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CURRICULUM VITAE

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Employment History

2008–Present Investigator, Howard Hughes Medical Institute
2006–Present Professor,
2001–2005 Assistant Professor,
Department of Human Genetics
Committees on Genetics and Evolutionary Biology
The University of Chicago

1998–2001 Postdoctoral Fellow, advised by Peter Donnelly
Department of Statistics, University of Oxford

Education

1998 Ph.D., advised by Marcus Feldman
Biological Sciences, Stanford University

1994 B.Sc., Biology (genetics concentration) and Mathematics
Honors project advised by Stephen Schaeffer
Pennsylvania State University

Research Support¹

2008–present Investigator, Howard Hughes Medical Institute.
2008-2011 RO1 MH084703: “Analysis and interpretation of DNA sequence data in association studies”,
with 1 year full cost supplement added
2010-2012 RO1 MH090951: “Statistical analysis of gene expression quantitative trait loci (eQTL)”

Previous grants/fellowships:

2003-2008 RO1 HG002772: “Linkage Disequilibrium Methods for Complex Trait Mapping”
2004–2009 Packard Foundation Fellowship: “Population genetics of genomic rearrangements”
2004-2006 Sloan Foundation Fellowship
1999-2003 Burroughs-Wellcome Fund Hitchings-Elion Postdoc-Faculty Award
“Population structure and linkage disequilibrium in association mapping”

¹Only showing grants for which JKP is/was the PI

- 1998 NIH (NRSA) 3-year Postdoctoral Award (replaced by BWF award)
"The impact of population history on association mapping"
- 1998 NSF funding to spend three months at Isaac Newton Institute, Cambridge, UK
- 1997 NSF travel award to TriNational Workshop on Molecular Evolution, Munich
- 1995 Santa Fe Institute Complex Systems Summer School, fellowship
- 1994-1998 Howard Hughes Medical Institute Predoctoral Fellowship
- 1994 NSF Predoctoral Fellowship (declined)
- 1989-1993 Penn State Braddock Scholarship (four-year full-tuition award)
- 1989-1993 Penn State Academic Excellence Scholarship

Awards and honors

- 2008 Selected as an investigator of the Howard Hughes Medical Institute
- 2008 Featured in Discover Magazine: "20 Best Brains Under 40" (Dec 2008 issue)
- 2007 "Best postdoc talk (basic research)" to my postdoc Graham Coop at Am. Soc. Hum. Genet. mtg.
- 2006 "Best Ph.D thesis award" to my student Ben Voight (for U of C Biological Sciences Division)
- 2006 New York Times front page news article on Voight et al paper on selection
- 2004 Selected Packard Fellow (see also Grants)
- 2004 Selected Alfred P. Sloan Fellow (see also Grants)
- 2003 Lancet's "Paper of the Year" (for any biomedical journal) was awarded to the paper of Rosenberg, Pritchard et al. (Science 2002) on human population structure (editorial in Lancet 362:2101-2103).
- 2002 Mitchell Prize from the American Statistical Association and the International Society of Bayesian Analysis, presented annually for "an outstanding paper describing how a Bayesian analysis has solved an important applied problem." Awarded for the *Genetics* paper of Pritchard et al (2000) on population structure.
- 1994 McCoy Award, given to the Penn State Outstanding Scholar-Athlete
- 1992 Stecker Award, given to a Penn State undergraduate in Mathematics

Selected Professional Activities

- 2001–present Teaching at University of Chicago: ~15-30 lecture hours per year: *Human Variation and Disease* (grad); *Simulation and Modeling of Evolutionary Processes* (grad/undergrad); *First Year Advanced Biology* (undergrad, starting 2012); small contributions to other classes.
- 2007–present Instructor at Conservation Genetics Workshop, Flathead Lake MT (biennial)
- 2001–present Member of various U of C internal committees (e.g., graduate admissions, graduate curriculum committee, many student thesis committees, BSD Cmte on Academic Promotions, various search committees, University Board of Academic Computing)
- 2001–present Reviewer for NIH, NSF, HHMI, Wellcome Trust, etc (on an *ad hoc* basis)
- 2006–present External referee for numerous promotion/tenure cases
- 1998–present Reviewer for many journals (Nature, Science, Cell, PNAS, PLoS, etc)
- 2012–present Editorial Board: *Current Biology*
- 2008–present Associate Editor: *Molecular Biology and Evolution*
- 2007–present Scientific Advisory Board, 23AndMe
- 2006–present Associate Editor: *PLoS Genetics*

