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 scientific track record includes the development of a broad range of impactful technologies for genetics, genomics, molecular biology and developmental biology. Technologies or areas of application or discovery to which I and/or my lab have made significant contributions include:

1) DNA sequencing technologies, including next-generation DNA sequencing (2005); multiplex targeted sequence capture (2007, 2009, 2013); exome sequencing (2009); subassembly or synthetic long reads (2010, 2014); tagmentation-based library construction (2010, 2012); optical sequencing (2012); haplotype-resolved whole genome sequencing (2011) and exploiting proximity ligation for chromosome-scale *de novo* genome assembly (2013), metagenome deconvolution (2014) or RNA structure inference (2015).

2) Multiplex molecular methods, including massively parallel reporter assays (MPRA; 2009, 2012, 2017, 2020); saturation genome editing (2014, 2018); multiplex programming and functional assessment of amino acid substitutions (2015, 2018) or precise deletions (2017, 2022); multiplex gene synthesis and tag-directed retrieval (2012, 2015); and CRISPR-based single-cell molecular screens (2019, 2019); combinatorial indexing to profile chromatin accessibility (2015), nuclear architecture (2017), gene expression (2017, 2019, 2020), genome sequence (2020), co-assays (2018, 2020), chemical transcriptomics (2020) and spatial transcriptomics (2021); genome editing-based lineage tracing (2016); and time-resolved, multi-symbol molecular recording of cell lineage (2022) and biological signals (2024).

3) Human genetics & medical diagnostics, including exome sequencing to identify causal genes for Mendelian disorders (2009, 2009, 2010, 2015), autism (2011, 2012, 2012, 2014, 2014) and cancer (2011, 2016, 2016); non-invasive inference of fetal genomes from cell-free DNA (2012, 2015) or embryo genotypes (2015); haplotype-resolved whole genome sequencing of the HeLa cancer cell line (2013); genome-wide computational prediction of the relative pathogenicity of human genetic variants (2014); prospective functional interpretation of variants of uncertain significance in *BRCA1* (2015, 2018, 2018); genome editing-based lineage tracing of metastatic cancer (2021); genomic surveillance for bacterial pathogens (2014, 2015) or viral pandemics (2020, 2020, 2022); and cancer detection and tissue-of-origin inference from cell-free DNA (2016).

4) Mammalian gene regulation, including genome-wide maps of nucleosome positioning based on cell-free DNA (2016); saturation mutagenesis of enhancers and promoters (2019); experimental and computational modeling of mammalian gene regulation (2013, 2018), including with deep convolutional neural networks (2020); multiplex assessment of enhancer-gene regulatory interactions (2019, 2024); quantitative single-cell expression reporters for cell type-resolved profiling of developmental enhancers (2024); and genome-wide dissection of epigenetic regulation of prime editing (2024);

5) Developmental biology, including organism-scale, single cell atlases of gene expression (worm: 2017, fly: 2022, mouse: 2019, human: 2020) and chromatin accessibility (fly: 2018, 2022, mouse: 2018, human: 2020); a data-driven ontogeny of mouse development from zygote to birth (2022, 2024); whole embryo reverse genetics (2023); the application of biological recording to embryonic development (2016); and advanced *in vitro* models of early human development (2024).

B. Positions, Scientific Appointments, and Honors

Professional Experience

2023 - Present	Lead Scientific Director, Seattle Hub for Synthetic Biology (Allen-CZI-UW)
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
2018 – present	Scientific Advisor	Chan Zuckerberg Initiative
2020 – present	Scientific Advisory Board	New York Genome Center
2021 – present	Cancer Basic Biology Co-Lead	Fred Hutch-UW-Seattle Children's Cancer Consortium
2021 – 2022	Scientific Advisory Board	Open Targets
2018 – 2022	Scientific Advisory Board	Allen Institute for Immunology
2017 – 2022	Advisory Council	Allen Institute for Cell Science
2017 – 2020	Advisory Committee to NIH Director	National Institutes of Health
2015	NIH ACD Working Group	AllOfUs / US Precision Medicine Initiative
2014 – 2018	National Advisory Council	National Human Genome Research Institute
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

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C. Contributions to Science

Genomic technologies or applications to which I and/or my lab made significant contributions fall into five areas, briefly discussed below together with four representative citations on which I am sole or joint corresponding author.

1. DNA sequencing technologies: 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 additional methods that have proven impactful, including exome sequencing, haplotype-resolved genome sequencing, chromatin interaction-based genome assembly, etc.
    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. 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.
    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. Burton JN, Adey A, Patwardhan RP, Qiu R, Kitzman JO, Shendure J. Chromosome-scale scaffolding of de novo genome assemblies based on chromatin interactions. Nature Biotechnology. 2013 Dec;31(12):1119-25. PubMed Central PMCID: PMC4117202.
2. Multiplex molecular methods: My lab has a longstanding, ongoing interest in developing multiplex, sequencing-based molecular methods. Areas in which we have made substantial contributions include massively parallel reporter assays, multiplex DNA synthesis, multiplex DNA mutagenesis, multiplex genome editing, multiplex functional assays, single cell assays based on combinatorial indexing, and genome editing-based biological recording.

