BIOGRAPHICAL SKETCH

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NAME: Shendure, Jay Ashok

eRA COMMONS USER NAME (credential, e.g., agency login): shendure

POSITION TITLE: Professor of Genome Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Princeton University, Princeton, New Jersey	AB	06/1996	Molecular Biology
Harvard University, Cambridge, Massachusetts	PHD	08/2005	Genetics
Harvard Medical School, Boston, Massachusetts	MD	08/2007	Medicine

A. Personal Statement

My background includes the development of a broad range of impactful technologies for genetics, genomics, and molecular biology. Technologies, or applications thereof, to which I and/or my lab made major contributions include next-generation DNA sequencing (2005); multiplex targeted sequence capture (2007, 2009, 2013); exome sequencing (2009) and its application to Mendelian disorders (2009, 2010) and autism (2011, 2012, 2012); massively parallel reporter assays (2009) and their application to enhancers (2012); subassembly, also known as synthetic long reads (2010); haplotype-resolved genome sequencing (2011), including of the HeLa cell line (2013); non-invasive inference of fetal genomes from cell-free DNA (2012); exploiting chromatin interactions for chromosome-scale *de novo* genome assembly (2013) or metagenome deconvolution (2014); genome-wide frameworks for interpreting genetic variants (CADD: 2014) and for mapping gene regulation (CRISPR-QTL: 2019); epigenetic maps and tissue-of-origin inference from cell-free DNA (2016); whole organism lineage tracing by genome editing (GESTALT: 2016); combinatorial cellular indexing for genome assembly (2014) and for single cell profiling of chromatin accessibility (2015), nuclear architecture (2017), gene expression (2017, 2019), genome sequence (2020), co-assays (2018) and chemical transcriptomics (2020); saturation genome editing (2014) and its application to prospective functional interpretation of variants of uncertain significance in *BRCA1* (2018); organism-scale, single cell atlases of gene expression (worm: 2017, fly: 2022, mouse: 2019, 2022, human: 2020) and chromatin accessibility (fly: 2018, 2022, mouse: 2018, human: 2020); whole embryo phenotyping of pleiotropic mouse mutants (2022); the DNA Typewriter and ENGRAM methods for time-resolved molecular recording (2021, 2022); precise genomic deletions with dual prime editing (2021); and sQers for multiplex, cell type-resolved profiling of developmental enhancers (2022).

More detail and a subset of citations are provided in the “Contributions to Science” section below.

B. Positions, Scientific Appointments, and Honors

Professional Experience

2017 - Present	Scientific Director, Allen Discovery Center for Cell Lineage Tracing
2017 - Present	Scientific Director, Brotman Baty Institute for Precision Medicine
2015 - Present	Full Professor (with tenure), Dept. of Genome Sciences, University of Washington
2015 - Present	Investigator, Howard Hughes Medical Institute
2010 - Present	Affiliate Professor, Division of Human Biology, Fred Hutchinson Cancer Research Center
2011 - 2015	Associate Professor (with Tenure), Dept. of Genome Sciences, University of Washington

2007 - 2011	Assistant Professor, Department of Genome Sciences, University of Washington
1998 - 2007	Medical Scientist Training Program (MSTP), Dept. of Genetics, Harvard Medical School
1997 - 1998	Research Scientist, Vaccine Division, Merck Research Laboratories, Rahway, NJ
1996 - 1997	Fulbright Scholar to India, Dept. of Pediatrics, Sassoon General Hospital , Pune

Academic Scientific Advisory Roles & Consortium Leadership

2017 – present	Board of Reviewing Editors	Science / AAAS
2017 – present	Advisory Council	Allen Institute for Cell Science
2018 – present	Scientific Advisory Board	Chan Zuckerberg Initiative (Single Cell Biology)
2020 – present	Scientific Advisory Board	New York Genome Center
2021 – 2022	Scientific Advisory Board	Open Targets
2018 – 2022	Scientific Advisory Board	Allen Institute for Immunology
2017 – 2020	Advisory Committee to NIH Director	National Institutes of Health
2014 – 2018	National Advisory Council	National Human Genome Research Institute
2015	NIH ACD Working Group	AllOfUs / US Precision Medicine Initiative
2012 – 2014	Scientific Advisory Board	Joint Genome Institute, Department of Energy
2012 – 2015	Steering Committee	NIH/NHGRI Centers for Mendelian Genomics
2009 – 2012	Steering Committee	NIH/NHLBI Exome Sequencing Project

