

HUNTER FRASER

EDUCATION

- 1997 – 2001 M.I.T. Cambridge, MA
B.S., Biology
- 2001 – 2005 U.C. Berkeley Berkeley, CA
Ph.D., Molecular and Cell Biology

RESEARCH POSITIONS

- 1996 – 1997 Harvard Medical School Boston, MA
• Worked in Fred Alt's lab on DNA knockout vectors which led to successful knockout mice.
- 1998 – 1999 M.I.T. Cambridge, MA
• Worked in Leonard Guarente's lab on gene expression and aging in yeast.
- 1999 Santa Fe Institute Santa Fe, NM
• Worked for one summer on computational analysis of genetic incompatibilities in mice.
- 2000 Stanford University Stanford, CA
• Worked in Marcus Feldman's lab on functional and evolutionary genomics.
- 2000 – 2001 M.I.T. Cambridge, MA
• Worked in Daniel Rothman's lab on mathematical models of aging.
- 2001 – 2005 U.C. Berkeley Berkeley, CA
• Ph.D. work in Michael Eisen's lab on functional and evolutionary genomics.
- 2004 Max Planck Institute Leipzig, Germany
• Worked for one month in Svante Pääbo's lab on aging and gene expression in the primate brain.
- 2005 Khao Chong Research Station Khao Chong, Thailand
• Worked for one month at a field station in the Khao Chong rainforest, collecting caterpillars as part of a biodiversity project led by Naomi Pierce.
- 2006 – 2007 Broad Institute of MIT and Harvard Cambridge, MA
• Studied polymorphic mRNA splicing in humans: its extent, and its impact on autoimmune diseases.
- 2008 – 2009 Rosetta Inpharmatics Seattle, WA
• Worked with Eric Schadt on the effects of genetic variation on gene expression in mouse and yeast.
- 2009 – 2016 Stanford University Stanford, CA
• Assistant Professor in the Department of Biology.
- 2016 – 2022 Stanford University Stanford, CA
• Associate Professor in the Department of Biology.
- 2022 – Present Stanford University Stanford, CA
• Professor in the Department of Biology.

PUBLICATIONS

- A.E. Hirsh and **H.B. Fraser**. Protein dispensability and rate of evolution. *Nature* 411: 1046 (2001).
- J.S. Weitz and **H.B. Fraser**. Explaining mortality rate plateaus. *PNAS* 98: 15383 (2001).
- S.B. Snapper, F. Takeshima, I. Anton, C.H. Liu, S.M. Thomas, D. Nguyen, D. Dudley, **H. Fraser**, D. Purich, M. Lopez-Illasaca, C. Klein, L. Davidson, R. Bronson, R.C. Mulligan, F. Southwick, R. Geha, M.B. Goldberg, F.S. Rosen, J.H. Hartwig, and F.W. Alt. N-WASP deficiency reveals distinct pathways for cell surface projections and microbial actin-based motility. *Nature Cell Biology* 3: 897 (2001).
- **H.B. Fraser**, A.E. Hirsh, L.M. Steinmetz, C. Scharfe, and M. Feldman. Evolutionary rate in the protein interaction network. *Science* 296: 750 (2002).
- A.E. Hirsh and **H.B. Fraser**. Genomic function: Rate of evolution and gene dispensability. *Nature* 421: 497 (2003).
- A.E. Hirsh, **H.B. Fraser**, and D.P. Wall. Detecting putative orthologs. *Bioinformatics* 19: 1710 (2003).
- **H.B. Fraser**, D.P. Wall, and A.E. Hirsh. A simple dependence between protein evolution rate and the number of protein-protein interactions. *BMC Evolutionary Biology* 3: 11 (2003).
- J.B. Plotkin, J.S. Dushoff, and **H.B. Fraser**. Detecting selection using a single genome sequence of *M. tuberculosis* and *P. falciparum*. *Nature* 428: 942 (2004).
- **H.B. Fraser**, A.E. Hirsh, G. Giaever, J. Kumm, and M.B. Eisen. Noise minimization in eukaryotic gene expression. *PLoS Biology* 2: 824 (2004).
- **H.B. Fraser** and A.E. Hirsh. Evolutionary rate depends on number of protein-protein interactions independently of gene expression level. *BMC Evolutionary Biology* 4: 13 (2004).
- **H.B. Fraser**, A.E. Hirsh, D.P. Wall, and M.B. Eisen. Coevolution of gene expression among interacting proteins. *PNAS* 101: 9033 (2004).
- A.P. Gasch, A.M. Moses, D.Y. Chiang, **H.B. Fraser**, M. Berardini, M.B. Eisen. Conservation and evolution of *cis*-regulatory systems in ascomycete fungi. *PLoS Biology* 2: e398 (2004).
- A.E. Hirsh, **H.B. Fraser**, and D.P. Wall. Adjusting for selection on synonymous sites in estimates of evolutionary distance. *Molecular Biology and Evolution* 22: 174 (2005).
- P.J. Lynch, **H.B. Fraser**, E. Sevastopoulis, J. Rine, and L.N. Rusche. A single amino acid substitution enhances the spreading ability of the promoter-specific repressor Sum1p from *S. cerevisiae*. *Molecular and Cellular Biology* 25: 5920 (2005).
- D.P. Wall, A.E. Hirsh, **H.B. Fraser**, J. Kumm, G. Giaever, M.B. Eisen, and M.W. Feldman. Functional genomic analysis of the rates of protein evolution. *PNAS* 102: 5483 (2005).
- **H.B. Fraser**, P. Khaitovich, J.B. Plotkin, S. Pääbo, and M.B. Eisen. Aging and gene expression in the primate brain. *PLoS Biology* 3: 274 (2005).
- **H.B. Fraser**. Modularity and evolutionary constraint on proteins.

