OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

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| --- |
| NAME: CHURCH, GEORGE |
| eRA COMMONS USER NAME (credential, e.g., agency login): gchurch |
| POSITION TITLE: Professor of Genetics |

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 DATEMM/YYYY | FIELD OF STUDY |
| Duke University, Durham, NC | BA | 10/1974 | Zoology and Chemistry  |
| Harvard University, Cambridge, MA | PHD | 06/1984 | Biochemistry and Molecular Biology |
| UCSF, San Francisco, CA | Postdoctoral Fellow | 1986 | Stem Cells and Genomics  |

### A. Personal Statement

In 1984 with Wally Gilbert, I developed the first direct genomic sequencing method and barcode-multiplexing tags. This led to automation and software used for the first cellular genome sequence (Helicobacter) in 1994, which evolved into “in situ sequencing” (1999 & 2014) and "next generation sequencing”. I pioneered chip-based DNA libraries, genome editing and stem cell engineering and new privacy, biosafety, human engineering, environmental, biosecurity, bioethics strategies and training. My group champions open-access human genome+trait data and cells and open-source sequencing instruments. I’ve trained over 400 people in my lab since 1986 and 1000 students in my classes.

**Training, mentoring, promoting inclusive & supportive scientific research environments.** Of 88 PhD students and 117 postdocs who have graduated from my lab, 47 became professors: Bar Ilan U., BU(2), Columbia (5), DTU, Duke(2), GA-Tech, Harvard(2), Hunter, Johns Hopkins, MIT(2), Northwestern, Rutgers, Stanford, UCLA, U.Conn, UCSD(2), U.d’Evry, U.Liverpool, U.MI, U.NM, USC, UCSF(2), U.Toronto, UW Seattle (2), Weizmann, Wash U (3),Vanderbilt(3), Yale, Yonsei U. A similar number have co-founded companies in medical diagnostics, synthetic biology, and therapeutics.

**Teaching trainees to conduct ethically sound and responsible scientific research.** I meet with students regularly to teach the importance of scientific integrity in 1:1 discussions and during regular lab meetings. Trainees learn the importance of data management, how to appropriately detail and document research experiments and related activities in lab notebooks, and for manuscripts, and the importance of rigor and reproducibility in research.

I **promote the use of the highest standards of practice to ensure the safety of all individuals in the research environment** and require annual lab safety training for all. I have a dedicated lab manager who is highly skilled and experienced, who serves as our lab safety representative.

**Maintaining a record of, & training in rigorous & unbiased experimental design, methodology, analysis, interpretation & reporting of results.** I co-lead a course HTGAA at MIT, Harvard (& globally) and teach a section in the required “Responsible Conduct of Science” course (MS300). I participate in 6 other courses (in systems biology, statistics, computational biology and/or synthetic biology), bridge different schools (HBS, HLS, HKS, HSPH, MIT) and outreach to wider community via Pged.org & 305 online videos totaling 180 hours.

**Supporting trainees in activities to identify and transition into careers in the biomedical research workforce consistent with trainees' skills, interests, values. Fulfilling the need of trainees to obtain Ph.D.s in a timely fashion with skills, credentials & experiences to transition into careers in the biomedical research workforce**. I participate in 25 PhD dissertation advisory committees (DAC). I encourage PhD students and advisors to publish and graduate with high quality yet swiftly. In my lab the mean time is 5 years (SD=1.4). I help expose students with a variety of realistic options, including biotech startups, presentations from entrepreneurs-in-residence, conflict avoidance, Harvard IP, etc. (Alumni from my group have co-founded over 40 such in the past 10 years, including Editas, Dyno, Nebula, and Egenesis).

