Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press



J. Craig Venter (1946–2026)

Mark D. Adams

Genome Res. published online November 23, 2026
Access the most recent version at doi:10.1101/gr.283001.126

P<P Published online November 23, 2026 in advance of the print journal.

Open Access Freely available online through the *Genome Research* Open Access option.

Creative Commons License This article, published in *Genome Research*, is available under a Creative Commons License (Attribution-NonCommercial 4.0 International), as described at http://creativecommons.org/licenses/by-nc/4.0/.

Email Alerting Service Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or **click here.**

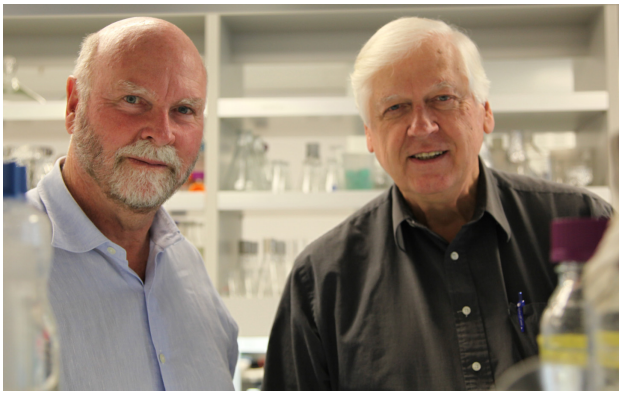


To subscribe to *Genome Research* go to:
https://genome.cshlp.org/subscriptions

© 2026 Adams; Published by Cold Spring Harbor Laboratory Press

Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press

J. Craig Venter (1946–2026)



Craig Venter and Hamilton "Ham" Smith (1931–2025). Image by Heather Kowalski, courtesy of J. Craig Venter Institute (2010).

J. Craig Venter, a giant in genomics, passed away this spring, having revolutionized the field several times over. Throughout his career, Craig Venter challenged conventional wisdom, sought funding to pursue his ideas from non-traditional sources, and always pushed others to see the potential of thinking big. Along the way, he attracted and inspired many people to join him in pushing frontiers and to have fun doing it.

Growing up in the San Francisco Bay area, Craig was a disinterested student, champion swimmer, and adventure lover who initially chose surfing over college. But faced with the draft for the war in Vietnam, he enlisted in the Navy, trained as a medic, and spent 1967–68 as a hospital corpsman in Da Nang. His experience of the seemingly random fragility and resilience of human life left him determined to return and make something of himself. He also taught himself to sail, kindling a passion that continued throughout his life. In 1969, he enrolled in community college, then transferred to the still-new University of California, San Diego. Six years later, he had completed a Ph.D. in physiology and pharmacology, working with Nathan Kaplan on the adrenaline receptor. Skipping a postdoc, he joined the faculty of the State University of New York at Buffalo and Roswell Park Comprehensive Cancer Center, where he continued to work on understanding how cells respond to neurotransmitters.

He joined the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health (NIH) in Bethesda in 1984. Frustrated by the difficulty of cloning new receptor genes, he embraced new DNA sequencing technologies and his lab was among the first to have automated DNA sequencing machines that read fluorescent DNA bases, introduced by Applied Biosystems in 1987.

I joined Craig's lab at NIH as a postdoc in May 1990. I'd seen an ad in the back of *Science* seeking both postdocs and software engineers to work on the Human Genome Project (HGP). At the time, like many in the biological sciences community, I wasn't yet convinced of the idea. It seemed blatantly unachievable with the available tools. But I was interested in the emerging field of bioinformatics, so it seemed like it would be a good opportunity.

