OTA WORKSHOP

REFINING COSTS FOR THE HUMAN GENOME PROJECT

WASHINGTON, D.C.—Some parts of the proposed Human Genome Project (see *Bio/Technology* **5:**933, Sept. '87; **5:**764, Aug. '87; **4:**925, Nov. '86), notably efforts to compile a crude genetic map of all the human chromosomes, now are expected to cost mere "small change." The price tags of other efforts—such as obtaining a more refined map, determining the full nucleotide sequence of entire chromosomes, storing cloned samples that are awaiting analysis, or developing computer software to handle masses of anticipated data—will be higher but are somewhat more difficult to estimate. Moreover, the requisite technology is expected to advance rapidly as the project continues—adding to up-front costs but also leading to overall savings and spin-off benefits. The entire 10-year effort is now predicted to cost perhaps $1–2 billion, down from earlier estimates of $3 billion for the sequencing alone.

These were some of the general conclusions thrashed out during a workshop convened by the Congressional Office of Technology Assessment (OTA) in August as part of its comprehensive study of the "Human Genome Project." Billed as an effort that will broadly address human genetic disease, the project has been attracting increased political interest. For instance, Senator Pete Domenici (R—NM) recently introduced legislation that would make the Department of Energy's (DOE) National Laboratories the hub of a new "human genome consortium," which also would involve universities and industry. Domenici proposed that the National Laboratories could be the answer to Japan's Ministry of International Trade and Industry, providing leadership and expertise to enhance U.S. international "competitiveness." A recent DOE report recommended an annual federal expenditure for the project of $40 million beginning in 1989, then growing steadily to $200 million per year by 1993.

Meanwhile, OTA's panel tried to estimate costs without specifying which federal agencies or private corporations would spend the money. The first category of effort is to build a crude genetic map consisting of restriction fragment length polymorphisms (RFLPs), whose resolution is measured in centimorgans, a unit corresponding in practice to about 1 million base pairs. According to Helen Donis-Keller of Collaborative Research Inc. (Bedford, MA), a map having 5 centimorgan resolution would be very useful and probably sufficient. Based on current technology, she estimates that $11 million in direct research costs, plus a capital outlay of $5 million for laboratories and equipment, is needed for constructing such a map. A map with 1 centimorgan resolution, which she claims is not needed but which is favored by some researchers, could cost 10–100-times as much. A map with resolution between 10 and 15 centimorgans probably could already be constructed.

Besides an RFLP map, scientists also are building a collection of human DNA fragments that eventually will establish a true physical map of the genome. Based on estimates developed by Anthony Carrano of Lawrence Livermore National Laboratory in California, the cost for cloning fragments and determining their proper order and relationship to one another would range from $50–$60 million. However, the cost for storing and maintaining the gene fragments as clones in living cells could be as high as $250 million, according to Robert Stevenson of the American Type Culture Collection (Rockville, MD). Much of this cost would come at the outset for building new facilities.

Uncertainties about costs continue to escalate when the next stage of the project, nucleotide sequencing, is considered. Current figures indicate that sequencing runs about $1–2 per base pair. When extrapolated directly, this amounts to at least $3 billion for the entire human genome. However, claims Leroy Hood of California Institute of Technology (Pasadena), "There is no area where the costs will change more dramatically." With steadily improving automation, he says, the average cost of sequencing could soon be reduced 100-fold. Juggling estimates to allow for repetitive runs, correction of errors, and eventual strategy changes dictated by later improvements in technology, participants at the OTA workshop suggested that, instead of $3 billion, $300 million is a more realistic projection of the actual cost for sequencing.

Some of those savings could come with an additional cost of their own, however. Hood insists that technology development costs need to be built into overall estimates for the project. He recommends separately budgeting between $50 million and $75 million per year toward this end.

Besides the development of laboratory instruments, cost estimates need to include figures for computer hardware and software for handling the massive data that will be generated. Moreover, project management costs and the need to ensure quality control should not be overlooked, OTA workshop participants pointed out. Depending on how many centers and satellite efforts are set up, costs could range from $12 million to perhaps $20 million per year for data acquisition and handling, plus research and development into better ways to use such information, according to Christian Burks of Los Alamos National Laboratory in New Mexico.

No one has affixed solid numbers to the management costs of the proposed project, and considerable uncertainty remains as to whether such a project should be absorbed into existing federal structures for conducting biomedical research or, instead, be put into an organization suited for something akin to "a moon mission." According to James Watson of Cold Spring Harbor Laboratory in New York, someone is needed "to shepherd the program" and keep it on track. **—Jeffrey L. Fox**