### B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

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| --- | --- |
| 2022 -  | Consultant, IntegraTX |
| 2021 -  | Consultant and Scientific Advisor, BioViva USA Inc. |
| 2021 -  | Advisor, Roswell Biotechnologies  |
| 2021 -  | Advisor, Alacris Theranostics GmbH |
| 2021 -  | Advisor, Bione  |
| 2021 -  | Consultant, Eterna  |
| 2021 -  | Consultant, G42 General Trading LLC |
| 2021 -  | Consultant, Outsized Ventures Limited |
| 2021 -  | Consultant, SNIPR Biome |
| 2020 -  | Advisor, Shenzhen Institutes of Advanced Technology, Chinese Academy of Science (SIAT) |
| 2020 -  | Advisor, Rejuvenate Bio, Inc. |
| 2020 -  | Advisor , Qihan-eGenesis Hongkong Limited |
| 2020 -  | Advisor, 4BaseCare |
| 2019 -  | Advisor, Center for Genome Engineering and Therapy, SIAT |
| 2017 -  | Visiting Professor, MIT Media Lab (Course: MAS.S61) |
| 2017 -  | Advisor, Regenesis Institute, Shenzhen |
| 2017 - 2019 | Advisor, Alibaba DAMO Academy, Hangzhou |
| 2016 -  | Director, Consortium for Space Genetics, Harvard Medical School |
| 2008 -  | Founding Core Faculty & Lead, Synthetic Biology, Wyss Institute  |
| 2006 -  | Senior Associate Faculty Member, Broad Inst. of Harvard & MIT  |
| 2005 -  | Director, Personal Genome Project  |
| 2005 -  | Editorial Boards, Nature/EMBO-MSB, Scientific American  |
| 2004 -  | Director, NIH NHGRI Center of Excellence in Genomic Science  |
| 2001 -  | Review Committee, NHGRI, BISTI, Pioneer grant, NHLBI BEE, NAS  |
| 1998 -  | Professor of Genetics, Harvard Medical School |
| 1998 -  | Director, Lipper Center for Computational Genetics  |
| 1994 - 1997 | Review Committee, National Center for Human Genome Research |
| 1990 - 1990 | Review Committee, NIH Genome Study Section  |
| 1988 -  | Faculty Member, HMS & MIT Health Sciences and Technology |
| 1988 - 1994 | Review Committee, Department of Energy Genome Project |
| 1987 -  | Director, DOE Technology development center  |
| 1986 - 1998 | Assistant/Associate Professor of Genetics, Harvard Medical School |
| 1986 - 1997 | Investigator, Howard Hughes Medical Institute  |
| 1985 - 1986 | Life Sciences Research Foundation Fellow, Anatomy, UCSF |
| 1984 - 1984 | Scientist, Biogen Research Corporation |
| 1976 - 1976 | Review Committee, National Science Foundation Program  |
| 1974 - 1975 | Predoctoral Fellow, National Science Foundation Dr. Church has disclosed key positions, appointments and affiliations in this Biosketch; however, listing all of Dr. Church’s affiliations or appointments would exceed the five page Biosketch limit, as required by the sponsor. Please contact Dr. Church for further information about their appointments and affiliations or see arep.med.harvard.edu/gmc/tech.html |

Honors

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| --- | --- |
| 2020 | Award for Outstanding Contributions to Biomolecular Technologies, ABRF |
| 2019 | Time 100 Summit Speaker, Time |
| 2019 | World Economic Forum Tech Pioneers, Inari Agriculture  |
| 2019 | Newsweek Innovators: The Creative Class of 2019, Newsweek |
| 2018 | Steven Beering Award for outstanding research contributions, Indiana School of Medicine |
| 2018 | Stem Cells and Regeneration Pioneer Award, University of Chicago Marine Biological Lab |
| 2018 | Liberty Science Genius Award, Liberty Science Center  |
| 2017 | Honorary Professor, Zhejiang University  |
| 2017 | Honorary Mayor, Hangzhou East Pharmaceutical Town |
| 2017 | Honorary Professor, Fudan University |
| 2017 | Mendel Award, European Human Genetics |
| 2017 | Time 100 Most Influential People-Titans, Time  |
| 2016 | Scripps Genomic Medicine Award, Scripps Translational Science Institute |
| 2015 | Science breakthrough of the year. CRISPR, Science |
| 2015 | Global Thinkers 100, Foreign Policy  |
| 2015 | World Economic Forum Tech Pioneers, Editas Medicine |
| 2013 | PA Andover Alumni Award of Distinction, Phillips Academy Andover  |
| 2012 | Top 10 science books (Regenesis), New Scientist  |
| 2012 | Member (Bioengineering), USA National Academy of Engineering  |
| 2012 | World changing experiments #1 ("Building a machine that can edit human DNA") , BBC |
| 2011 | Member (Chemistry), National Academy of Sciences USA  |
| 2011 | Bower Prize for Achievement in Science, Franklin Institute |
| 2011 | Lifetime Achievement Award, Personalized Medicine World Conference |
| 2010 | Steven Hoogendijk Award, Triennial International  |
| 2010 | US Presidential & EPA Green Chemistry Award (LS9), EPA |
| 2009 | Biotechnology Research Award, American Society for Microbiology  |
| 2008 | Technology Pioneer Awards (LS9 & 23andme), World Economic Forum  |

### C. Contribution to Science

**1.** Our “Genomic **Sequencing**” in 1984 and “Multiplex sequencing” in 1988 established concepts of molecular multiplexing/ barcoding, degenerate oligos and cycles of probing & imaging, which became the core of NGS along with our 1999 demonstration of in situ single-molecule amplification. In 2003 and 2005 we showed sequencing by synthesis and by ligation [1a] and tied 454 for the first NGS genome (ours larger by 8-fold than the 454 genome). By 2009, our DNA nanoball unchained ligation was producing human genomes at $1500 consumables cost [1b] and in 2012 the first human haplotype phasing (and 1E-7 consensus error rate for most of the genome). More than half of the high quality whole human genomes were being done using these 20 CGI machines and over 350,000 non-invasive prenatal aneuploidy clinical tests by 2014. In 1999 we published the first FISSEQ experiments evolving by 2014 to subcellular resolution and multicellular context [1c] combining the speed and comprehensiveness of single-cell NGS with the precision and ease-of-use of in situ hybridization and today protein & RNA barcodes [1d].

