

Stanford



Jonathan Pritchard

Professor of Genetics and of Biology

Bio

BIO

Jonathan Pritchard grew up in England before moving to Pennsylvania during high school. He received his BSc in Biology and Mathematics from Penn State University in 1994, and his PhD in Biology at Stanford in 1998. After that he moved to a postdoc in the Department of Statistics at Oxford University and then to his first faculty job at the University of Chicago in 2001. He has been an Investigator of the Howard Hughes Medical Institute since 2008. Pritchard returned to Stanford University in 2013, where he is now a Professor in the Departments of Biology and Genetics.

ACADEMIC APPOINTMENTS

- Professor, Genetics
- Professor, Biology
- Member, Bio-X

ADMINISTRATIVE APPOINTMENTS

- Investigator, Howard Hughes Medical Institute, (2008- present)
- Co-Director, Stanford's Center for Computational, Evolutionary and Human Genomics, (2017- present)

LINKS

- Lab web site: <http://pritchardlab.stanford.edu>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My group has expertise in the development of new statistical methods for genetic analysis and in their application to genomic data from humans and other organisms. We focus on questions relating to genetic variation and evolution: How does genetic variation impact phenotypic traits and evolution, both at the organismal and cellular level? What can we learn from genome sequences of modern and ancient humans about the relationships among human populations, and the the nature of adaptation in these populations?

We often work on problems where there are no off-the-shelf statistical methods. Thus, an important part of our work is in developing appropriate statistical and computational approaches that can yield new insights into biological data. In the past, we have made important contributions to a variety of problems in human population genetics, including methods for complex trait mapping, inference of population structure and history, and studies of natural selection. We have a strong track record of producing user-friendly resources that are widely used in the community, and in applied data analysis to tackle important biological questions. Notably, our Structure algorithm and software package for inferring population structure from genetic data have received >30,000 total citations spread across several papers.

Since 2008 an important emphasis of my group has focused on understanding gene regulation, and in particular how genetic variation may impact regulation.

Ultimately, we would like to be able to predict which noncoding variants in the genome are likely to have regulatory effects in any given cell type, and how these link to phenotypic variation and disease. My lab has been deeply involved in developing new computational methods to interpret various types of modern genomic assays and in linking these to genetic variation.

Secondly, we have had a major focus on understanding the genetic architecture of complex traits, and the implications for understanding evolution. We have argued that much--if not most--evolution in humans likely proceeds through a process that we call "polygenic adaptation" in which populations evolve through small allele frequency shifts at many loci.

We have also written extensively about conceptual models for understanding the genetic architecture of trait variation (Boyle et al, 2017). We have argued that the data are consistent with a model in which essentially every regulatory variant in disease-relevant cell types can affect risk, and proposed that most of these effects act through trans-regulatory networks. Testing this model is an ongoing focus of our work.

Teaching

COURSES

2019-20

- Advanced Genetics: GENE 205 (Win)
- Genomic approaches to the study of human disease: BIO 247, GENE 247 (Win)

2018-19

- Advanced Genetics: GENE 205 (Win)
- Genomic approaches to the study of human disease: BIO 247, GENE 247 (Aut)

2017-18

- Advanced Genetics: GENE 205 (Win)

2016-17

- Advanced Genetics: GENE 205 (Win)
- Statistical and Machine Learning Methods for Genomics: BIO 268, BIOMEDIN 245, CS 373, GENE 245, STATS 345 (Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Rachel Agolia, Daniel Cotter, Emily Ebel, Nicole Ferraro, Pablo Eduardo Garcia Nieto, Alissa Severson, Craig Smail, Theo Susanto, Adele Xu, Siming Zhang

Orals Chair

Stephen Bates

Postdoctoral Faculty Sponsor

Jake Freimer, Hakhamanesh Mostafavi, Shaila Musharoff, Yuval Simons, Jeff Spence, Clemens Weiss

Doctoral Dissertation Advisor (AC)

Matthew Aguirre, Margaret Antonio, Alyssa Lyn Fortier, Roshni Patel, Nasa Sinnott-Armstrong, Courtney Smith

Doctoral (Program)