On the day of my interview, I flew from Detroit and took the metro to Twinbrook—Craig's lab was in an off-NIH-campus building with several others from NINDS. As someone who worked on amino acid transport in *E. coli* and had sequenced only a single six-gene operon, I really had no idea what my prospects were. Throughout the day, I got to meet the talented, lively, and collegial group that made up the Venter lab, many of whom would continue to work with Craig for years. In what I would learn was typical Craig fashion, he made me an offer before I left but I had another interview set up the next day at Parke-Davis, a pharmaceutical company in Ann Arbor. Toward the end of my day there, who should I see in the hall but Craig! He was on a consulting visit and told my host in no uncertain terms that they should not hire me, perhaps only half in jest. I took it as a sign of confidence and let him know the next day that I'd be joining his lab.

When I started in the lab, most of the group was working on sequencing cosmids, which carry 30–50 kb of DNA. Careful analysis of the first three cosmids, mapping to a suspected Huntington's disease locus and sequenced over a period of several weeks, revealed the presence of only a few likely exons. While these represented among the largest contiguous stretches of the human genome sequenced to date, it was also clear what a long road lay ahead.

Another part of the lab was working on cloning genes for G protein-coupled receptors (GPCRs) that are activated by acetylcholine—a major regulator of key bodily functions. The state of the art at the time was to make radioactively labeled probes from the sequence of one receptor cDNA and hybridize it to a cDNA library consisting of tens of thousands of different sequences. For genes expressed at low levels, like GPCRs, there was often only a single "hit," which then required tedious work to recover and confirm the clone.

A few weeks into my post-doc, Craig returned from a trip to Japan and said that while he had a lot of time on the plane, he wondered what we would find if we selected cDNA clones *at random* from the library. He was interested in GPCRs, but others were interested in all sorts of other genes that hadn't yet been cloned—what if there was something for everyone?

I had been working on a double-stranded sequencing protocol to expand the types of clones, such as cDNAs, that could be run on automated sequencers beyond the commonly used single-stranded templates from bacteriophage M13 libraries. Running with Craig's idea, I isolated DNA from 96 random cDNA clones from a human brain library and sequenced them.

In that first batch of cDNA clones sequenced, two stood out like clarion calls to the future of genomics. They were the first (at the time) mammalian homologs of *Drosophila* genes encoding Notch and Enhancer of split. The Enhancer of split gene cluster encodes key downstream effectors of the Notch signaling pathway that are critical for cellular differentiation during development.

Corresponding author: mark.adams@jax.org
Article published online before print. Article and publication date are at https://www.genome.org/cgi/doi/10.1101/gr.283001.126. Freely available online through the *Genome Research* Open Access option.

© 2026 Adams This article, published in *Genome Research*, is available under a Creative Commons License (Attribution-NonCommercial 4.0 International), as described at http://creativecommons.org/licenses/by-nc/4.0/.

Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press

It was immediately clear that random sequencing of cDNAs could be a powerful approach for discovering human genes at an accelerated pace and larger scale than cosmid sequencing. Tony Kerlavage coined the term "expressed sequence tags" or ESTs for these single-read sequences of cDNA clones, an homage to the "sequence tagged sites" or STSs that were introduced in 1989 as a way of simplifying genome mapping (Olson et al. 1989).

As the EST paper was nearing submission to *Science*, it went through the standard internal review process for manuscripts at NIH. One well-respected scientific reviewer was adamant that the paper should not be published because the sequences were incomplete, which he thought was an affront to good science. He was overruled.

The manuscript also caught the attention of Reid Adler in the Office of Technology Transfer. With encouragement from an attorney at Genetech, NIH decided to file patents on ESTs. The rationale was that ESTs would be considered as prior art—making cloning of the full-length cDNA "obvious" in patent parlance—and implying that it would no longer be possible to gain patent protection on the few genes where that protection might be necessary to warrant the drug development investment to bring the invention to patients. Reid also felt that NIH should pursue the filings so that the patentability debate could occur publicly, rather than being driven by companies with no interest in sharing their strategies.