Nature Genetics 37: 351 (2005).

- J.B. Plotkin, J. Dushoff, M.M. Desai, and **H.B. Fraser**. Estimating selection pressures from limited comparative data.
Molecular Biology and Evolution. 23: 1457 (2006).
- J.B. Plotkin, J. Dushoff, M.M. Desai, and **H.B. Fraser**. Codon usage and selection on proteins.
Journal of Molecular Evolution, 63: 635 (2006).
- N. Bertin, N. Simonis, D. Dupuy, M.E. Cusick, J.D. Han, **H.B. Fraser**, F.P. Roth, and M. Vidal. Confirmation of organized modularity in the yeast interactome.
PLoS Biology 5: e153 (2007).
- J.B. Plotkin and **H.B. Fraser**. Assessing the determinants of evolutionary rates in the presence of noise.
Molecular Biology and Evolution, 24: 1113 (2007).
- **H.B. Fraser** and J.B. Plotkin. Using protein complexes to predict phenotypic effects of gene mutation.
Genome Biology, 8: R252 (2007).
- M. Yassour, T. Kaplan, **H.B. Fraser**, J. Levin, J. Pfiffner, X. Adiconis, G. Schroth, S. Luo, I. Khrebtkova, A. Gnirke, C. Nusbaum, D. Thompson, N. Friedman, and A. Regev. *Ab initio* construction of a eukaryotic transcriptome by massively parallel mRNA sequencing.
PNAS 106: 3264 (2009).
- **H.B. Fraser** and X. Xie. Common polymorphic transcript variation in human disease.
Genome Research 19: 567 (2009).
- **H.B. Fraser** and E.E. Schadt. The quantitative genetics of phenotypic robustness.
PLoS ONE 5: e8635 (2010).
- **H.B. Fraser**, A. Moses, and E.E. Schadt. Evidence for widespread adaptive evolution of gene expression in budding yeast.
PNAS 107: 2997 (2010).
- T. Babak, P. Garrett-Engele, C. Armour, C. Raymond, M. Keller, R. Chen, C. Rohl, J. Johnson, A. Attie, **H.B. Fraser***, and E.E. Schadt* (*equal contribution and corresponding authorship). Genetic validation of whole-transcriptome sequencing for mapping expression affected by *cis*-regulatory variation.
BMC Genomics 11: 473 (2010).
- Lamb JR, Zhang C, Xie T, Wang K, Zhang B, Hao K, Chudin E, **H.B. Fraser**, Millstein J, Ferguson M, Suver C, Ivanovska I, Scott M, Philippar U, Bansal D, Zhang Z, Burchard J, Smith R, Greenawalt D, Cleary M, Derry J, Loboda A, Watters J, Poon RT, Fan ST, Yeung C, Lee NP, Guinney J, Molony C, Emilsson V, Buser-Doepner C, Zhu J, Friend S, Mao M, Shaw PM, Dai H, Luk JM, and Schadt EE. Predictive genes in adjacent normal tissue are preferentially altered by sCNV during tumorigenesis in liver cancer and may be rate limiting.
PLoS ONE 6: e20090 (2011).
- **H.B. Fraser**, T. Babak, J. Tsang, Y. Zhou, M. Mehrabian, and E.E. Schadt. Systematic detection of polygenic *cis*-regulatory evolution.
PLoS Genetics 7: e1002023 (2011).
- **H.B. Fraser**, L. Lam, S. Neumann, and M.S. Kobor. Population-specificity of human DNA methylation.
Genome Biology, 13: R8 (2012).
- L. Lam, E. Emberly, **H.B. Fraser**, S. Neumann, E. Chen, G. Miller, and M.S. Kobor. Factors Underlying Variable DNA Methylation in a Human Community Cohort.
PNAS, 109 Suppl 2: 17253 (2012).
- **H.B. Fraser**, S. Levy, A. Chavan, H.B. Shah, S. Kowli, J.C. Perez, Y. Zhou, M.L. Siegal, and H. Sinha. Polygenic *cis*-regulatory adaptation in the evolution of yeast pathogenicity.
Genome Research, 22: 1930 (2012).
- M. Irimia, J.J. Tena, M.S. Alexis, A. Fernandez-Minan, I. Maeso, O. Bogdanovic, E. de la Calle-Mustienes, S.W. Roy, J.L. Gómez-Skarmeta, and **H.B. Fraser**. Extensive conservation of ancient microsynteny across metazoans due to *cis*-regulatory constraint.