1. Shendure J, Porreca GJ, Reppas NB, Lin X, McCutcheon JP, Rosenbaum AM, Wang MD, Zhang K, Mitra RD, Church GM (2005) Accurate Multiplex Polony Sequencing of an Evolved Bacterial Genome. **Science** 309:1728-32. PMID: 16081699
2. Drmanac R, et al. (2009) Human Genome Sequencing Using Unchained Base Reads on Self-assembling DNA Nanoarrays. **Science** 327:78-81. PMID: 19892942
3. Lee J, Daugharthy E, Scheiman J, Kalhor R, Terry R, Yang JL, Li C, Amamoto R, Peters D, Ferrente TC, Marblestone A, Bernard A, Turczyk BM, Conway N, Inverso S, Levner D, Mali P, Rios X, Jeanty SSF, Jones AR, Aach J, Church GM (2014) Highly multiplexed three-dimensional subcellular transcriptome sequencing in situ. **Science** 343:1360-3. PMCID:PMC4140943
4. Goodwin DR, Vaughan A, Leible D, Alon S, Henry GL, Cheng A, Chen X, Zhang R, Xue AG, Wassie AT, Sinha A, Bando Y, Kajita A, Marblestone AH, Zador AM, Boyden ES, Church GM, Kohman RE Expansion Sequencing of RNA Barcoded Neurons in the Mammalian Brain: Progress and Implications for Molecularly Annotated Connectomics. Biorxiv. 2022. doi.org/10.1101/2022.07.31.502046

2. **I**nnovative **Neurotechnologies** (BRAIN) and epigenetic programming[2a] We worked with the Cepko lab to establish the first barcoded developmental lineage tracing methods[2b]. Since then we have sought other ways to combine synthetic biology and in situ sequencing [1c][1d] with neurobiology to enable input/output at the scale of all individual neurons [2c][2d] as well as development ex vivo cultures of complex organoids and multicellular tissues able to restore function in preclinical transplants with resistance to autoimmunity.[2a]

1. Ng AHM, Khoshakhlagh P, Arias JER, Pasquini G, Wang K, Swiersy A, Shipman S, Appleton E, Kiaee K, Kohman R, Vernet K, Dysart M, Leeper K, Saylor W, Huang J, Graveline A, Taipale J, Hill D, Vidal M, Melero-Martin JM, Busskamp V, Church GM. A comprehensive library of human transcription factors for cell fate engineering. Nature Biotech. Nov-2020. PMID: 33257861.
2. Walsh C, Ryder L, Cepko C, Church GM, Tabin C (1992) The dispersion of neuronal clones across the cerebral cortex. **Science** 258: 317-320. PMID: 1411530
3. Marblestone AH, Zamft BM, Maguire YG, Shapiro MG, Cybulski T, Glaser JI, Amodei D, Stranges B, Kalhor R, Dalrymple DA, Seo D, Alon E, Maharbiz MM, Carmena JM, Rabaey JM, Boyden E, Church GM, Kording KP (2013) Physical Principles for Scalable Neural Recording. **Frontiers in Neuroscience.** 7(137)1-24. PMCID: PMC3807567
4. Alivisatos AP, Chun M, Church GM, Deisseroth K, Donoghue JP, Greenspan RJ, McEuen PL, Roukes ML, Sejnowski TJ, Weiss PS, Yuste R (2013) The Brain Activity Map **Science** 339:1284-5. PMCID: PMC3722427

3. Multiplex Oligonucleotide libraries **Genome Engineering** via. In 2004 we established the first methods for utilizing DNA from chips with error correction to make synthetic genes, libraries and operons [3a]. These technologies have been made available through Agilent, CustomArray and Gen9. We were the first to apply such oligo libraries to bacterial metabolic optimization [3b], GROs[4b][3d], cis-regulatory libraries [3c] and to human CRISPR genome editing libraries [4c]. We have also established ways to do library-vs-library selections and screens.