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. Nature Biotechnology. 2009 Dec;27(12):1173-5. PubMed Central PMCID: PMC2849652.

b. 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.

c. 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.

d. Choi J, Chen W, Minkina A, Chardon FM, Suiter CC, Regalado SG, Domcke S, Hamazaki N, Lee C, Martin B, Daza RM, Shendure J. A time-resolved, multi-symbol molecular recorder via sequential genome editing. Nature. 2022 Aug;608(7921):98-107. PubMed Central PMCID: PMC9352581.

3. Human genetics & medical diagnostics: My lab pioneered the application of genomic methods to various goals in human genetics and medical diagnostics, including the application of exome sequencing to identify the genetic basis of Mendelian disorders and autism, computational prediction of the relative pathogenicity of human genetic variants, prospective functional interpretation of variants of uncertain significance, and cell-free DNA-based cancer diagnostics.

   a. 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. Nature Genetics. 2010 Jan;42(1):30-5. PubMed Central PMCID: PMC2847889.

   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. Nature Genetics. 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. 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. Cell. 2016 Jan 14;164(1-2):57-68. PubMed Central PMCID: 26771485.

4. Mammalian gene regulation: My lab has a long-standing, ongoing interest in the development and application of experimental and computational methods to systematically measure and model mammalian gene regulation. We are increasingly focused on understanding how developmental enhancers and other aspects of the *cis*-regulatory landscape orchestrate mammalian embryonic development.

   a. 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.

   b. 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.

   c. Lalanne JB, Regalado SG, Domcke S, Calderon D, Martin BK, Li X, Li T, Suiter, CS, Lee C, Trapnell C, Shendure J. Multiplex profiling of developmental cis-regulatory elements with quantitative single-cell expression reporters. Nature Methods. 2024 Jun;21(6):983-993. PubMed Central PMCID: PMC11166576.

   d. Li X, Chen W, Martin BK, Calderon D, Lee C, Choi J, Chardon FM, McDiarmid T, Daza RM, Kim H, Lalanne JB, Nathans JF, Lee DS, Shendure J. Chromatin context-dependent regulation and epigenetic manipulation of prime editing. Cell. 2024 May 9;187(10):2411-2427.e25. PubMed Central PMCID: PMC11088515.

5. Developmental biology: My lab is increasingly focused on the application of genomic methods in the field of developmental biology, with a long-term goal of achieving a consensus ontogeny, inclusive of lineage histories, molecular states and other information, spanning the life cycle of *Mus musculus.* .

    a. 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.

    b. Huang X, Henck J, Qiu C, Sreenivasan V, Balachandran S, Amarie O, Hrabe de Angelis M, Behncke R, Chan W, Despang A, Dickel D, Duran M, Feuchtinger A, Fuchs H, Gailus-Durner V, Haag N, Hagerling R, Hansmeier N, Hennig F, Marshall C, Rajderkar S, Ringer A, Robson M, Saunders L, Silva-Buttkus P, Spielmann N, Srivatsan S, Ulferts S, Wittler L, Zhu Y, Kalscheuer V, Ibrahim D, Kurth I, Kornak W, Visel A, Pennacchio L, Beier D, Trapnell C, Cao J, Shendure J, Spielmann M. Single-cell, whole-embryo phenotyping of mammalian developmental disorders. Nature 2023 Nov 15; 623(7988):772-781. PubMed Central PMCID: PMC10665194.

    c. Qiu C, Martin BK, Welsh IC, Daza RM, Le TM, Huang X, Nichols EK, Taylor ML, Fulton O, O'Day DR, Gomes AR, Ilcisin S, Srivatsan S, Deng X, Disteche CM, Noble WS, Hamazaki N, Moens CB, Kimelman D, Cao J, Schier AF, Spielmann M, Murray SA, Trapnell C, Shendure J. A single-cell time-lapse of mouse prenatal development from gastrula to birth. Nature. 2024 Feb;626(8001):1084-1093. PubMed Central PMCID: PMC10901739.

    d. Hamazaki N, Yang W, Kubo CA, Qiu C, Martin BK, Garge RK, Regalado SG, Nichols EK, Pendyala S, Bradley N, Fowler DM, Lee C, Daza RM, Srivatsan S, Shendure J. Retinoic acid induces human gastruloids with posterior embryo-like structures. Nature Cell Biology. 2024 Oct;26(10):1790-1803. PubMed Central PMCID: PMC11469962.