- Genome Research*, 22: 2356 (2012).
- A. Ariza-Cosano, A. Visel, L.A. Pennacchio, **H.B. Fraser**, J.L. Gómez-Skarmeta, M. Irimia, and J. Bessa. Differences in enhancer activity in mouse and zebrafish reporter assays are often associated with changes in gene expression. *BMC Genomics*, 13: 713 (2012).
 - **H.B. Fraser**. Gene expression drives local adaptation in humans. *Genome Research*, 23: 1089 (2013).
 - J. Chang, Y. Zhou, X. Hu, L. Lam, C. Henry, E.M. Green, R. Kita, M.S. Kobor, and **H.B. Fraser**. The molecular mechanism of a *cis*-regulatory adaptation in yeast. *PLoS Genetics*, 9: e1003813 (2013).
 - J.D. Smith, K. McManus, and **H.B. Fraser**. A novel test for selection on *cis*-regulatory elements reveals positive and negative selection acting on mammalian transcriptional enhancers. *Molecular Biology and Evolution*, 30: 2509 (2013).
 - **H.B. Fraser**. Cell-cycle regulated transcription associates with DNA replication timing in yeast and human. *Genome Biology*, 14: R111 (2013).
 - C.G. Artieri and **H.B. Fraser**. Evolution at two levels of gene expression in yeast. *Genome Research*, 24: 411 (2014).
 - C.G. Artieri and **H.B. Fraser**. Transcript length mediates developmental timing of gene expression across *Drosophila*. *Molecular Biology and Evolution*, 31: 2879 (2014).
 - C.G. Artieri and **H.B. Fraser**. Accounting for biases in riboprofiling data indicates a major role for proline in stalling translation. *Genome Research*, 24: 2011 (2014).
 - R. Jiang, M.J. Jones, E. Chen, S.M. Neumann, **H.B. Fraser**, G.E. Miller, and M.S. Kobor. Discordance of DNA methylation variance between two accessible human tissues. *Scientific Reports* 5: 8257 (2015).
 - R.C. McCoy, Z. Demko, A. Ryan, M. Banjevic, M. Hill, S. Sigurjonsson, M. Rabinowitz, **H.B. Fraser**, and D.A. Petrov. Common variants spanning *PLK4* are associated with increased rate of mitotic-origin aneuploidy in human embryos. *Science*, 348: 235 (2015).
 - T. Babak, B. DeVeale, E. Tsang, Y. Zhou, X. Li, K.S. Smith, K.R. Kukurba, R. Zhang, J.B. Li, D. van der Kooy, S.B. Montgomery, and **H.B. Fraser**. Genetic conflict reflected in tissue-specific maps of genomic imprinting in human and mouse. *Nature Genetics*, 47: 544 (2015).
 - I.M. Kaplow, J.L. MacIsaac, S.M. Mah, M.S. Kobor, and **H.B. Fraser**. A pooling-based approach to mapping genetic variants associated with DNA methylation. *Genome Research*, 25: 907 (2015).
 - R.M. Agolia and **H.B. Fraser**. Disentangling sources of selection on exonic transcriptional enhancers. *Molecular Biology and Evolution*, 33: 585 (2015).
 - S. Naranjo, J.D. Smith, C.G. Artieri, M. Zhang, Y. Zhou, M.E. Palmer, and **H.B. Fraser**. Dissecting the genetic basis of a complex *cis*-regulatory adaptation. *PLoS Genetics*, 11: e1005751 (2015). [Winner of the **PLoS Genetics Research Prize**, awarded to the most outstanding paper published in PLoS Genetics in 2015.]
 - A.K. Tehranchi, M. Myrthil, T. Martin, B. Hie, D. Golan, and **H.B. Fraser**. Pooled ChIP-seq links variation in transcription factor binding to complex disease risk. *Cell*, 165: 730 (2016).
 - E. Sharon, L.V. Sibener, A. Battle, **H.B. Fraser**, K.C. Garcia, and J.K. Pritchard. Genetic variation in MHC protein-coding genes is associated with T-cell receptor expression biases. *Nature Genetics*, 48: 995 (2016).
 - R. Kita and **H.B. Fraser**. Local adaptation of sun-exposure-dependent gene expression regulation in human skin. *PLoS Genetics*, 12: e1006382 (2016).