Honors, Awards, Named Lectures

2022	Mendel Lecture	European Society of Human Genetics
2022	Election to Membership	National Academy of Sciences
2022	Election to Membership	National Academy of Inventors
2022	Election to Membership	Washington Academy of Sciences
2019	Richard Lounsbery Award	National Academy of Sciences
2019	AAAS Fellow	American Assc. Advancement of Science
2019	Jeffrey M. Trent Lectureship in Cancer Research	National Human Genome Research Institute
2019	Paul D. Gottlieb Distinguished Lectureship	University of Texas, Austin
2018	Allan C. Wilson Memorial Lectureship	University of California, Berkeley
2018	Richard and Carol Hertzberg Prize	University of California, San Diego
2018	Nancy Andrews Physician-Scientist Lectureship	Duke University
2017	British Society of Genetic Medicine Lectureship	British Society of Genetic Medicine
2014	Cell “40 under 40”, Cell 40th Anniversary	Cell Press
2014	7th Annual Scripps Genomic Medicine Award	Scripps Health
2014	HudsonAlpha Prize for Life Sciences	HudsonAlpha Institute for Biotechnology
2013	FEDERAprijs	Fed. of Dutch Medical Scientific Societies
2013	NIH Director’s Pioneer Award	National Institutes of Health
2012	Curt Stern Award	American Society of Human Genetics
2010	Lowell Milken Young Investigator	Prostate Cancer Foundation
2008	Science in Medicine New Investigator Lecture	University of Washington
2008	3rd Annual Tomorrow’s PIs	Genome Technology Magazine
2007	James Tolbert Shipley Prize	Harvard Medical School
2006	TR35 Young Innovator Award	M.I.T. Technology Review

1998	Medical Science Training Program Fellowship	National Institutes of Health
1996	Fulbright Scholarship	U.S. State Department
1996	*summa cum laude*	Princeton University
1996	Honorary Major in Anthropology	Princeton University
1996	Sigma Chi Thesis Award for Molecular Biology	Princeton University
1996	Senior Prize for Best Thesis in Anthropology	Princeton University

C. Contributions to Science

My major scientific achievements comprise methodological advances that promise to or already have had broad impacts in human genetics and molecular biology. I am sole or joint corresponding author on all publications referenced below.

1. Next-generation DNA sequencing: My doctoral research laid the conceptual groundwork and achieved early milestones for massively parallel or next-generation DNA sequencing (NGS), including the first proof-of-concept of NGS for genome resequencing in 2005. After establishing my lab in 2007, I led the development and application of a diversity of enabling methods in genome sequencing, e.g. haplotype-resolved genome sequencing and its application to infer the genome of a fetus via samples obtained non-invasively from its parents; chromatin contact-based scaffolding of genome assemblies and its application to the HeLa genome; etc. We have also sought to apply NGS in creative ways, e.g. the inference of nucleosome positions and tissues-of-origin of cell-free DNA based on fragmentation patterns, and the use of that information for cancer diagnostics.

    a. Shendure J, Porreca GJ, Reppas NB, Lin X, McCutcheon JP, Rosenbaum AM, Wang MD, Zhang K, Mitra RD, Church GM. Accurate multiplex polony sequencing of an evolved bacterial genome. Science. 2005 Sep 9;309(5741):1728-32. PubMed PMID: 16081699.
    b. Kitzman JO, Snyder MW, Ventura M, Lewis AP, Qiu R, Simmons LE, Gammill HS, Rubens CE, Santillan DA, Murray JC, Tabor HK, Bamshad MJ, Eichler EE, Shendure J. Noninvasive whole-genome sequencing of a human fetus. Sci Transl Med. 2012 Jun 6;4(137):137ra76. PubMed Central PMCID: PMC3379884.
    c. Adey A, Burton JN, Kitzman JO, Hiatt JB, Lewis AP, Martin BK, Qiu R, Lee C, Shendure J. The haplotype-resolved genome and epigenome of the aneuploid HeLa cancer cell line. Nature. 2013 Aug 8;500(7461):207-11. PubMed Central PMCID: PMC3740412.
    d. Snyder MW, Kircher M, Hill AJ, Daza RM, Shendure J. Cell-free DNA Comprises an In Vivo Nucleosome Footprint that Informs Its Tissues-Of-Origin. Cell. 2016 Jan 14;164(1-2):57-68. PubMed Central PMCID: PMC4715266.