Alyssa Lyn Fortier

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biology (School of Humanities and Sciences) (Phd Program)
- Biomedical Informatics (Phd Program)
- Genetics (Phd Program)

Publications

PUBLICATIONS

- **Landscape of stimulation-responsive chromatin across diverse human immune cells.** *Nature genetics*
Calderon, D., Nguyen, M. L., Mezger, A., Kathiria, A., Muller, F., Nguyen, V., Lescano, N., Wu, B., Trombetta, J., Ribado, J. V., Knowles, D. A., Gao, Z., Blaeschke, et al
2019
- **Public Discussion Affects Question Asking at Academic Conferences.** *American journal of human genetics*
Telis, N., Glassberg, E. C., Pritchard, J. K., Gunter, C.
2019
- **Trans Effects on Gene Expression Can Drive Omnigenic Inheritance.** *Cell*
Liu, X., Li, Y. I., Pritchard, J. K.
2019; 177 (4): 1022
- **Reduced signal for polygenic adaptation of height in UK Biobank** *ELIFE*
Berg, J. J., Harpak, A., Sinnott-Armstrong, N., Joergensen, A., Mostafavi, H., Field, Y., Boyle, E., Zhang, X., Racimo, F., Pritchard, J. K., Coop, G.
2019; 8
- **Interpreting polygenic scores, polygenic adaptation, and human phenotypic differences.** *Evolution, medicine, and public health*
Rosenberg, N. A., Edge, M. D., Pritchard, J. K., Feldman, M. W.
2019; 2019 (1): 26–34
- **High-resolution mapping of cancer cell networks using co-functional interactions.** *Molecular systems biology*
Boyle, E. A., Pritchard, J. K., Greenleaf, W. J.
2018; 14 (12): e8594
- **Evidence for Weak Selective Constraint on Human Gene Expression.** *Genetics*
Glassberg, E. C., Gao, Z., Harpak, A., Lan, X., Pritchard, J. K.
2018
- **Functional Genetic Variants Revealed by Massively Parallel Precise Genome Editing.** *Cell*
Sharon, E., Chen, S. A., Khosla, N. M., Smith, J. D., Pritchard, J. K., Fraser, H. B.
2018
- **Post-translational buffering leads to convergent protein expression levels between primates** *GENOME BIOLOGY*
Wang, S. H., Hsiao, C., Khan, Z., Pritchard, J. K.
2018; 19: 83
- **Determining the genetic basis of anthracycline-cardiotoxicity by response QTL mapping in induced cardiomyocytes.** *eLife*
Knowles, D. A., Burrows, C. K., Blischak, J. D., Patterson, K. M., Serie, D. J., Norton, N., Ober, C., Pritchard, J. K., Gilad, Y.
2018; 7
- **Remodeling the Specificity of an Endosomal CORVET Tether Underlies Formation of Regulated Secretory Vesicles in the Ciliate Tetrahymena thermophila** *CURRENT BIOLOGY*
Sparvoli, D., Richardson, E., Osakada, H., Lan, X., Iwamoto, M., Bowman, G. R., Kontur, C., Bourland, W. A., Lynn, D. H., Pritchard, J. K., Haraguchi, T., Dacks, J. B., Turkewitz, et al
2018; 28 (5): 697-+
- **Impact of regulatory variation across human iPSCs and differentiated cells** *GENOME RESEARCH*

