New Haven, CT

Degree awarded cum laude

APPOINTMENTS

Instructor in Genetics and Genomic Sciences at ICAHN SCHOOL OF 2020-Present

MEDICINE AT MOUNT SINAI, New York, NY

Charles Bronfman Institute for Personalized Medicine Icahn Institute of Data Science and Genomic Technology

Note: in fall 2022 my research output was affected by parental leave due to the birth of

my daughter.

Postdoctoral Fellow in Genetics and Genomic Sciences at ICAHN SCHOOL 2015-2020

> OF MEDICINE AT MOUNT SINAI, New York, NY Mentors: Prof. Eric E. Schadt and Dr. Ron Do

Charles Bronfman Institute for Personalized Medicine Icahn Institute of Data Science and Genomic Technology

Note: from 2017-2021 my research output was affected by becoming primary caretaker

to my temporarily disabled partner.

PUBLICATIONS AS LEAD OR SENIOR AUTHOR

For all publications, * indicates equal contribution from lead authors and \dagger indicates equal contribution from senior authors. CRediT roles describing my contribution are listed below each publication.

2022

D. J. Balick*, **D. M. Jordan***, S. R. Sunyaev[†], R. Do[†]. "Overcoming constraints on the detection of recessive selection in human genes from population frequency data." *Am. J. Hum. Genet.* **109**:33–49, doi:10.1016/j.ajhg.2021.12.001.

conceptualization, methodology, data curation, formal analysis, software, visualization, writing – initial draft, writing – review & editing

2021

B. O. Petrazzini, D. J. Balick, I. S. Forrest, J. Cho, G. Rocheleau, **D. M. Jordan**[†], R. Do[†]. "Prediction of recessive inheritance for missense variants in human disease." $medR\chi iv$ 2021.10.25.21265472, doi:10.1101/2021.10.25.21265472.

conceptualization, methodology, supervision, formal analysis, writing – original draft, writing – review & editing

H. M. T. Vy*, **D. M. Jordan***, D. J. Balick*, R. Do. "Probing the aggregated effects of purifying selection per individual on 1,380 medical phenotypes in the UK biobank." *PLOS Genet.* 17:e1009337, doi:10.1371/journal.pgen.1009337.

methodology, writing - original draft, writing - review & editing

A. T. Cohain*, W. T. Barrington*, **D. M. Jordan*** (co-first of 26), ..., J. L. M. Bjorkegren†, E. E. Schadt†. "An integrative multiomic network model links lipid metabolism to glucose regulation in coronary artery disease." *Nat. Commun.* 12:547, doi:10.1038/s41467-020-20750-8

conceptualization, methodology, formal analysis, visualization, writing - review & editing

2019

D. M. Jordan*, M. Verbanck*, R. Do. "HOPS: a quantitative score reveals pervasive horizontal pleiotropy in human genetic variation is driven by extreme polygenicity of human traits and diseases." *Genome Biol.* **20**:222, doi:10.1186/s13059-019-1844-7.

conceptualization, data curation, formal analysis, investigation, methodology, writing — original draft, writing — review & editing

C. A. Cassa*, D. Weghorn*, D. J. Balick*, **D. M. Jordan***, D. Nusinow, K. E. Samocha, A. O'Donnell-Luria, D. G. MacArthur, M. J. Daly, D. R. Beier[†], S. R. Sunyaev[†]. "Reply to 'Selective effects of heterozygous protein-truncating variants." *Nat. Genet.* **51**:3–4, doi:10.1038/s41588-018-0301-y.

formal analysis

D. M. Jordan*, H. K. Choi*, M. Verbanck*, R. Topless, H.-H. Wong, G. Nadkarni, T. R. Merriman, R. Do. "No causal effects of serum urate levels on the risk of chronic kidney disease: a Mendelian randomization study." *PLOS Med.* 16:e1002725, doi:10.1371/journal.pmed.1002725.

formal analysis, investigation, methodology, writing – original draft, writing – review & editing

2018

D. M. Jordan, R. Do. "Using full genomic information to predict disease: breaking down the barriers between complex and Mendelian disease." *Annu. Rev. Genom. Hum. Genet.* **19**:289–301, doi:10.1146/annurevgenom-083117-021136.

formal analysis, visualization, writing - original draft

C. A. Cassa*, D. Weghorn*, D. J. Balick*, **D. M. Jordan***, D. Nusinow, K. E. Samocha, A. O'Donnell Luria, D. G. MacArthur, M. J. Daly, D. R. Beier[†], S. R. Sunyaev[†]. "Estimating the selective effect of heterozygousprotein truncating variants from human exome data." *Nat. Genet.* **49**:806–810, doi:10.1038/ng.3831.