The EST paper, published in *Science* in June 1991 (Adams et al. 1991), made waves. ESTs embodied the promise of the HGP without the 15 year wait—a shortcut to the genes. The attendant outcry about patents fed the fire. Incyte Corp., a newly founded biotech company, immediately shifted its entire focus to building an EST database to support drug discovery. Several months later, Craig was approached by Wally Steinberg from HealthCare Investment Corp. to start a company based on ESTs. It was becoming difficult to extend EST sequencing to tissues outside the mandate of NINDS, so Craig was considering leaving, but he wanted to do science, not run a company. At a lunch at Andalucia, a Spanish restaurant near the lab, Craig proposed the idea of two companies—a non-profit run by him and a for-profit that would own and license out the non-profit's intellectual property. The idea stuck, and The Institute for Genomic Research (TIGR) and Human Genome Sciences (HGS) were founded in June 1992, with a $70M commitment to TIGR from HealthCare Ventures. Only a year later, SmithKline Beecham (now GlaxoSmithKline) paid HGS $125M for a license to the TIGR/HGS database.

The arrival of Bill Haseltine as the CEO of HGS disrupted the relationship between the two organizations. Craig fiercely protected TIGR's scientific independence, and Bill insisted that TIGR existed solely to make HGS successful. Joint work to rapidly expand the EST database proceeded but was increasingly fraught. TIGR's initial right to publish data within six months ended up negotiated away based on leverage from HGS. The $70M wasn't paid up front, but on a quarterly schedule. A delayed payment from HGS would have meant a missed payroll at TIGR. When the large EST compendium was published in a special supplemental issue of *Nature* in 1995 (Adams et al. 1995), the sequences were accessible only through a Material Transfer Agreement with restrictive terms and "reach-through" intellectual property rights. In response to the continued delays and restricted access to the TIGR EST data, a large public EST sequencing consortium was founded, with support from Merck. This effort went on to sequence hundreds of thousands of ESTs, placing them in the public domain, and leading to the current standards for rapid release of genomic data. After publication of the human genome drafts in 2001, an in-depth comparison of the EST database with the annotated genome showed that the vast majority of protein-coding genes were matched by an EST sequence, confirming that this shortcut strategy had been highly effective (Nekrutenko 2004).

While HGS was attempting to control TIGR's EST work, Craig was thinking about the future—and areas of genomics that wouldn't be a target for conflict with HGS. He met Hamilton ("Ham") Smith at a genome ethics meeting in Bilbao, Spain in early 1993. An initial conversation in a bar turned into a 30 year friendship and scientific partnership. At a TIGR retreat soon after that, Ham proposed that TIGR apply whole genome sequencing (WGS) to the complete genome of *Haemophilus influenzae* Rd, the bacterium that he had been working on for many years and the source of the restriction enzyme HindII that was the basis of his Nobel Prize in Physiology or Medicine in 1978. Ham was a tinkerer and an amateur programmer; he still worked in the lab (and continued to do so for years). He had done the math and estimated that it would take about a month of TIGR's sequencing capacity to collect the sequence reads and he promised to write the computer program to assemble the data. We were sold from the start. Ham's computer program didn't pan out, but Granger Sutton had been working for months on software to assemble EST sequences into full-length cDNAs—and there were four times as many ESTs as the number of sequence fragments we planned to acquire for the *Haemophilus* project. He set to work modifying the software, creating what would become a lynchpin of bacterial genomics, the TIGR Assembler.

The complete sequence and annotation of the *H. influenzae* genome was published in *Science* in July 1995 (Fleischmann et al. 1995). The paper arrived like a thunderclap in the genomics community, reinforced a few months later with publication of the genome sequence of *Mycoplasma genitalium* (Fraser et al. 1995). The power of the shotgun strategy, plus directed sequencing to fill the gaps, opened wide opportunities for microbiology. At least as impactful as the speed was the immediate appreciation of the value of completeness. Craig insisted that TIGR set a high bar for genome sequence quality, setting the standard for microbial genome projects for years to come. With 100% of the bases covered, everything that was known about the biology of *H. influenzae* now needed to be understood in the context of its genome.