- O. Carja, J.L. MacIsaac, S.M. Mah, B.M. Henn, M.S. Kobor, M.W. Feldman, and **H.B. Fraser**. Worldwide patterns of human epigenetic variation. *Nature Ecology and Evolution*, 1: 1577-1583 (2017).
- C.G. Artieri, A. Naor, I. Turgeman-Grott, Y. Zhou, R. York, U. Gophna, and **H.B. Fraser**. *Cis*-regulatory evolution in prokaryotes revealed by interspecific archaeal hybrids. *Scientific Reports*, 7: 3986 (2017).
- R. Kita, S. Venkataram, Y. Zhou, and **H.B. Fraser**. High-resolution mapping of *cis*-regulatory variation in budding yeast. *PNAS*, 114: E10736-E10744 (2017).
- E. Sharon, S.A. Chen, N.M. Khosla, J.D. Smith, J.K. Pritchard, and **H.B. Fraser**. Functional genetic variants revealed by massively parallel precise genome editing. *Cell*, 175: 544-557 (2018).
- P.A. Combs and **H.B. Fraser**. Spatially varying *cis*-regulatory divergence in *Drosophila* embryos elucidates *cis*-regulatory logic. *PLoS Genetics*, 14: e1007631 (2018).
- R.A. York, C. Patil, K. Abdilleh, Z.V. Johnson, M. Conte, M.J. Genner, P.T. McGrath, **H.B. Fraser***, R.D. Fernald*, and J.T. Streelman*. Behavior-dependent *cis*-regulation implicates genes and pathways associated with bower building in cichlid fishes. (*Corresponding authors) *PNAS*, 115: E11081-E11090 (2018).
- P.A. Combs, J.J. Krupp, N.M. Khosla, D. Bua, D.A. Petrov, J.D. Levine, and **H.B. Fraser**. Tissue-specific *cis*-regulatory divergence implicates *eloF* in inhibiting interspecies mating in *Drosophila*. *Current Biology*, 28: 3969-3975 (2018).
- T. Martin and **H.B. Fraser**. Phylogenetic expression profiling reveals widespread coordinated evolution of gene expression. *Nature Communications*, 9: 4963 (2018).
- **H.B. Fraser**. Improving estimates of compensatory *cis-trans* regulatory divergence. *Trends in Genetics*, 35: 88 (2019).
- A.K. Tehranchi, B. Hie, M. Dacre, I.M. Kaplow, K.P. Pettie, P.A. Combs, and **H.B. Fraser**. Fine-mapping *cis*-regulatory variants in diverse human populations. *eLife*, 8: e39595 (2019).
- P.E. García-Nieto, A.J. Morrison, and **H.B. Fraser**. The somatic mutation landscape of the human body. *Genome Biology*, 20: 298 (2019). [Selected as a top 20 paper in *Genome Biology* published from 2000-2020]
- Q. Zhao, M. Dacre, T. Nguyen, M. Pjanic, B. Liu, D. Iyer, P. Cheng, R. Wirka, J.B. Kim, **H.B. Fraser**, and T. Quertermous. Molecular mechanisms of coronary disease revealed using quantitative trait loci for TCF21 binding, chromatin accessibility, and chromosomal looping. *Genome Biology*, 21: 135 (2020).
- **H.B. Fraser**. Detecting selection from a genetic cross. *PNAS*, 117: 22323 (2020).
- A.F. Kern, G.X. Yang, N.M. Khosla, R.M.L. Ang, M.P. Snyder, **H.B. Fraser**. Divergent patterns of selection on metabolite levels and gene expression. *BMC Ecol Evol*, 21: 185 (2021).
- C.V. Weiss, L. Harshman, F. Inoue, **H.B. Fraser**, D.A. Petrov, N. Ahituv, D. Gokhman. The *cis*-regulatory effects of modern human-specific variants. *eLife* 10: e63713 (2021).
- A. Nivina, S. Herrera Paredes, **H.B. Fraser**, C. Khosla. GRINS: genetic elements that recode assembly-line polyketide synthases and accelerate their diversification. *PNAS*, 118: e2100751118 (2021).
- S.D. Singh-Babak, T. Babak, **H.B. Fraser**, and A.D. Johnson. Lineage-specific selection and the evolution of virulence in the *Candida* clade. *PNAS*, 118: e2016818118 (2021).
- R.M. Agoglia, D. Sun, F. Birey, S. Yoon, Y. Miura, K. Sabatini, S.P. Pasca, and **H.B. Fraser**. Primate cell fusion disentangles gene regulatory divergence in neurodevelopment.