conceptualization, formal analysis, writing - review & editing

D. M. Jordan*, S. Frangakis*, C. Golzio, C. Cassa, J. Kurtzberg, Task Force for Neonatal Genomics, E. E. Davis, S. R. Sunyaev[†], N. Katsanis[†]. "Identification of *cis*-suppression of human disease mutations by comparative genomics." *Nature* **524**:225–9, doi:10.1038/nature14497.

conceptualization, formal analysis, investigation, methodology, software, writing - original draft, writing - review & editing

D. M. Jordan*, A. Kiezun*, S. M. Baxter*, V. Agarwala, R. C. Green, M. F. Murray, T. Pugh, M. S. Lebo, H. L. Rehm, B. H. Funke, S. R. Sunyaev. "Development and validation of a computational method for assessment of missense variants in hypertrophic cardiomyopathy." *Am. J. Hum. Genet.* 18:183–92, doi:10.1016/j.ajhg.2011.01.011.

conceptualization, data curation, formal analysis, investigation, methodology, software, writing — original draft, writing — review & editing

D. M. Jordan, V. E. Ramensky, S. R. Sunyaev. "Human allelic variation: perspective from protein function, structure, and evolution." *Curr. Opin. Struct. Biol.* 20:591–7, doi:10.1016/j.sbi.2010.03.006. writing – original draft

D. M. Jordan, K. M. Mills, I. Andricioaei, A. Bhattacharya, K. Palmo, E. R. P. Zuiderweg. "Parameterization of peptide ¹³C carbonyl chemical shielding anisotropy in Molecular Dynamics simulations." *ChemPhysChem* 8:1375–85, doi:10.1002/cphc.200700003.

formal analysis, investigation, methodology, software

OTHER PUBLICATIONS

For all publications, * indicates equal contribution from lead authors and † indicates equal contribution from senior authors. CRediT roles describing my contribution are listed below each publication.

2022 G. Rocheleau, I. S. Forrest, Á. Duffy, S. Bafna, A. Dobbyn, M. Verbanck, H.-H. Won, D. M. Jordan, R. Do. "A tissue-level phenome-wide network map of colocalized genes and phenotypes in the UK Biobank." Commun. Biol. 5, 849, doi:10.1038/s42003-022-03820-z.

I. S. Forrest, K. Chaudhary, H. M. T. Vy, S. Bafna, D. M. Jordan, G. Rocheleau, R. J. F. Loos, J. H. Cho, R. Do. "Population-Based Penetrance of Deleterious Clinical Variants." *JAMA* **327**:350–359, doi:10.1001/jama.2021.23686.

methodology, writing - review & editing

J. K. Park, S. Bafna, I. S. Forrest, Á. Duffy, C. Marquez-Luna, B. O. Petrazzini, H. M. Vy, D. M. Jordan, M. Verbanck, J. Narula, R. S. Rosenson, G. Rocheleau, R. Do. "Phenome-wide Mendelian randomization study of plasma triglycerides and 2,600 disease traits." medRxiv 2022.07.21.22277900, doi:10.1101/2022.07.21.22277900.

methodology, writing - review & editing

G. Butler-Laporte, G. Povysil, J. Kosmicki, ..., D. Jordan (19th of 143), ..., J. B. Richards. "Exome-wide association study to identify rare variants influencing COVID-19 outcomes: Results from the Host Genetics Initiative." PLoS Genet. in press, preprint available: $medR\chi iv$ 2022.03.28.22273040, doi:10.1101/2022.03.28.22273040.

data curation, software

2021 A. N. Barbeira*, R. Bonazzola*, E. R. Gamazon*, Y. Liang*, Y.-S. Park*, ..., D. M. Jordan (18th of 30), ..., H. K. Im. "Exploiting the GTEx resources to decipher the mechanisms at GWAS loci." Genome Biol. 22:49, doi:10.1186/s13059-020-02252-4.

formal analysis, methodology

A. Schoech, D. Jordan, P.-R. Loh, S. Gazal, L. O'Connor, D. J. Balick, 2019 P. F. Palamara, H. Finucane, S. R. Sunyaev, A. Price. "Quantification of frequency-dependent genetic architectures and action of negative selection in 25 UK Biobank traits." Nat. Commun. 10:790, doi:10.1038/s41467-019-08424-6.

formal analysis, investigation

C. A. Cassa, D. M. Jordan, I. Adzhubei, S. Sunyaev. "A literature review 2018 at genome scale: improving clinical variant assessment." Genet. Med. 20:936-941, doi:10.1038/gim.2017.230.