Graduate Student/Postdoc Mentoring:

- 2011–Present Zia Khan (postdoc)
- 2011–Present Stoyan Georgiev (postdoc)

2011–Present Shyam Gopalakrishnan (postdoc)
 2011–Present Anil Raj (postdoc)
 2010–Present Graham McVicker (postdoc)
 2009–Present Roger Pique-Regi (postdoc)

2011–Present Bryce van der Geijn (PhD student, GGSB)
 2011–Present Paul Grabowski (PhD student, Ecology and Evolution)
 2008–Present Jack Degner (PhD student, GGSB)

2008–2011 Daniel Gaffney (postdoc); now junior group leader, Sanger Institute, UK
 2009–2011 Pall Melsted (postdoc); now assistant professor, University of Iceland
 2009–2011 Ying Wang (postdoc)
 2008–2009 Jordana Bell (postdoc); now Wellcome Trust Fellow, Oxford
 2006–2007 Jean-Baptiste Veyrieras (postdoc); now group leader at bioMerieux
 2004–2008 Graham Coop (postdoc); now assistant professor, U. of California, Davis
 2001–2005 Sebastian Zöllner (postdoc); now assistant professor, Biostatistics, U. of Michigan
 2002–2004 Giovanni Montana (postdoc); now assoc. prof equivalent, Statistics, Imperial College London
 2002–2003 Jeffrey Wall (postdoc); now associate professor, UCSF

2007–2011 Joseph Pickrell (PhD student, Human Genetics); now postdoc with D Reich, Harvard Med School
 2004–2008 Sridhar Kudaravalli (PhD, Human Genetics, 2008)
 2004–2008 Su Yeon Kim (PhD, Statistics, 2008; joint with P. McCullagh)
 went to postdoc with R. Nielsen, UC Berkeley; now postdoc with Terry Speed, UC Berkeley

2003–2007 Donald Conrad (PhD, Human Genetics, 2008)
 went to postdoc with M. Hurler, Sanger Institute; now asst. prof. Wash U.

2006–2008 Melissa Hubisz (M.S., Human Genetics; now programmer, Siepel lab, Cornell)
 2002–2006 Benjamin Voight (PhD, Human Genetics, 2006; joint with N. Cox)
 went to postdoc with M. Daly, Broad Institute; now asst. prof., Univ of Pennsylvania

2004–2006 Daniel Davison (PhD, Comm Ev. Biol., 2006; joint with S. Hackett)
 went to postdoc in Statistics with P. Donnelly, U. of Oxford; now in industry?

Research Interests

A central problem facing modern human genetics is to make sense of the vast quantity of human genetic variation. Which of the ~10 million common SNPs and thousands of deletions or duplications contribute to complex diseases or other traits? How important are rare variants in driving phenotypic variation? How can we identify the functional variants that underlie observed disease associations? What impact do purifying selection and adaptation have on genetic differences within and between populations, or between different species?

My group is interested in these and similar questions relating to the causes and consequences of genetic variation. Our work is primarily computational, with emphasis on data analysis, development of statistical methods and modeling—often working closely with experimental groups. Recently we have become interested in understanding how genetic variation within and between species impacts gene regulation, and we are now focusing much of our effort in this area, in close collaboration with Yoav Gilad's group at the University of Chicago.

Our past research contributions and current interests include the following:

- **Inference of population structure.** My colleagues and I have developed a model-based clustering approach (named *structure*) for using multilocus genotype data to infer population structure, and assign

individuals to populations [66, 54, 35, 20]. This method is now widely used in a range of fields, including in human genetics, forensics, and perhaps most widely in molecular ecology and conservation genetics. In 2002, our original paper [66] won the Mitchell Prize from the International Society for Bayesian Applications and it has been highly cited (> 6000 times according to Google Scholar). Our application to human data [56] won Lancet's Paper of the Year award in 2003.