In 1997, before the idea of Celera was even conceived, Jim Weber and Gene Myers proposed a WGS-focused strategy for the human genome in a perspective piece in *Genome Research* (Weber and Myers 1997), while Phil Green laid out the arguments against the strategy (Green 1997).

In early 1998, Steve Lombardi at Applied Biosystems (ABI) left several messages for Craig, wanting to talk about starting a company to sequence the human genome. I was Principal Investigator (PI) of one of the early NHGRI-funded sequencing centers at TIGR, working with Mel Simon at Caltech to map and sequence Chromosome 16. The idea of a company to sequence the genome seemed ludicrous. Craig eventually called back and in February, Craig, Tony Kerlavage, and I flew to Foster City for a meeting with Mike Hunkapiller, Bill Efcavitch, and others to see a new 96-capillary automated sequencer that was under development. They thought that the increased throughput and automation, combined with the shotgun sequencing strategy, would be a successful pairing to make genome sequencing faster and less expensive. And ABI's parent company, PerkinElmer, was interested in "moving up the value chain" from selling tools and reagents

Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press

toward higher value products. We estimated how long it would take to collect 7×–8× coverage of the human genome and concluded that 200 sequencers running flat out for a year could do the job; it seemed feasible.

By early May 1998, the PerkinElmer board had approved the investment to create Celera Genomics. The announcement came the day before the Cold Spring Harbor Genome Mapping and Sequencing meeting started. The PIs of the initial NHGRI-funded sequencing centers were meeting ahead of the conference to exchange information and plan at a time of slow progress. The announcement of Celera disrupted that agenda.

Just before the PI meeting started, Craig pulled aside Gerry Rubin from UC Berkeley and asked if he would collaborate to sequence the genome of *Drosophila melanogaster* as a warm-up exercise for the human genome. Gerry had been working on bacterial artificial chromosome (BAC)-based sequencing for several years and had completed over a third of the genome. Once assured that the data would be made freely public, he agreed.

After Celera's founding in May 1998, it took a year for production-scale sequencing to start, following renovations to the Rockville facility, development of the sequencing methods at scale, hiring of 500 people, and deployment of the new ABI 3700 sequencers. The sequencer room spanned the length of a football field, with rows of 3700s lined up in pairs and a giant double helix hung from the ceiling across the entire expanse. Downstairs was the DNA prep room that would produce 100,000 plasmid templates and 200,000 sequencing reactions each day. There resided the most closely held secret at Celera: an instrument for DNA extraction that used a magnet to raise and lower ball bearings in a 96-well plate to get efficient mixing. In their own separate wing of the building, Gene Myers, newly recruited from the University of Arizona, assembled a team of 40 Ph.D. computer scientists to build the genome-scale assembly software.

Craig's office witnessed an endless stream of meetings and phone calls with the science team, the business team that relied on his charisma and contacts to sell database subscriptions, and frequently, reporters. He was a strong believer in the adage that any press is good press. The writer James Shreeve would spend nearly a year "embedded" with Craig and the Celera team, culminating in his terrific account "The Genome War" with its provocative subtitle: "How Craig Venter Tried to Capture the Code of Life and Save the World." Somehow, Craig continued to find time to go sailing.

We devoted the summer of 1999 to sequencing the *Drosophila* genome as proof of principle for a larger-scale shotgun assembly program. The collaboration with Gerry Rubin's lab culminated in an annotation jamboree that brought together over two dozen *Drosophila* experts who got a first look at the annotated genome and contributed to the manuscripts interpreting the sequence that were published in *Science* (Adams et al. 2000; Myers et al. 2000; Rubin et al. 2000). The jamboree was an intense and remarkable gathering that fulfilled Craig's promise of a freely available genome sequence. At the end of each day, participants from the highly collaborative *Drosophila* community would give brief descriptions of what they found, often with a sense of awe. Gerry Rubin described it as "the most intellectually stimulating time of [his] career."

