BIOGRAPHICAL SKETCH

NAME: **George M. Church, PhD**

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

POSITION TITLE: **Professor of Genetics**

EDUCATION/TRAINING

| INSTITUTION & LOCATION | DEGREE | Completion Date | FIELD OF STUDY |
| --- | --- | --- | --- |
| **Duke University, Durham, NC** | **B.A.** | **10/1974** | **Zoology & Chemistry** |
| **Harvard University, Cambridge, MA** | **Ph.D.** | **06/1984** | **Biochem. & Mol. Biology** |

# A. Personal Statement: training & mentoring

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 411 people in my lab since 1986 and 900 students in my classes.

**Training, mentoring, promoting inclusive & supportive scientific research environments.**Of 65 PhD students and 81 postdocs who have graduated from my lab, 44 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. PhDs from my lab include 14 females.

**Maintaining a record of, & training in rigorous & unbiased experimental design, methodology, analysis, interpretation & reporting of results.** I teach a discussion section and Didactic Sessions of the required “Responsible Conduct of Science” course (MS300). I participate in 6 other courses (my role typically systems biology, statistics, computational biology and/or synthetic biology), bridge different schools (HBS, HLS, HKS, HSPH) and outreach to the wider community via Pged.org & 178 recent open online videos totaling 97 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 15 such in the past years, including Abvitro/Juno/Celgene, Editas and Egenesis).

# B. Positions and Honors

**Positions and Employment**

1974-1975 National Science Foundation Predoctoral Fellow

1984 Scientist, Biogen Research Corporation, Cambridge, MA

1985-1986 Life Sciences Research Foundation Fellow, Anatomy, Univ. Calif., San Francisco, CA

1986-1997 Howard Hughes Medical Institute Investigator

1986-1998 Assistant/Associate Professor of Genetics, Harvard Medical School, Boston, MA

1998-present Professor of Genetics, Harvard Medical School, Boston, MA

1987-present Director of the DOE Technology development center

2004-present Director of NIH NHGRI Center of Excellence in Genomic Science

2005-present Director of the Personal Genome Project

2006-present Broad Inst. of Harvard & MIT (1990 Genome Center Co-founder)

2008-present Wyss Institute for Biologically Inspired Engineering

**Scientific Review & Advisory Roles**

1976 National Science Foundation Program Project Grant Review Committee

1988,1992,1994 Department of Energy Genome Project Grant Review Committee

1990 NIH Genome Study Section Grant Review

1994-1997 National Center for Human Genome Research Review Committee

2001-present NHGRI, BISTI, Pioneer grant review committees, NHLBI BEE, NAS committees

2005-present Editorial Boards Nature/EMBO-MSB, Scientific American

**Honors, Awards**

2008 World Economic Forum Technology Pioneer Awards (LS9 & 23andme)

2009 American Society for Microbiology Biotechnology Research Award

2010 Consumer Genetics Champion & Public Initiative Awards

2010 US Presidential & EPA Green Chemistry Award (LS9)

2010 Triennial International Steven Hoogendijk Award

2011 Personalized Medicine World Conference Lifetime Achievement Award

2011 Franklin Institute Bower Prize for Achievement in Science

2011 National Academy of Sciences USA (Chemistry)

2011 National Academy of Engineering USA (Bioengineering)

# C. Contribution to Science

**1. Next-Generation Sequencing (NGS): Fluorescent Next-generation, In situ.**

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 and in 2012 the first human haplotype phasing (and bonus of 1E-7 consensus error rate for most of the genome). Arguably more than half of the high quality whole human genomes were being done using these 20 CGI machines plus over 350,000 non-invasive prenatal aneuploidy tests by 2014. In 1999 we published the first FISSEQ experiments evolving by 2014 to subcellular resolution and multicellular context [1d] combining the speed and comprehensiveness of single-cell NGS with the precision and ease-of-use of in situ hybridization.

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. Peters BA, et al. (2012) Accurate whole genome sequencing and haplotyping from 10-20 human cells. **Nature** 487: 190-195. PMCID: PMC3397394
4. 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

**2. Innovative Neurotechnologies (BRAIN)**

We helped the Cepko lab establish the first barcoded developmental lineage tracing methods[2a]. Since then we have sought other ways to combine synthetic biology and in situ sequencing [1d] with neurobiology to enable input/output at the scale of all individual neurons [2b][2c] as well as development ex vivo cultures of complex brain-like organoids[2d].

