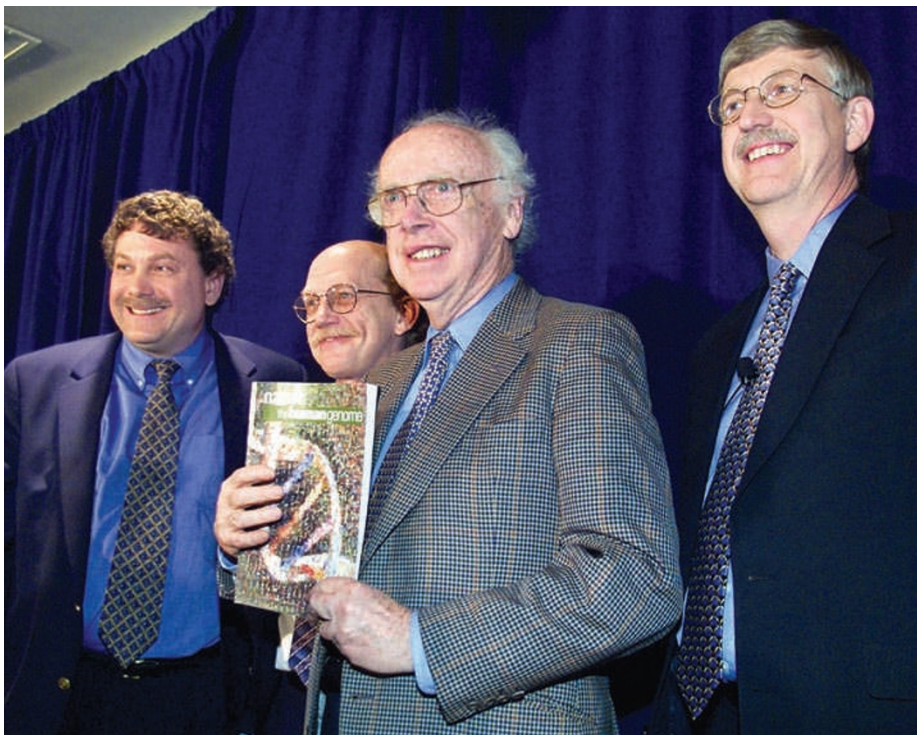
BOOKS & ARTS

Long view of the Human Genome Project

A bold attempt to tell the complicated story behind the human DNA sequence highlights that social change is needed before personalized medicine can take off, finds **Jan Witkowski**.

Drawing the Map of Life: Inside the Human Genome Project
by Victor K. McElheny
Basic Books: 2010. 384 pp. $28, £16.99



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Genome-project pioneers: (left to right) Eric Lander, Robert Waterston, James Watson and Francis Collins.

In 1985, Robert Sinsheimer, then chancellor of the University of California, Santa Cruz, convened a workshop to discuss sequencing the human genome. It was an audacious proposal: the longest genome that had been sequenced at the time was that of the Epstein-Barr virus, at 172,282 base pairs compared with 3 billion in human DNA. Sinsheimer's initiative failed.

Yet the idea gained momentum when, in 1988, James Watson was appointed associate director of the Office of Genome Research, part of the US National Institutes of Health (NIH). Watson declared 1990 the official start of the publicly funded NIH Human Genome Project (HGP). In 1998, Craig Venter and his company Celera Genomics, then in Rockville, Maryland, joined the race. Ten years ago in June, both projects announced a finish-line draw from President Bill Clinton's White House. February 2011 will mark a decade since the draft sequences were published.

In *Drawing the Map of Life,* science journalist and author Victor McElheny relates the story of the HGP, from its methods to the people involved. He describes the project's tortuous path to success, and asks whether its medical impacts live up to expectations. Weaving together so many threads is a formidable task. McElheny offers an entertaining narrative, but his book stops short of being a comprehensive history.

He opens in the 1980s, when many of the technologies central to gene sequencing were developed: the polymerase chain reaction that multiplies DNA fragments for analysis; the use of restriction enzymes to sever DNA strands at particular sites; and the use of restriction fragment length polymorphisms as markers in early searches for the genes involved in inherited disorders. The mapping of the genes underlying Huntington's disease, Duchenne muscular dystrophy and cystic fibrosis in the late 1980s had a huge impact on clinical genetics: suddenly the arrangement of the gene itself, rather than secondary markers, could be used to reveal mutations.

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McElheny traces the various stages of the HGP and the power struggles it engendered. The project had two phases under different directors. Watson led the NIH effort from 1988 until his resignation in 1992, after questions were raised about his holding of stock in biotechnology companies. McElheny describes the resignation, but not the finding by the US Department of Health and Human Services that Watson had done nothing unethical. Francis Collins then took over directorship of the HGP, and saw it through to the completion of the sequence in 2003.