2. Exome sequencing and Mendelian genetics: My lab pioneered the development of exome sequencing as well as its earliest applications to identify the genetic basis of Mendelian disorders that resist conventional analysis. This paradigm that has been widely adopted in human genetics since we first reported it in 2009 and has been used to identify the genes underlying hundreds of rare diseases. In related work, we co-developed de novo mutation-focused approaches for discovering and validating genes underlying autism spectrum disorders.

    a. Ng SB, Turner EH, Robertson PD, Flygare SD, Bigham AW, Lee C, Shaffer T, Wong M, Bhattacharjee A, Eichler EE, Bamshad M, Nickerson DA, Shendure J. Targeted capture and massively parallel sequencing of 12 human exomes. Nature. 2009 Sep 10;461(7261):272-6. PubMed Central PMCID: PMC2844771.
    b. Ng SB, Buckingham KJ, Lee C, Bigham AW, Tabor HK, Dent KM, Huff CD, Shannon PT, Jabs EW, Nickerson DA, Shendure J, Bamshad MJ. Exome sequencing identifies the cause of a mendelian disorder. Nat Genet. 2010 Jan;42(1):30-5. PubMed Central PMCID: PMC2847889.
    c. O'Roak BJ, Vives L, Girirajan S, Karakoc E, Krumm N, Coe BP, Levy R, Ko A, Lee C, Smith JD, Turner EH, Stanaway IB, Vernot B, Malig M, Baker C, Reilly B, Akey JM, Borenstein E, Rieder MJ, Nickerson DA, Bernier R, Shendure J, Eichler EE. Sporadic autism exomes reveal a highly interconnected protein

network of de novo mutations. Nature. 2012 Apr 4;485(7397):246-50. PubMed Central PMCID: PMC3350576.

d. O'Roak BJ, Vives L, Fu W, Egertson JD, Stanaway IB, Phelps IG, Carvill G, Kumar A, Lee C, Ankenman K, Munson J, Hiatt JB, Turner EH, Levy R, O'Day DR, Krumm N, Coe BP, Martin BK, Borenstein E, Nickerson DA, Mefford HC, Doherty D, Akey JM, Bernier R, Eichler EE, Shendure J. Multiplex targeted sequencing identifies recurrently mutated genes in autism spectrum disorders. Science. 2012 Dec 21;338(6114):1619-22. PubMed Central PMCID: PMC3528801.

3. Mutational analysis: My lab pioneered a new generation of methods for experimentally measuring or computationally predicting the functional consequences of mutations, including massively parallel reporter assays and saturation genome editing. We also developed combined annotation dependent depletion (CADD), a unifying and widely used framework for prioritizing variants observed in human genomes. We are applying these methods to goals including the prospective functional interpretation of variants of uncertain significance, e.g. at the BRCA1 locus.

   a. Patwardhan RP, Lee C, Litvin O, Young DL, Pe'er D, Shendure J. High-resolution analysis of DNA regulatory elements by synthetic saturation mutagenesis. Nat Biotechnol. 2009 Dec;27(12):1173-5. PubMed Central PMCID: PMC2849652.

   b. Kircher M, Witten DM, Jain P, O'Roak BJ, Cooper GM, Shendure J. A general framework for estimating the relative pathogenicity of human genetic variants. Nat Genet. 2014 Mar;46(3):310-5. PubMed Central PMCID: PMC3992975.

   c. Findlay GM, Daza RM, Martin B, Zhang MD, Leith AP, Gasperini M, Janizek JD, Huang X, Starita LM, Shendure J. Accurate classification of BRCA1 variants with saturation genome editing. Nature. 2018 Oct;562(7726):217-222. PubMed Central PMCID: PMC6181777.

   d. Findlay GM, Boyle EA, Hause RJ, Klein JC, Shendure J. Saturation editing of genomic regions by multiplex homology-directed repair. Nature. 2014 Sep 4;513(7516):120-3. PubMed Central PMCID: PMC4156553.