conceptualization, formal analysis, investigation

C. A. Cassa, S. Akle, D. M. Jordan, J. A. Rosenfeld. "When 'N of 2' is not enough: Integrating functional validation data in rare disease gene discovery." Cold Spring Harb. Mol. Case Stud. 3:a001099, doi:10.1101/mcs.a001099.

software

T. L. Lenz, V. Spirin, D. M. Jordan, S. R. Sunyaev. "Excess of deleterious 2016 mutations around HLA genes reveals evolutionary cost of balancing selection." Mol. Biol. Evol. 33:2555-2564, doi:10.1093/molbev/msw127. formal analysis

H.-H. Won, P. Natarajan, A. Dobbyn, **D. M. Jordan**, P. Roussos, K. Lage, S. Raychaudhuri, E. Stahl[†], R. Do[†]. "Disproportionate contributions of select genomic compartments and cell types to genetic risk for coronary artery disease." *PLOS Genet.* 11:e1005622, doi:10.1371/journal.pgen.1005622.

writing - review & editing

S. Akle, S. Chun, **D. M. Jordan**, C. A. Cassa. "Mitigating false-positive associations in rare disease gene discovery." *Hum. Mutat.* **36**:998–1003, doi:10.1002/humu.22847.

software

N. Sahni*, S. Yi*, M. Taipale*, J. I. Fuxman Bass*, J. Coulombe-Huntington*, ..., **D. M. Jordan** (27th of 48), ..., F. P. Roth[†], Y. Xia[†], A. J. M. Walhout[†], S. Lindquist[†], M. Vidal[†]. "Widespread macromolecular interaction perturbations in human genetic disorders." *Cell* **161**:647–60, doi:10.1016/j.cell.2015.04.013.

formal analysis, methodology

1. Seim*, X. Fang*, Z. Xiong, ..., **D. Jordan** (15th of 29), ..., V. N. Gladyshev. "Genome analysis reveals insights into physiology and longevity of the Brandt's bat *Myotis brandtii*." *Nat. Commun.* 4:2212, doi:10.1038/ncomms3212.

formal analysis

C. A. Cassa, M. Y. Tong, **D. M. Jordan**. "Large numbers of genetic variants considered to be pathogenic are common in asymptomatic individuals." *Hum. Mutat.* **9**:1216–20, doi:10.1002/humu.22375.

formal analysis, investigation, methodology, visualization

I. A. Adzhubei, **D. M. Jordan**, S. R. Sunyaev. "Predicting functional effect of human missense mutations using PolyPhen-2." *Curr. Prot. Hum. Genet.* **7.20**, doi:10.1002/0471142905.hg0720s76.

writing - review and editing

2012 J. A

J. A. Tennessen*, A. W. Bigham*, T. D. O'Connor*, ..., **D. Jordan** (12th of 25), ..., J. M. Akey, Broad GO, Seattle GO, on behalf of the NHLBI Exome Sequencing Project. "Evolution and functional impact of rare coding variation from deep sequencing of human exomes." *Science* 337:64–9, doi:10.1126/science.1219240.

formal analysis, investigation, methodology, visualization

GRANTS AND AWARDS

- 2018 Conference Registration Award, Society for Molecular Biology and Evolution (SMBE)
- 2017 Reviewer's Choice Poster Award, American Society for Human Genetics (ASHG)
- Trainee on T32 Institutional Postdoctoral Training Grant, "Training program in molecular and cellular cardiology" (HL007824, PIs: Profs. Bruce D. Gelb and Roger J. Hajjar), NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)
 - 2015 Young Investigator Travel Award, SMBE
 - Semifinalist for Charles J. Epstein Trainee Award for Excellence in Human Genetics Research, ASHGGraduate Student Travel Award, SMBE

- 2011 Semifinalist for Human Genetics Trainee Research Award for abstract submission to the 12th International Congress of Human Genetics, ASHG
- 2008-2010 Trainee on T32 Institutional Predoctoral Training Grant, "Molecular biophysics training grant" (GM008313, PI: Prof. James M. Hogle), NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