Although it didn't feel like it at the time, the human genome "race" transpired quite quickly. Over only about eight months, from the fall of 1999 into the spring of 2000, Celera collected 5.3× coverage of the human genome, with about 60% contributed by Craig's DNA. Faced with whether to include the data from the Human Genome Sequencing Consortium (HGSC, aka "the public project") or ignore it, a decision was made to try to produce the best possible product by integrating the two data sets, adding the BAC-scale scaffolding information from the HGSC to Celera's paired-end sequencing from a wide range of clone sizes. This led to much discussion about whether Celera's genome was simply a repackaging of the HGSC data.

Later, Gene's group determined that the HGSC contribution to the Celera assembly was "≈1% of sequence length and 35,000 errors of order … that were overcome by reliance on Celera's mate-pair data" (Adams et al. 2003). It seems that the variable quality of BAC assemblies introduced more uncertainty into the assembly than it solved. Ultimately, it is the WGS strategy that has endured, complemented by long-range linking information that is now primarily in the form of Pacific Biosciences and Oxford Nanopore Technologies long reads that can span complex repetitive regions of the genome, leading to full "telomere-to-telomere" assemblies (Nurk et al. 2022). Today, only a few species have genome-wide BAC maps, while genomes from over 5000 eukaryotic species have been sequenced using the WGS strategy, according to the Earth BioGenome Project (https://www.earthbiogenome.org/).

At the press conference announcing the end of the race to sequence the human genome on June 26, 2000, President Bill Clinton called the result "the most important, most wondrous map ever produced by humankind." Craig emphasized humanity's commonality. There were high expectations that the initial genome sequence would transform medicine. Craig returned to these themes many times over the years. In 2007, his was the first personal genome to be sequenced and published (Levy et al. 2007), considered to be the beginning of individualized genomic information. He co-founded Human Longevity, Inc. in 2013, to merge genomics, deep phenotyping, and precision medicine to bring this knowledge directly to patients. Earlier this year, Craig co-founded Diploid Genomics, Inc., another milestone in his continual search for ways to make the genome relevant for each person as the foundation for interpretation of clinical information and informed decision-making.

After the human genome was published (Venter et al. 2001), Celera went on to produce a WGS version of the mouse genome (Mural et al. 2002), and even got NIH funding to participate in consortiums to sequence the rat (Gibbs et al. 2004) and *Anopheles gambiae* genomes (Holt et al. 2002). Celera, mired in conflict about the directions for the business, fired Craig in 2002 and he returned to TIGR and a series of affiliated non-profits that eventually merged to become the J. Craig Venter Institute (JCVI).

At JCVI, Craig's focus shifted to metagenomes—primarily the human and ocean microbiomes—opening a window into entire ecosystems that weren't amenable to study in the laboratory. Craig's lab at JCVI was among the first to apply scale to metagenome studies—essentially a shotgun sequencing strategy for microbial ecosystems—including from the Sargasso Sea (Venter et al. 2004) and the human gut (Gill et al. 2006). These projects again were driven by curiosity about the unknown.

The ocean was thought to be boring, microbially speaking, prior to the Sargasso Sea study. Over the next decade, with public and private funding and his 95-foot sailboat *Sorcerer II*, the Global Ocean Sampling expedition proved otherwise, revealing that the world's oceans harbor a massive, previously hidden universe of microscopic life, identifying millions of new genes and entirely new protein families, and exposing the extraordinary diversity of genes involved in carbon acquisition and transformation. Craig's group at JCVI along with Larry Smarr and Paul Gilna at UC San Diego,

Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press

with funding from the Gordon and Betty Moore Foundation, created the CAMERA resource that served as a portal to metagenomics data for the scientific community.