- Nature*, 592: 421-427 (2021).
- D. Gokhman, R.M. Agoglia, M. Kinnebrew, W. Gordon, D. Sun, V.K. Bajpai, S. Naqvi, C. Chen, A. Chan, C. Chen, D.A. Petrov, N. Ahituv, H. Zhang, Y. Mishina, J. Wysocka, R. Rohatgi, and **H.B. Fraser**. Human-chimpanzee fused cells reveal *cis*-regulation underlying skeletal evolution. *Nature Genetics*, 53: 467-476 (2021).
 - P.E. García-Nieto, B. Wang, and **H.B. Fraser**. Transcriptome diversity is a systematic source of variation in RNA-sequencing data. *PLoS Computational Biology*, 18: e1009939 (2022).
 - C.K. Hu, R.A. York, H.C. Metz, N.L. Bedford, **H.B. Fraser**, and H.E. Hoekstra. Cis-regulatory changes in locomotor genes are associated with the evolution of burrowing behavior. *Cell Reports*, 38: 110360 (2022).
 - B. Zhao, S.A. Chen, J. Lee, **H.B. Fraser**. Bacterial Retrons Enable Precise Gene Editing in Human Cells. *CRISPR Journal*, 5: 31-39 (2022).
 - **H.B. Fraser**. Existing methods are effective at measuring natural selection on gene expression. *Nature Ecology & Evolution*, 6: 1836 (2022).
 - R.M.L. Ang, S.A. Chen, A.F. Kern, Y. Xie, and **H.B. Fraser**. Widespread epistasis among beneficial genetic variants revealed by high-throughput genome editing. *Cell Genomics*, 3: 100260 (2023).
 - S.A. Chen, A.F. Kern, R.M.L. Ang, Y. Xie, and **H.B. Fraser**. Gene-by-environment interactions are pervasive among natural genetic variants. *Cell Genomics*, 3: 100273 (2023).
 - A.L. Starr, D. Gokhman, and **H.B. Fraser**. Accounting for cis-regulatory constraint prioritizes genes likely to affect species-specific traits. *Genome Biology*, 24: 11 (2023).
 - K.L. Mack, T.A. Square, B. Zhao, C.T. Miller, and **H.B. Fraser**. Evolution of spatial and temporal cis-regulatory divergence between marine and freshwater sticklebacks. *Molecular Biology and Evolution*, in press (2023).
 - K.L. Mack, H.E. Talbott, M. Griffin, N.J. Guardino, J.B.L. Parker, A.F. Spielman, M.F. Davitt, S. Mascharak, M.J. Berger, D.C. Wan, **H.B. Fraser***, and M.T. Longaker*. Allele-specific expression reveals genetic drivers of tissue regeneration in mice. (*equal contribution and corresponding authorship) *Cell Stem Cell* 30: 1368 (2023).
 - B. Wang, A.L. Starr, and **H.B. Fraser**. Cell type-specific cis-regulatory divergence in gene expression and chromatin accessibility revealed by human-chimpanzee hybrid cells. *eLife* (2023).