- Banovich, N. E., Li, Y. I., Raj, A., Ward, M. C., Greenside, P., Calderon, D., Tung, P., Burnett, J. E., Myrthil, M., Thomas, S. M., Burrows, C. K., Romero, I., Pavlovic, et al
2018; 28 (1): 122–31
- **Annotation-free quantification of RNA splicing using LeafCutter** *NATURE GENETICS*
Li, Y. I., Knowles, D. A., Humphrey, J., Barbeira, A. N., Dickinson, S. P., Im, H., Pritchard, J. K.
2018; 50 (1): 151–+
 - **Large-Scale Clonal Analysis Resolves Aging of the Mouse Hematopoietic Stem Cell Compartment.** *Cell stem cell*
Yamamoto, R., Wilkinson, A. C., Oechara, J., Lan, X., Lai, C. Y., Nakauchi, Y., Pritchard, J. K., Nakauchi, H.
2018; 22 (4): 600–607.e4
 - **Frequent nonallelic gene conversion on the human lineage and its effect on the divergence of gene duplicates** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Harpak, A., Lan, X., Gao, Z., Pritchard, J. K.
2017; 114 (48): 12779–84
 - **Inferring Relevant Cell Types for Complex Traits by Using Single-Cell Gene Expression** *AMERICAN JOURNAL OF HUMAN GENETICS*
Calderon, D., Bhaskar, A., Knowles, D. A., Golan, D., Raj, T., Fu, A. Q., Pritchard, J. K.
2017; 101 (5): 686–99
 - **Quantification of transplant-derived circulating cell-free DNA in absence of a donor genotype** *PLOS COMPUTATIONAL BIOLOGY*
Sharon, E., Shi, H., Kharbanda, S., Koh, W., Martin, L. R., Khush, K. K., Valantine, H., Pritchard, J. K., De Vlaminck, I.
2017; 13 (8): e1005629
 - **An Expanded View of Complex Traits: From Polygenic to Omnigenic** *CELL*
Boyle, E. A., Li, Y. I., Pritchard, J. K.
2017; 169 (7): 1177–86
 - **Rapid evolution of the human mutation spectrum** *ELIFE*
Harris, K., Pritchard, J. K.
2017; 6
 - **Tracing the peopling of the world through genomics.** *Nature*
Nielsen, R., Akey, J. M., Jakobsson, M., Pritchard, J. K., Tishkoff, S., Willerslev, E.
2017; 541 (7637): 302-310
 - **Batch effects and the effective design of single-cell gene expression studies** *SCIENTIFIC REPORTS*
Tung, P., Blischak, J. D., Hsiao, C. J., Knowles, D. A., Burnett, J. E., Pritchard, J. K., Gilad, Y.
2017; 7
 - **Mutation Rate Variation is a Primary Determinant of the Distribution of Allele Frequencies in Humans** *PLOS GENETICS*
Harpak, A., Bhaskar, A., Pritchard, J. K.
2016; 12 (12)
 - **A Bibliometric History of the Journal GENETICS** *GENETICS*
Telis, N., Lehmann, B. V., Feldman, M. W., Pritchard, J. K.
2016; 204 (4): 1337-1342
 - **Detection of human adaptation during the past 2000 years.** *Science*
Field, Y., Boyle, E. A., Telis, N., Gao, Z., Gaulton, K. J., Golan, D., Yengo, L., Rocheleau, G., Froguel, P., McCarthy, M. I., Pritchard, J. K.
2016
 - **Lineage-specific and single-cell chromatin accessibility charts human hematopoiesis and leukemia evolution.** *Nature genetics*
Corces, M. R., Buenrostro, J. D., Wu, B., Greenside, P. G., Chan, S. M., Koenig, J. L., Snyder, M. P., Pritchard, J. K., Kundaje, A., Greenleaf, W. J., Majeti, R., Chang, H. Y.
2016; 48 (10): 1193-1203
 - **Genetic variation in MHC proteins is associated with T cell receptor expression biases.** *Nature genetics*
Sharon, E., Sibener, L. V., Battle, A., Fraser, H. B., Garcia, K. C., Pritchard, J. K.
2016; 48 (9): 995-1002