1. 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
2. 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. 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. Busskamp V, Lewis NE, Guye P, Ng AHM, Shipman S, Byrne SS, Sanjana NE, Li Y, Weiss R, Church GM (2014) Rapid neurogenesis through transcriptional activation in human stem cells. **Molecular Systems Biology** 10:760: 1-21. PMCID: PMC4299601

**3. Oligonucleotide libraries and Multiplex Accelerated Genome Engineering (MAGE)**

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 been made available through Agilent, CustomArray and Gen9. We were the first to apply such oligo libraries to bacterial metabolic optimization [3b], GROs[4a], cis-regulatory libraries [3c] and to human CRISPR genome editing libraries [4b]. We have also established ways to do library-vs-library selections and screen [3d].

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. Gu L, Li C, Aach J, Hill DE, Vidal M, Church GM (2014) Multiplex single-molecule interaction profiling of DNA-barcoded proteins. **Nature.** 515:554-7. PMCID: PMC4246050

**4. Genome Editing: Genomically Recoded Organisms (GRO), CRISPR.**

The 2009 MAGE method [3b] allowed us to make the most radically altered bacteria genome (4.7 Mbp GRO), including genome change of 1 of the 64 triplet codons, enabling resistance to multiple viruses and full dependence on an amino acid not found in nature -- undetectable escape at one in a trillion cells [4a]. In 2007, researchers at Danisco harnessed CRISPR to protect bacteria.  In January 2013, we (and two other labs) adapted CRISPR for homologous recombination in eukaryotic (human) genomes [4b].  By August 2013 we helped make CRISPR much more specific [4c] and work efficiently in many animals and plants. We developed the first CRISPR gene-drive and associated safety features for use against disease vectors and invasive species[4d].

1. 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
2. Mali P, Yang L, Esvelt KM, Aach J, Guell M, DiCarlo JE, Norville J, Church GM (2013) RNA-guided human genome engineering via Cas9. **Science** 339: 823-6. PMCID: PMC3712628
3. Mali P, Aach J, Stranges PB, Esvelt KM, Moosburner M, Kosuri S, Yang L, Church GM (2013) Cas9 transcriptional activators for target specificity screening and paired nickases for cooperative genome engineering. **Nature Biotech** 31:833-8. PMCID: PMC3818127
4. Esvelt KM, Smidler AL, Catteruccia F, Church GM (2014) Concerning RNA-Guided Gene Drives for the Alteration of Wild Populations. **eLife** 3:e03401. PMCID: PMC4117217

**5.** **Nanopore sequencing and DNA nanostructures**

In 1988 the first AFM images of single DNA molecules inspired me to survey all single-molecule methods and settle on onto patch-clamp electrophysiology (in use since 1976). This led to the first nanopore-sequencing patent [5a] 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 [5b] and the first nanorobot [5c] which has since been scaled-up in pre-clinical trials in Israel. The full integration [5d] of chip-based oligonucleotide libraries [3a] writing, copying and NGS-reading of barcode-indexed digital information is now in production phase for two (early-stage) commercial products.

1. Church GM, Deamer DW, Branton D, Baldarelli R, Kasianowicz J (1998) US Patent # 5,795,782 Characterization of individual polymer molecules based on monomer-interface interactions.
2. 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
3. Douglas SM, Bachelet I, Church GM (2012) A logic-gated nanorobot for targeted transport of molecular payloads. Science 335, 831-834. PMID: 22344439
4. Church GM, Gao Y, Kosuri S (2012) Next-generation Digital Information Storage in DNA. **Science** 337(6102):1628. PMID: 22903519

**Public db URL:** <http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/41157672>

**D. Research Support**

**Ongoing Research Support**

A27136 Church 09/01/15 – 08/31/18

Charoen Pokphand Group

*Porcine Genome Editing for Pathogen Resistance*

We propose to use CRISPR systems to produce pigs resistant to Porcine Reproductive & Respiratory Syndrome Virus (PRRSV) and main Porcine Epidemic Diarrhea Virus (PEDV).

MCB-1330914 Keasling (UCBerkeley) 09/15/13 – 08/31/18

NSF

*Synthetic Biology for Yeast*

The project goal is to design and build a module consisting of three polyketide synthases for yeast.