4. Molecular methods: My lab has a long-standing and ongoing interest in developing new molecular methods for a broad range of goals in genomics and biomedical research more broadly. Recent examples include single cell combinatorial indexing ("sci-") assays or co-assays, genome editing of synthetic target arrays for lineage tracing (GESTALT), and a genome-wide framework for mapping gene regulation (CRISPR-QTL).

   a. Cusanovich DA, Daza R, Adey A, Pliner HA, Christiansen L, Gunderson KL, Steemers FJ, Trapnell C, Shendure J. Multiplex single cell profiling of chromatin accessibility by combinatorial cellular indexing. Science. 2015 May 22;348(6237):910-4. PubMed Central PMCID: PMC4836442.

   b. McKenna A, Findlay GM, Gagnon JA, Horwitz MS, Schier AF, Shendure J. Whole-organism lineage tracing by combinatorial and cumulative genome editing. Science. 2016 Jul 29;353(6298):aaf7907. PubMed Central PMCID: PMC4967023.

   c. Cao J, Cusanovich DA, Ramani V, Aghamirzaie D, Pliner HA, Hill AJ, Daza RM, McFaline-Figueroa JL, Packer JS, Christiansen L, Steemers FJ, Adey AC, Trapnell C, Shendure J. Joint profiling of chromatin accessibility and gene expression in thousands of single cells. Science. 2018 Sep 28;361(6409):1380-1385. PubMed Central PMCID: PMC6571013.

   d. Gasperini M, Hill AJ, McFaline-Figueroa JL, Martin B, Kim S, Zhang MD, Jackson D, Leith A, Schreiber J, Noble WS, Trapnell C, Ahituv N, Shendure J. A Genome-wide Framework for Mapping Gene Regulation via Cellular Genetic Screens. Cell. 2019 Jan 10;176(1-2):377-390.e19. PubMed Central PMCID: PMC6690346.

5. Global views of development: Recently, we have begun applying single cell profiling and lineage tracing methods developed in the lab towards obtaining global views of development across a range of key organisms, including worm, fly, mouse and human.

   a. Cao J, Packer JS, Ramani V, Cusanovich DA, Huynh C, Daza R, Qiu X, Lee C, Furlan SN, Steemers FJ, Adey A, Waterston RH, Trapnell C, Shendure J. Comprehensive single-cell transcriptional profiling

of a multicellular organism. Science. 2017 Aug 18;357(6352):661-667. PubMed Central PMCID: PMC5894354.

b. Cusanovich DA, Reddington JP, Garfield DA, Daza RM, Aghamirzaie D, Marco-Ferreres R, Pliner HA, Christiansen L, Qiu X, Steemers FJ, Trapnell C, Shendure J, Furlong EEM. The cis-regulatory dynamics of embryonic development at single-cell resolution. Nature. 2018 Mar 22;555(7697):538-542. PubMed Central PMCID: PMC5866720.

c. Cusanovich DA, Hill AJ, Aghamirzaie D, Daza RM, Pliner HA, Berletch JB, Filippova GN, Huang X, Christiansen L, DeWitt WS, Lee C, Regalado SG, Read DF, Steemers FJ, Disteche CM, Trapnell C, Shendure J. A Single-Cell Atlas of In Vivo Mammalian Chromatin Accessibility. Cell. 2018 Aug 23;174(5):1309-1324.e18. PubMed Central PMCID: PMC6158300.

d. Cao J, Spielmann M, Qiu X, Huang X, Ibrahim DM, Hill AJ, Zhang F, Mundlos S, Christiansen L, Steemers FJ, Trapnell C, Shendure J. The single-cell transcriptional landscape of mammalian organogenesis. Nature. 2019 Feb;566(7745):496-502. PubMed Central PMCID: PMC6434952.

Complete List of Published Work:

https://pubmed.ncbi.nlm.nih.gov/?term=Shendure%2C+Jay%5BAuthor%5D&sort=date