The fundamental question of "what does it take to be alive?" stimulated Craig throughout his career. He was intrigued by the "genes of unknown function" in the early genomes sequenced by TIGR. Working with Clyde Hutchison, Ham Smith, Dan Gibson, John Glass, and many others, the team at TIGR and later at JCVI and Synthetic Genomics, Inc. (co-founded by Craig) chipped away at this question, first by making genome-wide knockouts of *Mycoplasma mycoides* to identify essential genes and then creating the synthetic biology toolkit that would enable comprehensive design of a genome that could be tested experimentally to determine the minimal set of genes necessary for life. *Mycoplasmas* were ideal platforms for this work, with small genomes and no cell walls. The JCVI synthetic biology team eventually developed methods to synthesize large genome segments from short oligonucleotides, use the yeast recombination machinery to assemble them into a circular genome, and then transplant that genome into a recipient cell from a different species, *Mycoplasma capricolum*. When the first "synthetic cell" was published in 2010 (Gibson et al. 2010), Craig described the result as the first cell whose "parent is a computer." JCVI-syn1.0 included four watermarks—text encoded as DNA—including a quote from James Joyce's *A Portrait of the Artist as a Young Man*: "To live, to err, to fall, to triumph, to recreate life out of life."

Genome minimization was even more complicated, revealing numerous examples of genetic redundancy, where the viability of individual gene knockouts was context dependent. After innumerable variants were tested, JCVI-syn3.0 was published in 2016 (Hutchison et al. 2016). Remarkably, despite all of its 438 protein-coding and 35 RNA genes being essential for growth, over a quarter of them were classified as genes of unknown or generic function. As Craig said, "It's a very humbling set of experiments."

Ten years after the publication of JCVI-syn3.0, it stands as a singular accomplishment. No other group has replicated the complete workflow of whole-genome synthesis and transplantation in another species, reflecting the diverse technical challenges and unique advantages of the *Mycoplasmas*. But many of the methods and approaches have become widely used in the synthetic biology field, and JCVI's John Glass leads a consortium of over 80 research groups that continue to explore the minimal set of genes necessary for life—and how they interact to create an efficient living system (Seidel et al. 2025; Thornburg et al. 2026).

Over the course of his career, Craig was at the leading edge of several tidal waves: gene discovery (ESTs), microbial genomes, the human genome, metagenome sequencing, and synthetic biology. Early on, recognizing the potential of this new area of biology, Craig co-organized (with Tom Caskey) the first Genome Sequencing Conference at The Barns of Wolf Trap Farm in October 1989, focusing on the technology of sequencing. Reflecting Craig's ambition for the meeting, the formal launch of the NIH-funded HGP, and love of a great party, the 1990 meeting moved to Hilton Head, South Carolina and marked the beginning of several years of the Genome Sequencing Conference (later Genome Sequencing and Analysis Conference or GSAC), with increasingly lavish banquet dinners sponsored by Qiagen, Applied Biosystems, and other providers of tools and reagents to the rapidly growing field.

Craig's labs had some of the first automated DNA sequencers. At various times in the years ahead he had among the largest numbers of active sequencers anywhere in the world. But scale wasn't a goal in itself. At each stage, it was a pressing scientific objective that was the goal. First gene discovery—ESTs leap-frogging the slow and tedious process of genome sequencing. Then microbial genomes—achieving something very rare in biology: completeness. The human genome followed, a "natural" extension of sequencing bacterial genomes, albeit 1000× larger and immeasurably more complex due to the repetitive nature of the genome. Then the ocean metagenome—providing the initial glimpses of the extraordinary diversity and interconnectedness of microbial life in the largest ecosystem on the planet. Craig wasn't the first to use or advocate for shotgun sequencing. He wasn't the first to use sequencing to characterize microbial diversity. But he showed what was possible by thinking bigger and acting with more urgency than anyone else.

Although his decisions to partner with for-profit industry were sometimes controversial, Craig managed to leverage corporate funding into some of the most important advances in genomics, and provided a foundation for the non-profit TIGR and JCVI to win over $500M in federal funding in the following years to expand on those advances. Despite the strings that came with the commercial funding, those programs culminated in publications illustrating both his commitment to science and his desire for conventional recognition of his work. And he was recognized, as a recipient of the U.S. National Medal of Science, the Leeuwenhoek Medal, the Gairdner International Award, the Paul Ehrlich Prize, and the King Faisal International Prize for Science, and as a member of the National Academy of Sciences.