- **Genome-wide association study of behavioral, physiological and gene expression traits in outbred CFW mice.** *Nature genetics*
Parker, C. C., Gopalakrishnan, S., Carbonetto, P., Gonzales, N. M., Leung, E., Park, Y. J., Aryee, E., Davis, J., Blizard, D. A., Ackert-Bicknell, C. L., Lionikas, A., Pritchard, J. K., Palmer, et al
2016; 48 (8): 919-926
- **Thousands of novel translated open reading frames in humans inferred by ribosome footprint profiling.** *eLife*
Raj, A., Wang, S. H., Shim, H., Harpak, A., Li, Y. I., Engelmann, B., Stephens, M., Gilad, Y., Pritchard, J. K.
2016; 5
- **Coregulation of tandem duplicate genes slows evolution of subfunctionalization in mammals** *SCIENCE*
Lan, X., Pritchard, J. K.
2016; 352 (6288): 1009-1013
- **RNA splicing is a primary link between genetic variation and disease** *SCIENCE*
Li, Y. I., van de Geijn, B., Raj, A., Knowles, D. A., Petti, A. A., Golan, D., Gilad, Y., Pritchard, J. K.
2016; 352 (6285): 600-604
- **Genetic Variation, Not Cell Type of Origin, Underlies the Majority of Identifiable Regulatory Differences in iPSCs.** *PLoS genetics*
Burrows, C. K., Banovich, N. E., Pavlovic, B. J., Patterson, K., Gallego Romero, I., Pritchard, J. K., Gilad, Y.
2016; 12 (1)
- **Abundant contribution of short tandem repeats to gene expression variation in humans.** *Nature genetics*
Gymrek, M., Willems, T., Guilmatre, A., Zeng, H., Markus, B., Georgiev, S., Daly, M. J., Price, A. L., Pritchard, J. K., Sharp, A. J., Erlich, Y.
2016; 48 (1): 22–29
- **Genetic Variation, Not Cell Type of Origin, Underlies the Majority of Identifiable Regulatory Differences in iPSCs** *PLOS GENETICS*
Burrows, C. K., Banovich, N. E., Pavlovic, B. J., Patterson, K., Romero, I. G., Pritchard, J. K., Gilad, Y.
2016; 12 (1)
- **Abundant contribution of short tandem repeats to gene expression variation in humans** *NATURE GENETICS*
Gymrek, M., Willems, T., Guilmatre, A., Zeng, H., Markus, B., Georgiev, S., Daly, M. J., Price, A. L., Pritchard, J. K., Sharp, A. J., Erlich, Y.
2016; 48 (1): 22-?
- **Whole Genome Sequencing Identifies a Novel Factor Required for Secretory Granule Maturation in Tetrahymena thermophila.** *G3 (Bethesda, Md.)*
Kontur, C., Kumar, S., Lan, X., Pritchard, J. K., Turkewitz, A. P.
2016; 6 (8): 2505-2516
- **WASP: allele-specific software for robust molecular quantitative trait locus discovery** *NATURE METHODS*
van de Geijn, B., McVicker, G., Gila, Y., Pritchard, J. K.
2015; 12 (11): 1061-1063
- **Genetic Control of Chromatin States in Humans Involves Local and Distal Chromosomal Interactions** *CELL*
Grubert, F., Zaugg, J. B., Kasowski, M., Ursu, O., Spacek, D. V., Martin, A. R., Greenside, P., Srivas, R., Phanstiel, D. H., Pekowska, A., Heidari, N., Euskirchen, G., Huber, et al
2015; 162 (5): 1051-1065
- **Genetic Control of Chromatin States in Humans Involves Local and Distal Chromosomal Interactions.** *Cell*
Grubert, F., Zaugg, J. B., Kasowski, M., Ursu, O., Spacek, D. V., Martin, A. R., Greenside, P., Srivas, R., Phanstiel, D. H., Pekowska, A., Heidari, N., Euskirchen, G., Huber, et al
2015; 162 (5): 1051-1065
- **The Genotype-Tissue Expression (GTEx) pilot analysis: Multitissue gene regulation in humans** *SCIENCE*
Ardlie, K. G., DeLuca, D. S., Segre, A. V., Sullivan, T. J., Young, T. R., Gelfand, E. T., Trowbridge, C. A., Maller, J. B., Tukiainen, T., Lek, M., Ward, L. D., Kheradpour, P., Iriarte, et al
2015; 348 (6235): 648-660
- **Reprogramming LCLs to iPSCs Results in Recovery of Donor-Specific Gene Expression Signature** *PLOS GENETICS*
Thomas, S. M., Kagan, C., Pavlovic, B. J., Burnett, J., Patterson, K., Pritchard, J. K., Gilad, Y.
2015; 11 (5)

