

Evolution of a Vision: Genome Project Origins,

In an interview at a DNA sequencing conference in Hilton Head, South Carolina, David Smith, a founder and former Director of the DOE Human Genome Program, recalled the establishment of this country's first human genome project. The impressive early achievements and spin-off benefits, he noted, offer more than mere vindication for project founders. They also provide a tantalizing glimpse into the future where, he observed, "scientists will be empowered to study biology and make connections in ways undreamt of before."*

The DOE Human Genome Program began as a natural outgrowth of the agency's long-term mission to develop better technologies for measuring health effects, particularly induced mutations. As Smith explained it, "DOE had been supporting mutation studies in Japan, where no heritable mutations could be detected in the offspring of populations exposed to the atomic blasts at Hiroshima and Nagasaki. The program really grew out of a need to characterize DNA differences between parents and children more efficiently. DOE led the development of many mutation tests, and we were interested in developing even more sensitive detection methods. Mortimer Mendelsohn of Lawrence Livermore National Laboratory, a member of the International Commission for Protection Against Environmental Mutagens and Carcinogens, and I decided to hold a workshop to discuss DNA-based methods (see Human Genome Project chronology, p. ii).

"Ray White (University of Utah) organized the meeting, which took place in Alta, Utah, in December 1984. It was a small meeting but very stimulating intellectually. We concluded the obvious—that if you really wanted to use DNA-based technologies, you had to come up with more efficient ways to characterize the DNA of much larger regions of the genome. And the ultimate sensitivity would be the capability to compare the complete DNA sequences of parents and their offspring."

Project Begins

Smith recalled reaction to the first public statement that DOE was starting a program with the aim of sequencing the human genome. "I announced it at the Cold Spring

“Genomics has come of age, and it is opening the door to entirely new approaches to biology.”

Harbor meeting in May 1986, and there was a big hullabaloo." After a year-long review, a National Academy of Sciences National Research Council panel endorsed the project and the basic strategy proposed. Smith pointed out that NIH and others were also having discussions on the feasibility of sequencing the human genome. "Once NIH got interested, many more people became involved. DOE and NIH signed a Memorandum of Understanding in October 1988 to coordinate our activities aimed at characterizing the human genome." But, he observed, it wasn't all smooth sailing. The nascent project had many detractors.

Responding to Critics

Many scientists, prominent biologists among them, thought having the sequence would be a misuse of scarce resources. Smith, laughing now, recalls one scientist complaining, "Even if I had the sequence, I wouldn't know what to do with it." Other critics worried that the genome project would siphon shrinking research funds away from individual investigator-initiated research projects. Smith takes the opposite

view. "In fact, individual investigators can do things they would never be able to do otherwise. We're beginning to see that demonstrated at this meeting. For the first time, we're finding people exploring systematic ways of looking at gene function in organisms. The genome project opens up enormous new research fields to be mined. Cottage-industry biologists won't need a lot of robots, but they will have to be computer literate to put the information all together."

The genome project also is providing enabling technologies essential to the future of the emerging biotechnology industry, catalyzing its tremendous growth. According to Smith, the technologies are

capable of more than elucidating the human genome. "We're developing an infrastructure for future research. These technologies will allow us to efficiently characterize any of the organisms out there that pertain to various DOE missions, with such applications as better fuels from biomass, bioremediation, and waste control. They also will lead to a greater understanding of global cycles, such as the carbon cycle, and the identification of potential biological interventions. Look at the ocean; an amazing number of microbes are in there, but we don't know how to use them to influence cycles to control some of the harmful things that might be happening. Up to now, biotechnology has been nearly all health oriented, but applications of genome research to modern biology really go beyond health. That's one of the things motivating our program to try to develop some of these other biotechnological applications."

Responding to criticism about not researching gene function early in the project, Smith reasserted that the purpose of the Human Genome Project is to build technologies and resources that will enable researchers to learn about biology in a much

*The Seventh International Genome Sequencing and Analysis Conference, September 1995.