Role: Co-Investigator

74178 Church 01/01/17 – 12/31/18

Robert Wood Johnson Foundation

*Harnessing patient participation as a means for sharing phenotypes for research*

The goal of this project is to investigate efficient methods for core phenotypic data collection and aggregation, and also to develop and deploy a tool or system for collecting and aggregating core data.

R01 HL130793 Cantor 09/10/15– 05/31/19

NIH/NHLBI

*Megakaryoctye Transcription Factor Activation to Enhance in vitro Platelet Production from Human* IPSCs

The Church laboratory will be responsible for performing FISSIQ on the bone marrow sections provided by the Cantor lab. The Church lab will assist the Cantor lab in overlaying the immunofluorescence and sequencing images for data analysis.

Role: Subcontract PI

W911NF-17-2-0079 Church 05/15/17 – 05/14/19

DARPA

*Design of Cellular Blocks, their Programmatic Assembly into Biological Meshes, and the Synthesis of Tissue-Like Structures*

The goal of this project is to develop a strategy for growing cellular shapes and patterns from a single progenitor human induced pluripotent stem cell (iPSC).

RF1 AG048056 Yankner / Church 08/15/14 – 06/30/19

NIH / NIA

*Genome Engineering an IPSC Model of Alzheimer's Disease*

The overall goal of this proposal is to bring together new genome engineering and stem cell technology to further our understanding of AD genetics and pathogenesis.

W911NF-17-2-0089 Church 06/13/17 – 12/12/19

IARPA

*A Cell-Type Specific Platform for Identifying Toxicity of Proteins and Polypeptides*

The goal of this project is to establish a set of methods for evaluating sequences of unknown function for their threat potential as toxic polypeptides through an vitro expression system and in an engineered bio-contained strain of E. coli.

U01 GM110714 Brady (Rockefeller) 07/01/15 – 04/30/20

NIH / NIGMS

*A minimally invasive synthetic biology-driven approach for natural products discovery*

The work outlined in this proposal is designed to establish a new turnkey natural product discovery platform -from the development of model strains and streamlined methods for the capture and bioinformatics identification of novel biosynthetic diversity, through to the expression and characterization of natural products themselves.

Role: Subcontract PI

OPP1175154 Church 11/22/17 – 05/31/20

Bill and Melinda Gates Foundation

*Engineering skin as a bioreactor for production and sustained delivery of therapeutic agents to the blood stream for immune augmentation*

We utilize skin as a delivery platform that can together address outstanding issues of: non-invasive delivery method administered at a single site, antibody production of serum concentration in the range of 10-100 µg/mL, and validation in human samples – human skin explants and human skin/mouse chimera models, an essential feature that expedites the design-build-test cycle of genetically modified human tissues.

RM1HG008525 Church 09/21/15 – 06/30/20

NIH / NHGRI

*Center for Genomically Engineered Organs*

The Center for Genomically Engineered Organs will develop methods for making tissues in laboratories that closely match normal or diseased tissues in humans and animals.

N66001-17-2-4056 Church 07/01/17 – 06/30/20

DARPA

*Molecular Control and Prevention of Genome Editing*

The goal of this project is to develop tools to control genome editing through a recoded viral delivery system, promoter engineering to enable tissue specific expression and guide RNA tuning for single nucleotide discrimination. We also plan on developing a CRISPR/Cas9-based genetic defense system to safeguard humans and other organisms from natural viral pathogens to neutralize the targeted threat.

D16PC00008 Church 01/15/16 – 01/14/21

IARPA

*Cortical architecture and algorithms for machine listening*

This project aims to combine three algorithmic ideas that are used simultaneously in the brain that are usually employed one at a time in machine learning: (1) deep learning (2) fast learning and readout (3) Bayesian integration and selection.

R01MH113279 Yankner 09/26/16 – 06/30/21

NIH/NIMH

*Exploring a Novel Paradigm of Schizophrenia and Bipolar Disorder*

This project aims to understand schizophrenia and bipolar disorder by capitalizing on genetically engineered mouse models and induced progenitor stem cell lines, and will advance new technology to sequence the transcriptome in single brain cells in situ, enabling the convergence of multiple data streams at single cell resolution.

Role: Co-Investigator

DE-FG02-02ER63445 Church 12/01/16 – 11/30/21

DOE

*Microbial Ecology, Proteogenomics & Computational Optima*

This project studies proteomics and cell models for Prochlorococcus and Pseudomonas.