

Tough Times Ahead for the Genome Project

As the genome project comes under increasing scrutiny, Congress is asking how much and how fast it should grow

THE HONEYMOON IS OVER for the genome project. After 2 years of hefty budget increases and what seemed like nearly universal support, the project is facing mounting criticism from its peers and increased scrutiny from Congress. In fact, the huge budget increase—from \$60 million to \$108 million—slated for the genome project at the National Institutes of Health for 1991 is in serious trouble. In a closed session on 20 June, the House appropriations subcommittee voted against giving the project the full amount requested by the President, according to one congressional source, who would not say how far shy of the request the appropriation actually is.

The reasons for the project's predicament are several, but chief among them is a perception that the genome budget has grown too big and too fast when the rest of biomedicine is strapped for funds (*Science*, 24 November 1989, p. 988). In Congress, no one is talking about dismantling the project, say committee aides. Rather, the question is simply, "Should the genome project be expanding when we can't do other things we would like to do at NIH, like [raise the]

number of grants?" as one key aide puts it.

There are other concerns as well. One is the project's budget, which the same aide says James Watson, director of the Center for Human Genome Research at NIH, "just backed into" without sufficient justification. In 1988 a National Academy of Sciences committee recommended that the genome project be funded at \$200 million a year, after an initial scaling-up period. Since then, that number, plus inflation, has become firmly embedded in planning at NIH and the Department of Energy, which is requesting \$48 million for next year.

There is also "nervousness, but not opposition" about concentrating research in large centers, as Watson has proposed. And Congressman David Obey (D-WI) has questioned the wisdom of expanding the project until some of the ethical questions surrounding the use of genetic knowledge are resolved.

Francis Collins of the University of Michigan, a codiscoverer of the cystic fibrosis gene who is actively involved in the genome project, puts it very simply: "We have a PR problem of major proportions." To Collins, while the majority of biologists are still behind the project, the "Camelot days" of intellectual debate are clearly over. "This is getting into turf," he says, referring to the two letter-writing campaigns now under way to stop the project (*Science*, 13 October 1989, p. 204). So far, the White House and NIH have received nearly 60 of these form letters from biologists around the country, and an untold number are circulating on Capitol Hill.

Now Watson and a number of leading scientists are frantically trying to repair the damage with a counteroffensive of their own. Watson has been going door to door on Capitol Hill, aggressively fighting for his budget—and threatening to quit if he doesn't get it. Last week, as the House appropriations subcommittee neared its crucial vote on the NIH budget, Collins, David Housman, a Massachusetts Institute of Technology researcher who studies the genes involved in cancer and other diseases, and Huntington's disease researcher Nancy Wexler of Columbia University all flew in to Washington to plead the project's case.

And since the genome center sounded the alarm a few weeks ago, letters of support have been pouring into congressional offices. Nobel laureates Paul Berg of Stanford and Renato Dulbecco, president of the Salk Institute, have written, for example. And these have not been mere form letters but eloquent pleas to maintain the President's budget request. "The genome project [is] an effort whose momentum, promise, and very lifeblood depend on plans previously set in motion to expand the project as quickly as possible to the \$200-million-a-year level," wrote Collins.

At the White House Office of Science and Technology Policy, James Wyngaarden has been urging the genome project critics to quit sniping at their peers and instead band together to lobby for more research funds. Wexler, too, is troubled by the split among people who should be allies. "You don't bomb your own house," she says. But even the more moderate critics of the project, like microbiologist Bernard Davis of Harvard, say that such pleas are coming too late. "The dissatisfaction is too deep and the rift too broad," Davis says.

For all the critics, the biggest gripe is money. They are convinced that the genome project is diverting funds from traditional—and in their view, far worthier—"small" biology. The hardcore among them—like Martin Rechsteiner of the University of Utah and Michael Syvanen of the University of California at Davis, who organized the letter campaigns—argue strenuously against brute-force sequencing of the entire genome, apparently without realizing that the genome center has yet to endorse it either. They call the project mediocre, mind-numbing work unfit for training young scientists. And they are leery of concentrating the effort in a few big centers instead of spreading the wealth.

Davis, on the other hand, supports the current goals of the project—mapping the chromosomes, developing new technologies, studying model organisms, and sequencing the DNA in interesting regions of the human genome—calling them "virtuous." But, asks Davis, "Is it worth a crash program?" He doesn't think so, and says his view is shared by almost all members of Harvard's Department of Microbiology and Molecular Genetics.

These attacks drive genome project proponents to distraction. "What are we doing wrong in our approach to our colleagues? Why do they so completely misunderstand what we are about?" asked Norton Zinder of Rockefeller University at last week's meeting of the NIH genome advisory committee, where members spoke as if they were under siege. Says Stanford's Berg: "How

Hubble Trouble

As *Science* went to press on 26 June, managers for the \$1.5-billion Hubble Space Telescope were reporting to NASA headquarters that the telescope suffers from a serious focusing problem, a condition known as spherical aberration, which causes the point-like images of stars to be surrounded by fuzzy haze. The aberration seems to result from a subtle warping in the telescope's mirrors as they adjust to the zero gravity of space, and cannot be eliminated simply by tweaking the telescope's focus. Ground controllers hope that they can correct the problem with a set of 24 pistons on the back of the 2.4-meter main mirror, using them to push and pull on that optically exquisite surface until the aberrations are eliminated by force. ■ M. MITCHELL WALDROP

can \$60 million or \$100 million have that big a negative impact on the \$5-billion NIH budget? It just doesn't make any sense."