- **Correcting for population structure in association mapping.** Case-control association mapping is widely perceived as a powerful tool for gene identification, but this approach fell out of favor in the human genetics community in the 1990s due to concern that unrecognized population structure could lead to false positives. Our work in this area helped to show that these problems can be greatly reduced by using random unlinked marker loci to detect, and correct for cryptic population structure [67, 65, 58]. (Similar ideas were developed independently by Bernie Devlin and Kathryn Roeder and slightly later by David Reich and colleagues.) The case-control design is now the most widely used approach in the field, and virtually all genome-wide association studies now use some sort of test for population structure.

In a separate line of work, in 2001 I used population genetic arguments to argue that rare variants are likely to make an important contribution to complex diseases; this has important implications for the likely success of different types of study design [59, 57]. These predictions may be consistent with the recent flurry of genome-wide association studies that, thus far, can explain only a modest fraction of the heritability of typical complex traits by common variants.

- **Human variation and history.** I have a long-standing interest in using patterns of genetic variation to learn about evolutionary or historical processes, in addition to our work on human population structure. My 1999 paper on inferring human demographic history from Y chromosome data [68] was among the first papers to apply Approximate Bayesian Computation in genetics. My lab provided the statistical analysis for the first successful autosomal sequencing of Neanderthal DNA [37]. We performed one of the first high-resolution surveys of deletions in the human genome, showing that copy number variation is extremely (and at the time, surprisingly) widespread [41].

Related work has considered how demography and the biology of recombination shape linkage disequilibrium in humans [61, 51, 38]. Working with Molly Przeworski, we provided the first pedigree-based approach to studying the genome-wide distribution of recombination events at very high resolution [28]. Our work showed that there was variation across individuals in the extent to which each individual used known recombination hotspots; subsequent work on PRDM9 (by other groups) has helped to define the underlying mechanism of this variation.

- **Adaptation in humans.** We have also put considerable effort into studying the extent of recent natural selection in humans [40, 23, 21, 14, 13, 15]. In our most recent work, we have argued that, while examples of strong, selective sweeps exist, the data suggest that strong, rapid selective sweeps are actually rare in humans [21, 14]. We propose that many adaptive events occur by a polygenic mechanism that allows rapid adaptation of populations, yet may leave relatively little trace in population genetic data [14, 13]
- **Population genetics of gene expression.** Since 2008 a major focus of my lab has been on understanding the links between genetic variation and functional variation in gene regulation [26, 11, 8, 1]. There is now strong evidence that genetic variants that impact gene regulation play important roles in complex traits and in adaptation. Yet we know relatively little about the detailed mechanisms by which variation impacts expression, or how to predict which SNPs are likely to affect expression in any given cell type.

We are now working on an intensive experimental and computational project in this area, in close collaboration with our colleague Yoav Gilad and his lab. At present much of our effort is going into an in-depth study of the variants (and mechanisms) that generate expression QTLs in the HapMap lymphoblastoid cell lines. These cells represent a unique resource for our purpose, as they have been sequenced by the

1000 Genomes Project, and characterized using a variety of genomic technologies. In this project we are developing statistical and computational methods to integrate diverse types of genome-wide information to better understand the links between genetic variation and gene expression. Ultimately we hope to gain much better understanding of the mechanisms by which genetic variation impacts gene regulation in a much broader range of cell types; we hope that this type of work will be of great value for interpreting population variation data.