CONF

ference Presentations and Posters	
2022	"Prediction of recessive inheritance for missense variants in human disease." Presentation at American Society of Human Genetics (ASHG) 32ND ANNUAL MEETING, Los Angeles, CA, October 25–29, 2022.
2019	"Measuring recessive selection using summary statistics of the site frequency spectrum." Poster at American Society of Human Genetics (ASHG) 29TH ANNUAL MEETING, Houston, TX, October 15–19, 2019.
2018	"Detection of pervasive horizontal pleiotropy in highly polygenic human traits." Poster at Society for Molecular Biology and Evolution (SMBE) 2019, Manchester, England, UK, July 21-25, 2019. "The landscape of pervasive horizontal pleiotropy is driven by extreme
20.0	polygenicity of human traits and diseases." Poster at American Society of Human Genetics (ASHG) 28th annual meeting, San Diego, CA, October 16–20, 2018.
	"Recent human demographic history confounds population genetic inference of recessive selection." Poster at Society for Molecular Biology and Evolution (SMBE) 2018, Yokohama, Japan, July 8–12, 2018. (Recipient of Registration Award)
2017	"Pervasive pleiotropy in the human genome revealed by a novel quantitative analysis of summary association statistics." Poster at ASHG 67TH ANNUAL MEETING, Orlando, FL, October 17–21, 2017. (Recipient of Reviewer's Choice Poster Award)
	"Using population genetics data to predict recessive human genes." Presentation at Gordon Research Conference (GRC) on Human Genetics and Genomics, Stowe, VT, July 9–14, 2017.
	"Successive gene duplications drive enrichment of dominance in ortholog models over evolutionary time." Poster at SMBE 2017, Austin, TX, July 2–6, 2017.
2016	"Detection of recessive selection identifies non-additive components of complex disease." Poster at ASHG 66TH ANNUAL MEETING, Vancouver, BC, Canada, October 17–22, 2016.
	"Recessive selection in complex disease and implications for variant discovery." Presentation at SMBE 2016, Gold Coast, QLD, Australia, July 3-7, 2016.
2015	"Parametric estimation of evolutionary constraint using amino acid sequences." Presentation at SMBE 2015, Vienna, Austria, July 12-16, 2015. (Recipient of Young Investigator Travel Award)
2014	"Bioinformatic prediction and <i>in vivo</i> validation of residue-residue interactions in human proteins." Presentation at AMERICAN PHYSICAL SOCIETY (APS) MARCH MEETING 2014, Denver, CO, March 3-7, 2014.
2013	"Computational prediction and <i>in vivo</i> validation of suppressors of human disease mutations." Presentation at ASHG 63RD ANNUAL MEETING, Boston, MA, October 22–26, 2013. (Semifinalist for Charles J. Epstein Award for Excellence in Human Genetics Research)
	"Computational prediction and <i>in vivo</i> validation of context dependencies in human disease mutations." Presentation at SMBE 2013,

Chicago, IL, July 7–11, 2013. (Recipient of Graduate Student Travel Award)

- 2012 "Evaluating epistatic models of protein evolution based on comparative genomics data." **Poster** at SMBE 2012, Dublin, Ireland, June 23–26 2012.
- "Compensatory amino acid changes as a signal of human disease."

 Poster at 12TH INTERNATIONAL CONGRESS OF HUMAN GENETICS (ICHG),
 Montreal, QC, Canada, October 11–15, 2011. (Semifinalist for ASHG 2011
 Trainee Research Award)
- "A computational approach to predict the pathogenic effect of missense mutations in genetic diagnostics of hypertrophic cardiomyopathy (HCM)." Poster at ASHG 59TH ANNUAL MEETING, Honolulu, HI, October 20–24 2009.
- 2007 "Parameterization of peptide ¹³C carbonyl chemical shielding anisotropy in Molecular Dynamics simulations." **Poster** at 48TH EXPERIMENTAL NUCLEAR MAGNETIC RESONANCE CONFERENCE, Daytona Beach, FL, April 22–8 2007.

TEACHING EXPERIENCE

FALL 2014 | Guest Instructor for 1.264: DATABASE, INTERNET, AND SYSTEM INTEGRA-TION TECHNOLOGIES

Taught by Dr. Christopher Cassa at MIT

Course for graduate students in engineering at MIT. Wrote lectures and homework assignments for a unit on data visualization and machine learning using Python's Orange framework.

FALL 2010 Teaching Fellow for MCB 293: PHYSICAL, CHEMICAL, AND MOLECULAR BIOLOGY

Taught by Asst. Profs. Andres Leschziner and Victoria D'Souza at Harvard Faculty of Arts and Sciences

Course for graduate students in Harvard's Molecular and Cellular Biology Ph.D. program, covering topics in biochemistry and biophysics, including biological imaging, protein structure and folding, thermodynamics, and enzyme kinetics.

SPRING 2010

Teaching Fellow for MCB 111: MATHEMATICS IN BIOLOGY
Taught by Asst. Prof. Sharad Ramanathan at Harvard Faculty of Arts and
Sciences

Course for graduate students in Harvard's Molecular and Cellular Biology Ph.D. program and advanced undergraduates, covering topics in linear algebra, probability, and dynamical systems.

