

What a long, strange trip it's been...

1985

In 1985, Charles DeLisi, then associate director for health and environmental research at the Department of Energy (DoE), begins to discuss a mammoth project — of a scale unprecedented in biology — to sequence the complete human genome. DoE funding begins in 1987.



1988

The National Institutes of Health (NIH) establishes the Office of Human Genome Research in September 1988. Renamed the National Center for Human Genome Research (NCHGR) a year later, its director is James Watson, co-discoverer of the double helix structure of DNA. Watson's testimony to the US Congress, in which he pledged to devote a small fraction of the project's budget to 'ethical, legal and social' issues, had proved instrumental in garnering political support.



Early 1990s

With sequencing still slow and expensive, the genome project adopts a 'map-first, sequence-later' strategy. In the early 1990s, two Parisian laboratories, the Centre d'Etude du Polymorphisme Humain and Génethon, have an integral role in mapping — underlining the project's international character. The labs' driving forces are Daniel Cohen (top) and Jean Weissenbach. Later, the genome project constructs a higher-resolution map that is used to sequence and assemble the human genome.



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1998



In May 1998, Venter forms a company to sequence the human genome within three years. The company, later named Celera, will use an ambitious 'whole genome shotgun' method, which involves assembling the genome without using maps. But its data release policy will not follow the Bermuda principles.

1999

The public project responds to Venter's challenge. By early 1999, it is on track to produce a draft genome sequence by 2000. Increasingly, the bulk of the sequencing takes place in five huge centres: at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts; the Sanger Centre near Cambridge, UK; Baylor College of Medicine in Houston; Washington University in St Louis; and the DoE's Joint Genome Institute (JGI) in Walnut Creek, California. The centres' leaders are dubbed the 'G5'. Here, Robert Waterston of Washington University in St Louis and John Sulston of the Sanger Centre are pictured in a rare moment of relaxation, while Trevor Hawkins and Elbert Branscomb of the JGI prepare samples.



Super models

The complete genome sequences of model organisms are proving immensely valuable to biologists working on these species, and will also help interpret the human genome sequence. Published highlights to date include the yeast *Saccharomyces cerevisiae* (May 1997), the nematode *Caenorhabditis elegans* (December 1998), the fruitfly *Drosophila melanogaster* (March 2000, right), and the plant *Arabidopsis thaliana* (December 2000, left).



The draft human genome sequence published in *Nature* this week is the culmination of 15 years of work, involving 20 sequencing centres in six countries. Here, we present a reminder of some of the key moments.

1992

Francis Collins of the University of Michigan replaces Watson as head of NCHGR in April 1992. Watson had earlier clashed with Craig Venter, then at NIH, over the patenting of DNA fragments known as expressed sequence tags.



1992

Later that year, Venter sets up The Institute for Genomic Research (TIGR) in Rockville, Maryland. TIGR later sequences a host of bacterial genomes, starting with *Haemophilus influenzae*.



1996



In February 1996, at a meeting in Bermuda, international partners in the genome project agree to formalize the conditions of data access, including release of sequence data into public databases within 24 hours. These came to be known as the 'Bermuda principles'.

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1999-2000



The first complete human chromosome sequence — number 22 — is published in December 1999. Chromosome 21 follows in May 2000, a collaborative effort led by German and Japanese groups under the direction of André Rosenthal and Yoshiyuki Sakaki, respectively. Sakaki (centre) is pictured here at *Nature's* chromosome 21 press conference in Tokyo.



2000



Outside, celebrations continue with Eric Lander of the Whitehead Institute, Baylor's Richard Gibbs, and Waterston and Richard Wilson from Washington University.



On 26 June 2000, leaders of the public project and Celera announce completion of a working draft of the human genome sequence. Collins and Venter are seen here on television with Ari Patrinos of the DoE, who cut through the animosity between the rival projects to broker the joint announcement at the White House in Washington.

This week



Finally, this week sees the publication of the draft genome, the public sequence in *Nature*, Celera's in *Science*.

We are grateful for contributions and input from Francis Collins, Richard Gibbs, Victor McKusick, John McPherson, David Stewart and the staff of the Cold Spring Harbor Laboratory.

Technical gurus



Without advances in sequencing technology, we would still be waiting to unveil our genetic blueprint. Double Nobel laureate Fred Sanger (pictured) of the Laboratory of Molecular Biology in Cambridge invented the basic technique of gene sequencing back in the 1970s. In the 1980s, Leroy Hood, then at the California Institute of Technology in Pasadena, introduced the first automated sequencing machine. But it was the ABI PRISM 3700 DNA Analyzer, developed by Michael Hunkapiller of PE Biosystems, which allowed the rapid sequencing progress made by both Celera and the public project over the past two years. Assembling fragments of the genome into a complete sequence, meanwhile, depended heavily on computer programs developed by Philip Green of the University of Washington in Seattle.