The supporters also argue that they are building a tool, like an accelerator, that will be of immense benefit to all biologists. And the genetic map, to be completed in the next few years, will dramatically speed the search for genes involved in human disease. And all the supporters argue that to cut back funding now, when the project is just hitting its stride, would be a disaster. "It's cutting the engine as the plane is getting off the ground," says Berg. "That is the most dangerous time."

Without a significant increase in funds, the first casualty will be the new research centers Watson has proposed to tackle major chunks of the project—say, mapping a human chromosome or sequencing the *Escherichia coli* genome. Two or three of these

centers will start later this year, funded at \$2 or \$3 million each, and Watson has requested an additional \$26 million for centers for 1991. About a dozen leading researchers have already applied. "If the centers can't go forward, all those who broke their backs during the past 9 months will be discouraged and find something else to do," warns Collins.

Exactly how the genome budget fared with the House appropriations subcommittee won't be made public until the full committee meets, probably in mid-July. The subcommittee's recommendation almost always stands, although the ongoing budget summit between Congress and the White House this year has thrown a wild card into all such deliberations.

Meanwhile, a subcommittee of the Senate Energy and Natural Resources Committee has scheduled a hearing on 11 July to rehash

some of earlier debate on "big" versus "small" biology. Rechsteiner, Syvanen, and Davis have been asked to testify. Ironically, staffers on the House appropriations subcommittee say they never even received the Rechsteiner and Syvanen letters that Watson and his staff are so exercised about. What they received instead are stacks of letters urging them to correct the grant squeeze at NIH, and that, they say, was their first priority this year.

One thing seems certain. Genome supporters will be back next year arguing their case. Says Collins: "We had this naïve idea that we had this debate several years ago, and through it the scientific community came to support the project. NIH set something up, and Congress gave it money. I didn't realize you have to go through this every year."

■ LESLIE ROBERTS

Women Left Out at NIH

A new study says the National Institutes of Health does too little to encourage scientists to include women in their research

IF A FEDERAL AGENCY can be hoist by its own petard, then the National Institutes of Health suffered that experience at a congressional hearing last week on women's health.

At issue was whether NIH is doing an adequate job of implementing its own policy to encourage the inclusion of women in studies that it funds. According to testimony presented at the 18 June hearing of the House Subcommittee on Health and the Environment by Mark V. Nadel, an associate director of the General Accounting Office, the answer is no. To illustrate the problem, Nadel pointed to a study of 22,000 physicians begun in 1981 that demonstrated a beneficial effect of an aspirin every other day on coronary heart disease. Not a single woman was included in the study, and it is impossible to know if women will also benefit from taking aspirin. Other large epidemiological studies, such as the Multiple Risk Factor Intervention Trials of coronary heart disease and the Baltimore Longitudinal Study of Aging, either included no women at all, or added them late to the protocol.

Did NIH deny the charges? Not exactly. Acting director of NIH William F. Raub was conciliatory as he tried to answer the pointed questions from committee members who wanted to know why NIH had promulgated the policy if it didn't plan to enforce it. He conceded that NIH's policy

has been poorly advertised and weakly worded, merely urging grant applicants to "consider the inclusion of women" in clinical trials. He assured the committee that the agency would do a better job in the future. "There was no point in being contentious about it," Raub told *Science* after the hearing, adding that he was aware that a small fraction of NIH staff had "disdain" for the policy, an attitude he said was unacceptable.



Malign neglect. Representative Schroeder says NIH policies put women's health at risk.

But if Raub agreed that the administrative policy needed modifying, he denied that women were being given short shrift by NIH-funded researchers. "I'm confident that the vast majority of clinical and epidemiological trials have women well represented in them," he said.

Representative Patricia Schroeder (D-CO), who cochairs the Congressional Caucus for Women's Issues and who requested the GAO investigation, disagreed. "American women have been put at risk by medical research practices that fail to include women," she said at the hearing. While opinions clearly differ on this point, there is unanimous agreement on another: at present, the data that might determine who is correct do not exist.

NIH instituted its policy encouraging inclusion of women in research protocols where appropriate in 1986, following a Public Health Service task force report recommending greater attention to women's health. The policy called for grant applicants to state whether women would be included in studies and, if not, to explain why. It also said researchers should note and evaluate gender differences in their research proposals. Presumably, this could have created a measurable track record.

But the GAO found that "the policy has not been well communicated or understood" at NIH or in the scientific community and "has been applied inconsistently." After spending several months looking into the question, GAO concluded that it was impossible to determine the impact of the policy. Many grant applications provide no information on the sex of their study populations, while others that excluded women