- **Genomic variation. Impact of regulatory variation from RNA to protein.** *Science*
Battle, A., Khan, Z., Wang, S. H., Mitrano, A., Ford, M. J., Pritchard, J. K., Gilad, Y.
2015; 347 (6222): 664-667
- **Impact of regulatory variation from RNA to protein** *SCIENCE*
Battle, A., Khan, Z., Wang, S. H., Mitrano, A., Ford, M. J., Pritchard, J. K., Gilad, Y.
2015; 347 (6222): 664-667
- **The Genetic and Mechanistic Basis for Variation in Gene Regulation** *PLOS GENETICS*
Pai, A. A., Pritchard, J. K., Gilad, Y.
2015; 11 (1)
- **msCentipede: Modeling Heterogeneity across Genomic Sites and Replicates Improves Accuracy in the Inference of Transcription Factor Binding.** *PloS one*
Raj, A., Shim, H., Gilad, Y., Pritchard, J. K., Stephens, M.
2015; 10 (9)
- **msCentipede: Modeling Heterogeneity across Genomic Sites and Replicates Improves Accuracy in the Inference of Transcription Factor Binding.** *PloS one*
Raj, A., Shim, H., Gilad, Y., Pritchard, J. K., Stephens, M.
2015; 10 (9)
- **Methylation QTLs Are Associated with Coordinated Changes in Transcription Factor Binding, Histone Modifications, and Gene Expression Levels** *PLOS GENETICS*
Banovich, N. E., Lan, X., McVicker, G., van de Geijn, B., Degner, J. F., Blischak, J. D., Roux, J., Pritchard, J. K., Gilad, Y.
2014; 10 (9)
- **fastSTRUCTURE: Variational Inference of Population Structure in Large SNP Data Sets** *GENETICS*
Raj, A., Stephens, M., Pritchard, J. K.
2014; 197 (2): 573-U207
- **The deleterious mutation load is insensitive to recent population history.** *Nature genetics*
Simons, Y. B., Turchin, M. C., Pritchard, J. K., Sella, G.
2014; 46 (3): 220-224
- **The functional consequences of variation in transcription factor binding.** *PLoS genetics*
Cusanovich, D. A., Pavlovic, B., Pritchard, J. K., Gilad, Y.
2014; 10 (3)
- **The chromatin architectural proteins HMGD1 and H1 bind reciprocally and have opposite effects on chromatin structure and gene regulation** *BMC GENOMICS*
Nalabothula, N., McVicker, G., Maiorano, J., Martin, R., Pritchard, J. K., Fondufe-Mittendorf, Y. N.
2014; 15
- **The effect of freeze-thaw cycles on gene expression levels in lymphoblastoid cell lines.** *PloS one*
Çalışkan, M., Pritchard, J. K., Ober, C., Gilad, Y.
2014; 9 (9)
- **Archaic humans: Four makes a party.** *Nature*
Birney, E., Pritchard, J. K.
2014; 505 (7481): 32-34
- **fastSTRUCTURE: variational inference of population structure in large SNP data sets.** *Genetics*
Raj, A., Stephens, M., Pritchard, J. K.
2014; 197 (2): 573-89
- **Methylation QTLs are associated with coordinated changes in transcription factor binding, histone modifications, and gene expression levels.** *PLoS genetics*
Banovich, N. E., Lan, X., McVicker, G., van de Geijn, B., Degner, J. F., Blischak, J. D., Roux, J., Pritchard, J. K., Gilad, Y.
2014; 10 (9): e1004663

- **Epigenetic modifications are associated with inter-species gene expression variation in primates** *GENOME BIOLOGY*
Zhou, X., Cain, C. E., Myrthil, M., Lewellen, N., Michelini, K., Davenport, E. R., Stephens, M., Pritchard, J. K., Gilad, Y.
2014; 15 (12)
- **Primate Transcript and Protein Expression Levels Evolve Under Compensatory Selection Pressures** *SCIENCE*
Khan, Z., Ford, M. J., Cusanovich, D. A., Mitrano, A., Pritchard, J. K., Gilad, Y.
2013; 342 (6162): 1100-1104
- **Identification of Genetic Variants That Affect Histone Modifications in Human Cells** *SCIENCE*
McVicker, G., van de Geijn, B., Degner, J. F., Cain, C. E., Banovich, N. E., Raj, A., Lewellen, N., Myrthil, M., Gilad, Y., Pritchard, J. K.
2013; 342 (6159): 747-749