RESEARCH EXPERIENCE

2020-Present

Instructor at Icahn School of Medicine at Mount Sinai, New York, NY

Laboratories of Prof. Eric E. Schadt and Dr. Ron Do, Charles Bronfman Institute for Personalized Medicine, Icahn Institute of Data Science and Genomic Technology, Department of Genetics and Genomic Sciences

Leading various research projects in systems biology and complex trait genetics, including projects on predicting specific phenotypic effects of variants from electronic health record data and and analyzing the effects of host genetics on COVID-19 disease progression; mentoring and assisting in research projects of students and postdocs.

2015-2020

Postdoctoral Researcher at Icahn School of Medicine at Mount Sinai, New York, NY

Laboratories of Prof. Eric E. Schadt and Dr. Ron Do, Charles Bronfman Institute for Personalized Medicine, Icahn Institute of Data Science and Genomic Technology, Department of Genetics and Genomic Sciences

Leading various research projects in systems biology and complex trait genetics, including projects related to causal inference of risk factors in complex disease, investigation of evolutionary dynamics in network models of systems biology, and detection of protective alleles in human patients.

2010-2015

Ph.D. Candidate at Brigham and Women's Hospital, Boston, MA Laboratory of Prof. Shamil R. Sunyaev, Division of Genetics, Department of Medicine

Researched theoretical and technical advances in PolyPhen, a computational tool to predict the phenotypic effect of variation in proteins, including the development of a detailed model of epistasis and the development of a parametric tree-based model of evolution.

2009-2010

Rotation Student at Harvard Medical School, Boston, MA Laboratory of Prof. Gerhard Wagner, Department of Biological Chemistry and Molecular Pharmacology

Conducted a fractional factorial screen of refolding conditions for the extracellular domains of CD45 in order to produce an NMR structure, with the goal of creating a generally applicable protocol for refolding extracellular protein domains.

2009

Rotation Student at Brigham and Women's Hospital, Boston, MA Laboratory of Prof. Shamil R. Sunyaev, Division of Genetics, Department of Medicine

Developed an accurate and clinically useful computational tool to predict the phenotypic effect of mutations in genes associated with hypertrophic cardiomyopathy (HCM).

2006-2008

Software Developer at STRIATUS, INC., Dexter, MI

Developed data analysis and visualization tools to support sophisticated laboratory automation systems used to conduct combinatorial screens of biofuel synthesis processes.

2005-2007

Research Assistant at UNIVERSITY OF MICHIGAN, Ann Arbor, MI Laboratory of Prof. Erik R. P. Zuiderweg, Biophysics Research Division, Department of Biological Chemistry

Developed an algorithm for predicting magnetic properties of model proteins, enabling simulation of nuclear magnetic resonance (NMR) spectroscopy at timescales faster than current experimental NMR can measure.

2004

Summer Student at University of Michigan Medical School, Ann Arbor MI

Laboratory of Prof. Robert A. Koeppe, Department of Radiology

Compared and analyzed computational image analysis methods for Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) scans of human brains, including methods for mapping images of individual brains onto standard brain atlases.

2003 Summer Student at University of Michigan School of Public Health, Ann Arbor, MI

Laboratory of Prof. Martin A. Philbert, Department of Toxicology

Developed and tested nanoprobes ("PEBBLEs") for in vivo imaging of calcium ion concentrations in cultured mammalian cells.

PROFESSIONAL SERVICE AND LEADERSHIP

Abstract reviewer for American Society of Human Genetics 2020 (ASHG) 30th annual meeting, San Diego, CA, October 27-31, 2020.

Judge for American Society of Human Genetics (ASHG) DNA Day

2017-present Essay Competition.

> Mentor for Undergraduate Award Recipient at Society for Molec-2016 ular Biology and Evolution (SMBE) 2016, Gold Coast, QLD, Australia, July 3-7, 2016.

Ad hoc peer reviewer for journals Nature Communications, eLife, 2011-present

American Journal of Human Genetics, Nucleic Acids Research, Communications Biology, Scientific Reports, Genome Biology and Evolution, Journal of the American Society of Nephrology, PLOS Genetics, PLOS Computational Biology, PLOS ONE, Genome Biology, Bioinfor-

matics, BMC Medical Genomics.

HOBBIES AND INTERESTS

I am an avid classical musician, with training in piano and viola. I frequently perform in amateur and semi-professional orchestras, chamber ensembles, and choirs. In addition to classical music, I play folk/pop piano and guitar and write songs. My current long-term project is an adaptation of Wagner's ring cycle into a series of folk/pop style songs. I am also a homebrewer and beer enthusiast, as well as an épée fencer.