fundamental as data on human DNA. But the debate subsided when Gilbert failed to raise sufficient funds.

NIH makes its move

As the genome project gained congressional funding and scientific respectability, NIH wrested control from DOE. Urged on by a group of advisers who met outside Washington, D.C., in Reston, Virginia, in March 1988, then–NIH director James Wyngaarden announced that NIH would create a special office for genome research (*Science*, 13 May 1988, p. 878). In short order, he nabbed Watson to head it, and with that coup, NIH was firmly ensconced as the lead agency. It has remained so, even as the project gathered international collaborators and Britain's Wellcome Trust took on a prominent role.

Watson proved a shrewd strategist, skilled in the care and feeding of those who controlled congressional purse strings, and a tough taskmaster. "My name was good," he says by way of explanation. Indeed, members of Congress were spellbound when the eccentric Nobel laureate swept in to testify. Watson was eloquent in touting the project's goal: "to find out what being human is." He also had the refreshing quality of saying what he thought, no matter how politically incorrect—an unusual quality in Washington, D.C.

Even as the project began, Watson's advisory panel was still debating the proper balance for the project—how much should be devoted to building tools, like maps and faster sequencing machines, and how much to actually using these tools to find disease genes? (*Science*, 13 January 1989, p. 167) Watson was adamant: Even though disease genes captured the public imagination and kept the dollars flowing, this project was designed to build the equivalent of a particle accelerator: They should not be sidetracked. As Botstein explained at a January 1989 meeting, "We are looking at the production of a set of tools that will enable human geneticists to do what they want. We are the Cray, if you like. We don't write software for your particular applications."

At the same time, Watson relentlessly pushed the first stage of the project and its most tangible goal—building maps of the human chromosomes. Knowing that Congress did not have the patience to wait 15 years for results, Watson staked his reputation on getting the maps done in five. With the maps in hand, genes would fall out in short order, including the putative Alzheimer's gene, which, Watson joked, should be a priority given the age of most members of Congress.

Progress was rapid. By 1990, Sulston and colleagues had nearly completed the physical map of the worm—changing worm biology forever—and Olson and colleagues were proceeding apace on yeast (*Science*, 15 June 1990, p. 1310). Faster and easier ways to clone and map DNA were coming on line, and sequencing trials were beginning. For a short time, the controversy that had dogged the project from the outset seemed to have dissipated.

Venter, round one

That newfound harmony was shattered in June 1991, when Venter, who ran a large sequencing lab at the National Institute for Neurological Disorders and Stroke, went public with an iconoclastic plan: Why not focus on finding the genes—the "real goods" that both scientists and companies were clamoring for—and leave tedious sequencing until later? Venter and colleague Mark Adams had developed a new technique, called expressed sequence tags, that enabled them to find genes at unprecedented speed. Never one of Watson's inner circle, Venter boasted that this new approach "was a bargain in comparison to the genome project" and claimed he could find 80% to 90% of the genes within a few years, for a fraction of the cost (*Science*, 21 June 1991, p. 1618).

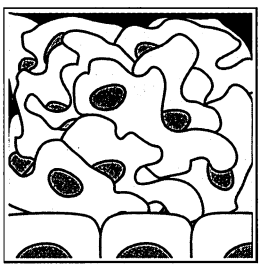
Watson dismissed Venter's "cream-skimming approach," but their feud remained subterranean until a few weeks later, when Venter described his work at a

NEW SCIENCE:

Nailing Down Cancer Culprits

A general sending troops out to battle wants as much intelligence about the enemy and its weaknesses as possible. Researchers fighting cancer hope the complete human genome sequence will help provide such information.

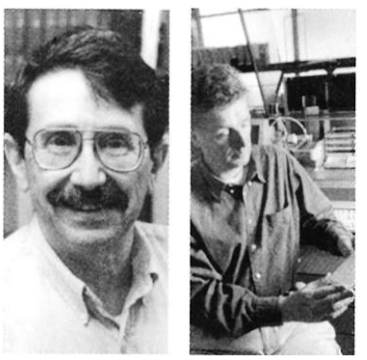
The sequence will greatly speed the identification of the genetic underpinnings of cancer. Over the past 15 years or so, researchers have learned that cancers are usually caused by the accumulation of several gene mutations, some of which activate cancer-promoting oncogenes, whereas others inactivate tumor suppressor genes. And though scientists have fingered roughly 100 oncogenes and 30 or so tumor suppressors, that's "only a fraction of the genes that cause cancer," says cancer gene expert Bert Vogelstein of the Johns Hopkins University School of Medicine in Baltimore, Maryland.



In the past, once researchers determined where in the genome a cancer gene resides, they could still spend months, or even years, scouring the region—often a megabase or two long—looking for likely candidate genes to test. Now, Vogelstein says, that can be done "literally with the click of a button. The availability of the sequence enormously simplifies the search for those [missing cancer] genes."

Researchers are also using microarrays and other techniques to measure changes in the expression of thousands of genes at a time—information that provides a very detailed picture of the alterations leading to cancer development and spread. Knowing all the human genes will make this picture more complete. Researchers have already found that tumors that look similar to a pathologist may display different gene expression patterns—and that these differences can reveal potentially lifesaving information about how the cancers will respond to therapy.

–JEAN MARX



UNSUNG HEROES: MEL SIMON & PIETER DE JONG

Although they were slow to win acceptance, the bacterial artificial chromosomes (BACs) created by geneticist Simon (left) of the California Institute of Technology in Pasadena soon became the "currency of the genome," as he says. These clones' large capacity and stability make them highly efficient. Using BACs, Caltech's de Jong created massive "libraries" of DNA from various human tissues for sequencing.

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