1. Tian J, Gong H, Sheng N, Zhou X, Gulari E, Gao X, Church GM (2004) Accurate Multiplex Gene Synthesis from Programmable DNA Chips. **Nature** 432: 1050-4. PMID: 16516567
2. Wang HH, Isaacs FJ, Carr PA, Sun ZZ, Xu G, Forest CR, Church GM (2009) Programming cells by multiplex genome engineering and accelerated evolution**. Nature.** 460(7257):894-8. PMID: 19633652
3. Goodman DB, Church GM, Kosuri S (2013) Causes and effects of N-terminal codon bias in bacterial genes. **Science** 342:475-9. PMID: 24702823
4. Nyerges A, Vinke S, Flynn R, Owen SV, Rand EA, Budnik B, Keen E, Narasimhan K, Marchand JA, Baas-Thomas M, Liu M, Chen K, Chiappino-Pepe A, Hu F, Baym M, Church GM (2023) Swapped genetic code prevents viral infections and gene transfer. Nature. 2023 PMID: 36922599

4**. Genomically Recoded Organisms** (GRO), CRISPR. The 2009 MAGE method [3b] allowed us to make a radically altered bacteria genome (4.7 Mbp GRO), including genome change of 1 of the 64 triplet codons, eventually 3 of 64, enabling resistance to (apparently) all viruses [3d] and full dependence on an amino acid not found in nature -- undetectable escape at one in a trillion cells [4b]. In 2007, researchers at Danisco harnessed CRISPR to protect bacteria.  In January 2013, our lab (side-by-side with a team lead by ex-lab members) adapted CRISPR for homologous recombination in eukaryotic (human) genomes. Our paper was the first using normal human cells, first with sgRNA libraries and first with computational avoidance of off-targets [4c] We developed the first CRISPR gene-drive and associated safety features for use against disease vectors and invasive species [4d]. We have extended multiplex editing from 1 to 5 edits per cell in populations of billions of cells in 2009 [3b] up to 27,000 per cell in 2020, and up to 69 edits per germline pig [4a].

1. Anand RP, et al. Design and testing of a humanized porcine donor for xenotransplantation. Nature. 2023 PMID: 37821590
2. Mandell DJ, Lajoie MJ, Mee MT, Takeuchi R, Kuznetsov G, Norville J, Gregg CJ, Stoddard BL, Church GM (2015) Biocontainment of genetically modified organisms by synthetic protein design. **Nature** 518:55-60. PMID: 25607366
3. Mali P, Yang L, Esvelt KM, Aach J, Guell M, DiCarlo JE, Norville JE, Church GM. RNA-guided human genome engineering via Cas9. Science. 2013 Feb 15;339(6121):823-6. PMCID: PMC3712628.
4. Esvelt KM, Smidler AL, Catteruccia F, Church GM. Concerning RNA-guided gene drives for the alteration of wild populations. Elife. 2014 Jul 17;3 PMCID: PMC4117217.

5**.** **Machine Learning for protein design**, **Nanopore sequencing, DNA nanostructures**: In 1988 the first AFM images inspired me to survey single-molecule methods and settle on patch-clamp electrophysiology (in use since 1976). This led us to the first nanopore-sequencing patent (#5,795,782) licensed to Agilent then to Oxford Nanopore Tech. Later we co-invented methods for tag-dNTP polymerase-pore fusions in use at Genia/Roche. In 1977, my experience with tRNA crystallography lead to a dream of designed DNA-nanostructures. Ned Seeman published the first examples in 1982 and my group published a tool for computer aided-design [5d] and the first nanorobot [5b]. The full integration of chip-based oligonucleotide libraries [3a] writing, copying and NGS-reading of barcode-indexed digital information [5c] is now the basis of a consortium of 41 teams (DNAstoragealliance.org). Further integration of DNA Read-Write with machine learning and accelerated evolution [3b] has enabled testing of millions of protein designs including useful gene therapy capsids [5a].

1. Bryant D, Bashir A, Sinai S, Jain N, Ogden P, Riley P, Church G, Colwell L, Kelsic E. Massively parallel deep diversification of AAV capsid proteins by machine learning. Nature Biotech 2020 PMID: 33574611.
2. Douglas SM, Bachelet I, Church GM (2012) A logic-gated nanorobot for targeted transport of molecular payloads. Science 335, 831-834. PMID: 22344439
3. Church GM, Gao Y, Kosuri S (2012) Next-generation Digital Information Storage in DNA. **Science** 337(6102):1628. PMID: 22903519
4. Douglas SM, Marblestone A, Teerapittayanon S, Vazquez A, Church GM, Shih WH (2009) Rapid prototyping of three-dimensional DNA-origami shapes with caDNAno **Nucleic Acids Res** 37(15):5001-6. PMCID: PMC2731887

Complete List of Published Work in My Bibliography:
<https://www.ncbi.nlm.nih.gov/myncbi/george.church.1/bibliography/public/>