The book also describes the fierce competition between various commercial and academic laboratories to isolate and sequence medically relevant genes. The most famous rival to the NIH project is Venter, a pioneer of large-scale sequencing who left the NIH to set up The Institute for Genome Research to sequence small genomes. In 1998 Venter announced the formation of a new company, Celera Genomics, that would target the human genome. The academics rallied to meet Celera's challenge.

In 2000, HGP and Celera jointly announced the draft human genome sequences to great fanfare. But acrimony and infighting continued over data release until the sequences were published in 2001. Celera published in *Science* but sought special conditions of access to its data for commercial scientists. The HGP opposed any such restrictions and instead published its sequence in *Nature*, depositing its data in the open-access GenBank database.

The completion of the HGP in 2003 was a great triumph. With draft sequences finished two years earlier than planned, it is transforming research. The pace of sequencing has since rocketed thanks to techniques that the project hastened. Many complex organisms have now been sequenced, and their genomes will be mined for years to come.

Yet the era of genomic medicine has not yet come to pass. McElheny is right to ask when we will see public-health returns on the huge investment in the HGP. He argues that social change will be needed before genomic information can be integrated into current medical practice and interpreted by the public. He asks,

for example, how physicians will use genetic data for diagnosis and treatment, and whether individuals will welcome or fear knowledge of what their genomes hold for the future.

Such social change will follow, I believe, when useful applications of genomic information become available. They might tell us how to alter our lifestyles to improve our health, or distinguish which drugs will be of benefit or have serious side effects, or may guide the development of new drugs. But this will take time. We are only at the beginning of interpreting the sequence and understanding what variants mean for the individual.

Drawing the Map of Life is one of many books that have been written about the HGP. The volume does not add much to earlier descriptions of the project's genesis, such as *Genome* by Jerry Bishop and Michael Waldholz (Simon and Schuster, 1990) and *The Gene Wars* by Robert Cook-Deegan (W. W. Norton, 1994). In *Cracking the Genome* (Free Press, 2001), Kevin Davies brought us up to the completion of the draft sequences. More recently, protagonists John Sulston and Venter have told their contrasting personal stories, while James Shreeve has written a detailed study of Venter's contributions.

All of these books are valuable; what is now needed is a scholarly history of the HGP. *Drawing the Map of Life* is not that book, but it offers an enjoyable account of the project from origin to conclusion and beyond. ■

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In Retrospect: *Science — The Endless Frontier*

Vannevar Bush's pivotal report that marked the beginning of modern science policy catapulted the phrase 'basic research' into popular usage, explains **Roger Pielke Jr**.

Science — The Endless Frontier. A Report to the President on a Program for Postwar Scientific Research
by Vannevar Bush
National Science Foundation: 1960 (reprint). First published 1945.

H. WALKER/TIME LIFE PICTURES/GETTY

Engineer Vannevar Bush's proposals led to the creation of the National Science Foundation in 1950.

The US government's landmark report *Science — The Endless Frontier* was published 65 years ago last month. Commissioned by President Franklin D. Roosevelt and prepared by electrical engineer Vannevar Bush, who directed US government research during the Second World War, the document distilled the lessons of wartime into proposals for subsequent federal support of science. Although its bold recommendations were only partly implemented, the document is ripe for reappraisal today: it marked the beginning of modern science policy.

Bush's report called for a centralized approach to government-sponsored science, largely shielded from political accountability. The creation of the National Science Foundation in 1950, a small agency with a limited mandate, was far from the sweeping reform set out in the 30-page report and its appendices. However, its publication ushered in a new era in which science was viewed as vital for progress towards national goals in health, defence and the economy. Government funding for research and development consequently increased by more than a factor of ten from the 1940s to the 1960s.

The influence of *Science — The Endless Frontier* stems largely from its timing, coming at the tail end of a war in which science-based technology had been crucial. The development of the atomic bomb, radar and penicillin meant that Bush's declaration that "scientific progress is essential" to public welfare found a receptive audience. Bush also adopted innovative language that capitalized on this new-found government credulity.

In particular, he broadened the meaning of the phrase 'basic research'. In using it to refer simultaneously to the demands of policy-makers for practical innovation and to the interests of scientists in curiosity-driven enquiry, he satisfied both sectors.

Before the report, pleas by scientists to expand government support for research had met with only limited success. Prominent calls along similar lines were made to no avail in 1924 by the UK National Union of Scientific Workers (NUSW) and in 1929 by US agriculture secretary Arthur Hyde. The poor response might have been due to the confused messages offered to protect the integrity of pure research. In a 1921 essay, for example, the NUSW president declared that scientific research has "no industrial bearing at all" but later stated that it is "the foundation of progress in industry". Not surprisingly, most policy-makers shrugged.

Some political leaders did champion government support for basic research before 1945. Prior to Hyde's appointment, US agriculture secretary Henry C. Wallace had argued in