Review articles

- **H.B. Fraser**. Coevolution, modularity, and human disease. *Current Opinion in Genetics & Development*, 16: 637 (2006).
- **H.B. Fraser**. Genome-wide approaches to the study of adaptive gene expression evolution. *Bioessays* 33: 469 (2011).
- M. Irimia, I. Maeso, S.W. Roy, and **H.B. Fraser**. Ancient *cis*-regulatory constraints and the evolution of genome architecture. *Trends in Genetics*, 29: 521 (2013).

AWARDS RECEIVED

- Stanford Prize in Population Genetics and Society (2022)
- Top 20 paper published in *Genome Biology* in the past 20 years, for “The somatic mutation landscape of the human body” (2020) <https://genomebiology.biomedcentral.com/20years>

- PLoS Genetics Research Prize, awarded to the most outstanding paper published in *PLoS Genetics* in the previous year, for “Dissecting the genetic basis of a complex *cis*-regulatory adaptation” (2016)
- NIH New Innovator Award (2011)
- Pew Scholar in the Biomedical Sciences (2011)
- Alfred P. Sloan Fellowship (2010)
- Frederick E. Terman Fellowship (2009)
- Life Science Research Foundation Postdoctoral Fellowship (2007)
- Merck/MIT Computational Systems Biology Initiative Postdoctoral Fellowship (2006)
- Belling Prize, awarded to the most outstanding Ph.D. graduate of the previous five years in Genetics at UC Berkeley (2005)
- National Science Foundation Predoctoral Fellowship (2002)
- Massachusetts Biotechnology Council Scholarship (1997)

CURRENT FUNDING

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|--|-------------------|-------------|
| • NIH R01 (R01GM097171)
Title: Evolutionary genomics of yeast | 8/1/20 – 7/31/25 | \$1,030,000 |
| • NIH R01 (R01HG012285)
Title: Investigating human cis-regulatory evolution with hybrid iPS cells | 5/25/22 – 3/31/26 | \$1,764,000 |

TEACHING

Current

- The science and ethics of personalized genomic medicine (Bio 4N)
- Evolutionary Genomics (Bio 332)

Past

- Introduction to Problem Solving in Infectious Disease (Bio 60)
- Evolution (Bio 43)