Craig was bold and lived life large. In his office at the eponymous J. Craig Venter Institute (JCVI), he displayed a life-sized 3D model of his brain on a table, a vintage motorcycle in the corner, and dramatic photos on the walls of *Sorcerer II* under sail. He relished disrupting the status quo and disquieting its defenders. I often thought of him as a nonlinear thinker—able to foresee a solution without dwelling on the process to get there. He also had an innate sense of what was possible, the knack to hire people who would work creatively and solve problems, and a remarkable ability to motivate them along the way.

Mark D. Adams
Professor & Interim Scientific Director, The Jackson Laboratory for Genomic Medicine, Farmington, Connecticut 06032, USA

References

Adams MD, Kelley JM, Gocayne JD, Dubnick M, Polymeropoulos MH, Xiao H, Merril CR, Wu A, Olde B, Moreno RF, et al. 1991. Complementary DNA sequencing: expressed sequence tags and human genome project. *Science* **252:** 1651–1656. doi:10.1126/science.2047873

Adams MD, Kerlavage AR, Fleischmann RD, Fuldner RA, Bult CJ, Lee NH, Kirkness EF, Weinstock KG, Gocayne JD, White O, et al. 1995. Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence. *Nature* **377**(Suppl)**:** 3–174.

Adams MD, Celniker SE, Holt RA, Evans CA, Gocayne JD, Amanatides PG, Scherer SE, Li PW, Hoskins RA, Galle RF, et al. 2000. The genome sequence of *Drosophila melanogaster*. *Science* **287:** 2185–2195. doi:10.1126/science.287.5461.2185

Adams MD, Sutton GG, Smith HO, Myers EW, Venter JC. 2003. The independence of our genome assemblies. *Proc Natl Acad Sci* **100:** 3025–3026. doi:10.1073/pnas.0637478100

Fleischmann RD, Adams MD, White O, Clayton RA, Kirkness EF, Kerlavage AR, Bult CJ, Tomb JF, Dougherty BA, Merrick JM, et al. 1995. Whole-genome random sequencing and assembly of *Haemophilus influenzae* Rd. *Science* **269:** 496–512. doi:10.1126/science.7542800

Fraser CM, Gocayne JD, White O, Adams MD, Clayton RA, Fleischmann RD, Bult CJ, Kerlavage AR, Sutton G, Kelley JM, et al. 1995. The minimal gene complement of *Mycoplasma genitalium*. *Science* **270:** 397–403. doi:10.1126/science.270.5235.397

Downloaded from genome.cshlp.org on November 24, 2026 . Published by Cold Spring Harbor Laboratory Press

Gibbs RA, Weinstock GM, Metzker ML, Muzny DM, Sodergren EJ, Scherer S, Scott G, Steffen D, Worley KC, Burch PE, et al. 2004. Genome sequence of the Brown Norway rat yields insights into mammalian evolution. *Nature* **428:** 493–521. doi:10.1038/nature02426

Gibson DG, Glass JI, Lartigue C, Noskov VN, Chuang RY, Algire MA, Benders GA, Montague MG, Ma L, Moodie MM, et al. 2010. Creation of a bacterial cell controlled by a chemically synthesized genome. *Science* **329:** 52–56. doi:10.1126/science.1190719

Gill SR, Pop M, Deboy RT, Eckburg PB, Turnbaugh PJ, Samuel BS, Gordon JI, Relman DA, Fraser-Liggett CM, Nelson KE. 2006. Metagenomic analysis of the human distal gut microbiome. *Science* **312:** 1355–1359. doi:10.1126/science.1124234

Green P. 1997. Against a whole-genome shotgun. *Genome Res* **7:** 410–417. doi:10.1101/gr.7.5.410