Publications

- [1] Degner J.F., A.A. Pai, Pique-Regi R., J.-B. Veyrieras, D.J. Gaffney, J.K. Pickrell, S. De Leon, K. Michelini, N. Lewellen, G.E. Crawford, M. Stephens, Y. Gilad, and J.K. Pritchard. DNaseI sensitivity QTLs are a major determinant of human expression variation. *Nature (accepted)*, 2012.
- [2] G.H. Perry, D. Reeves, P. Melsted, A. Ratan, W. Miller, K. Michelini, E.E. Louis Jr, J.K. Pritchard, C.E. Mason, and Y. Gilad. A genome sequence resource for the aye-aye (*Daubentonia madagascariensis*), a nocturnal lemur from madagascar. *Genome Biology and Evolution*, 2011.
- [3] L. Huang, M. Jakobsson, T.J. Pemberton, M. Ibrahim, T. Nyambo, S. Omar, J.K. Pritchard, S.A. Tishkoff, and N.A. Rosenberg. Haplotype variation and genotype imputation in African populations. *Genetic Epidemiology*, 35(8):766–780, 2011.
- [4] J.K. Pritchard. Whole-genome sequencing data offer insights into human demography. *Nature Genetics*, 43(10):923–925, 2011.
- [5] P. Melsted and J. Pritchard. Efficient counting of k-mers in DNA sequences using a Bloom filter. *BMC Bioinformatics*, 12(1):333, 2011.
- [6] J.K. Pickrell, D.J. Gaffney, Y. Gilad, and J.K. Pritchard. False positive peaks in ChIP-seq and other sequencing-based functional assays caused by unannotated high copy number regions. *Bioinformatics*, 27(15):2144–2146, 2011.
- [7] A.M. Hancock, D.B. Witonsky, G. Alkorta-Aranburu, C.M. Beall, A. Gebremedhin, R. Sukernik, G. Utermann, J.K. Pritchard, G. Coop, and A. Di Rienzo. Adaptations to climate-mediated selective pressures in humans. *PLoS Genetics*, 7(4):e1001375, 2011.
- [8] R. Pique-Regi, J.F. Degner, A.A. Pai, D.J. Gaffney, Y. Gilad, and J.K. Pritchard. Accurate inference of transcription factor binding from DNA sequence and chromatin accessibility data. *Genome Research*, 21(3):447–455, 2011.
- [9] J.T. Bell, A.A. Pai, J.K. Pickrell, D.J. Gaffney, R. Pique-Regi, J.F. Degner, Y. Gilad, and J.K. Pritchard. DNA methylation patterns associate with genetic and gene expression variation in HapMap cell lines. *Genome Biology*, 12(1):R10, 2011.
- [10] A.A. Pai, J.T. Bell, J.C. Marioni, J.K. Pritchard, and Y. Gilad. A Genome-Wide Study of DNA Methylation Patterns and Gene Expression Levels in Multiple Human and Chimpanzee Tissues. *PLoS Genetics*, 7(2), 2011.
- [11] J.K. Pickrell, J.C. Marioni, A.A. Pai, J.F. Degner, B.E. Engelhardt, E. Nkadori, J.B. Veyrieras, M. Stephens, Y. Gilad, and J.K. Pritchard. Understanding mechanisms underlying human gene expression variation with RNA sequencing. *Nature*, 464(7289):768–772, 2010.
- [12] J.K. Pickrell, A.A. Pai, Y. Gilad, and J.K. Pritchard. Noisy splicing drives mRNA isoform diversity in human cells. *PLoS Genet*, 6(12):e1001236, 2010.

- [13] J.K. Pritchard and A. Di Rienzo. Adaptation—not by sweeps alone. *Nature Reviews Genetics*, 11(10):665–667, 2010.
- [14] J.K. Pritchard, J.K. Pickrell, and G. Coop. The genetics of human adaptation: hard sweeps, soft sweeps, and polygenic adaptation. *Current Biology*, 20(4):R208–R215, 2010.
- [15] J.K. Pritchard. How we are evolving. *Scientific American*, 301(10):41–47, 2010.
- [16] G. Coop, D. Witonsky, A. Di Rienzo, and J.K. Pritchard. Using environmental correlations to identify loci underlying local adaptation. *Genetics*, 185(4):1411–1423, 2010.
- [17] A.M. Hancock, D.B. Witonsky, E. Ehler, G. Alkorta-Aranburu, C. Beall, A. Gebremedhin, R. Sukernik, G. Utermann, J. Pritchard, G. Coop, and A. Di Rienzo. Human adaptations to diet, subsistence, and ecoregion are due to subtle shifts in allele frequency. *Proceedings of the National Academy of Sciences*, 107(Supplement 2):8924–8930, 2010.
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- [28] G. Coop, X. Wen, C. Ober, J.K. Pritchard, and M. Przeworski. High-resolution mapping of crossovers reveals extensive variation in fine-scale recombination patterns among humans. *Science*, 319(5868):1395–1398, 2008.
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