Holt RA, Subramanian GM, Halpern A, Sutton GG, Charlab R, Nusskern DR, Wincker P, Clark AG, Ribeiro JM, Wides R, et al. 2002. The genome sequence of the malaria mosquito *Anopheles gambiae*. *Science* **298:** 129–149. doi:10.1126/science.1076181

Hutchison CA, Chuang RY, Noskov VN, Assad-Garcia N, Deerinck TJ, Ellisman MH, Gill J, Kannan K, Karas BJ, Ma L, et al. 2016. Design and synthesis of a minimal bacterial genome. *Science* **351:** aad6253. doi:10.1126/science.aad6253

Levy S, Sutton G, Ng PC, Feuk L, Halpern AL, Walenz BP, Axelrod N, Huang J, Kirkness EF, Denisov G, et al. 2007. The diploid genome sequence of an individual human. *PLoS Biol* **5:** e254. doi:10.1371/journal.pbio.0050254

Mural RJ, Adams MD, Myers EW, Smith HO, Miklos GL, Wides R, Halpern A, Li PW, Sutton GG, Nadeau J, et al. 2002. A comparison of whole-genome shotgun-derived mouse chromosome 16 and the human genome. *Science* **296:** 1661–1671. doi:10.1126/science.1069193

Myers EW, Sutton GG, Delcher AL, Dew IM, Fasulo DP, Flanigan MJ, Kravitz SA, Mobarry CM, Reinert KH, Remington KA, et al. 2000. A whole-genome assembly of *Drosophila*. *Science* **287:** 2196–2204. doi:10.1126/science.287.5461.2196

Nekrutenko A. 2004. Reconciling the numbers: ESTs versus protein-coding genes. *Mol Biol Evol* **21:** 1278–1282. doi:10.1093/molbev/msh125

Nurk S, Koren S, Rhie A, Rautiainen M, Bzikadze AV, Mikheenko A, Vollger MR, Altemose N, Uralsky L, Gershman A, et al. 2022. The complete sequence of a human genome. *Science* **376:** 44–53. doi:10.1126/science.abj6987

Olson M, Hood L, Cantor C, Botstein D. 1989. A common language for physical mapping of the human genome. *Science* **245:** 1434–1435. doi:10.1126/science.2781285

Rubin GM, Yandell MD, Wortman JR, Gabor Miklos GL, Nelson CR, Hariharan IK, Fortini ME, Li PW, Apweiler R, Fleischmann W, et al. 2000. Comparative genomics of the eukaryotes. *Science* **287:** 2204–2215. doi:10.1126/science.287.5461.2204

Seidel ZP, Kumar R, Conroy Araujo MM, Glass SA, Rodriguez R, Goshia T, Glass JI. 2025. Meeting proceedings from 4th minimal cell workshop: exploring JCVI minimal cell fundamental insights and integrative applications. *ACS Synth Biol* **14:** 1905–1911. doi:10.1021/acssynbio.5c00159

Thornburg ZR, Maytin A, Kwon J, Brier TA, Gilbert BR, Fu E, Gao YL, Quenneville J, Wu T, Li H, et al. 2026. Bringing the genetically minimal cell to life on a computer in 4D. *Cell* **189:** 2582–2597.e27. doi:10.1016/j.cell.2026.02.009

Venter JC, Adams MD, Myers EW, Li PW, Mural RJ, Sutton GG, Smith HO, Yandell M, Evans CA, Holt RA, et al. 2001. The sequence of the human genome. *Science* **291:** 1304–1351. doi:10.1126/science.1058040

Venter JC, Remington K, Heidelberg JF, Halpern AL, Rusch D, Eisen JA, Wu D, Paulsen I, Nelson KE, Nelson W, et al. 2004. Environmental genome shotgun sequencing of the Sargasso Sea. *Science* **304:** 66–74. doi:10.1126/science.1093857

Weber JL, Myers EW. 1997. Human whole-genome shotgun sequencing. *Genome Res* **7:** 401–409. doi:10.1101/gr.7.5.401

Received October 19, 2026; accepted in revised form October 19, 2026.