Varmus Tapped to Head NIH

The long-anticipated nomination of the UCSF biologist was announced last week. Picked more for his scientific credentials than administrative experience, Varmus will face some tough challenges

Harold Varmus was getting ready for the annual softball game between his team and J. Michael Bishop's—a summer ritual for the two Nobel Prize–winning biologists at the University of California, San Francisco—when the news came through last week: The White House had issued a long-awaited statement naming Varmus the next director of the National Institutes of Health (NIH). The nomination won't go to the Senate floor before late September. But now, 6 weeks after Varmus' selection was leaked, it's official. Reached at his lab, Varmus said he is glad the White House has finally tied the knot—especially since he's already made an emotional and financial commitment to the job.

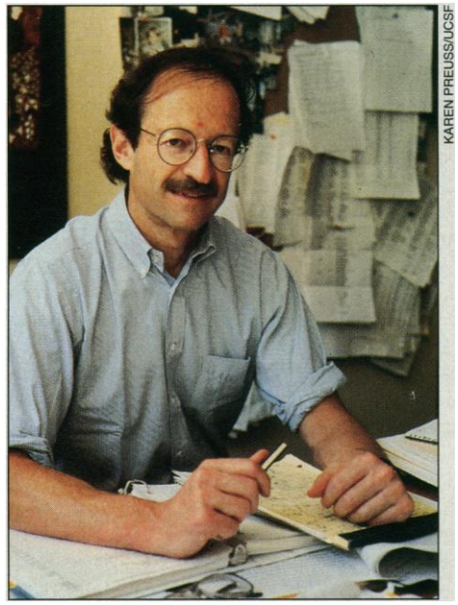
He bought a house in Washington in July; his wife Constance Casey this week got a job as a book editor at *The Washington Post*; his younger son has a place at a local school; and Varmus himself has been reading the fine print of Washington's subway rules to see when he can take his bicycle home on the train. At 53, he still bikes to work. Asked why it took so long to announce his nomination, Varmus professes ignorance. There have been reports that his complex finances slowed down the process, but Varmus says he has "no idea" what this refers to. "I have some biotech stock; once I'm confirmed, I'll sell all that," he says.

Most academics, Varmus says, move to new jobs the way the Queen Mary shifts course: "very, very slowly." But in his case, "there was no other way to do it" than to "take a risk and hope it works out." It is not just Varmus who is taking a risk, however. The Administration picked Varmus knowing that he had little administrative experience beyond running his 20-person lab. Varmus will therefore face a big challenge in mastering the Byzantine ways of NIH's 16,000-person staff. He is inheriting an agency that has lost several key researchers in the past few years, recent budget increases have barely kept pace with inflation, and powerful groups such as AIDS activists and advocates for increased breast cancer funding are arguing for new ways of doing business.

Varmus does, however, have two major assets to help him tackle these issues: His prestige as a Nobelist will open doors in Washington, and he is coming into the job with almost universal backing from the biomedical research community. Moreover, although a neophyte in management, he is no stranger to biomedical politics, having helped resolve a bitter dispute over the naming of the AIDS virus, gotten involved in debates over indirect costs and funding for breast cancer research, and briefed Congress several times on research topics.

A scientist's scientist

If the Senate confirms him, Varmus will be the first Nobel Prize–winner to head NIH—also the first with a master's degree in English literature (Harvard, 1962). Varmus says he developed a taste for literature while an undergraduate at Amherst and wanted to continue exploring it. But in graduate school "I found myself jealous of my classmates who were studying medicine and doing science and were a part of the contemporary world." He read Freud and considered becoming a psychiatrist but settled on medicine, partly because "it was hard to sit still in a room with one other person for an hour."



KAREN PREUSS/UCSF

Risk-taker. Harold Varmus.

He studied medicine at the Columbia College of Physicians and Surgeons, taking 3 months to work in a mission hospital in India and receiving his M.D. in 1966. After a residency and internship at Columbia Presbyterian Hospital, he moved to NIH in 1968 to do research on bacterial genetics in Ira Pastan's lab. Two years later, he joined Bishop at UCSF and was elected a member of the National Academy of Sciences in 1984.

The 1989 Nobel Prize Varmus shares with Bishop was awarded for research showing that a retrovirus gene that causes cancer in chickens first existed as a normal gene in chickens and even in mammals. Early in its evolution, the virus acquired genetic material—key instructions affecting cell growth—from one of its hosts and incorporated this information in its own genetic code, altering it in such a way that it often produces cancer. The discovery put retroviruses in a new light and suggested ways of exploring the genetic causes of cancer (*Science*, 20 October 1989, p. 326).

That stellar research career put him on almost everybody's short list of candidates for the top NIH job (see box). He is a scientist's scientist, getting praise across the board, including from the likes of James Watson, director of the Cold Spring Harbor Laboratory, who spoke of Varmus as "acutely intelligent" and "a delightful person." And as soon as his nomination became official on 3 August, the biomedical societies broadcast their approval with faxed words of praise. The Association of American Medical Colleges called Varmus "a man of high integrity and unquestioned scientific accomplishment," while the Federation of American Societies for Experimental Biology noted that he "understands the importance of basic research."

Indeed, basic research is so important to Varmus that he insisted on continuing to run a lab while directing NIH. It's vital for his new job, he says, that he "retain a clear idea of what it is to do science." He has already negotiated to have his lab—"a scaled-down operation" involving six to eight people—moved to the NIH campus. But some of Varmus' colleagues wonder whether this dual role is too ambitious. Maxine Singer, who is president of the Carnegie Institution of Washington and also runs a lab at NIH, says she told Varmus a few weeks ago that she "thought it was unrealistic" for him to follow her example; Carnegie, she notes, is "a lot smaller than NIH." Nevertheless, she says "he should try it anyway....He might pull it off."

A political scientist

Although the biomedical establishment was delighted by Varmus' nomination, rumblings of discontent from one quarter have already given him a taste of the political pressures he will have to deal with. In July, AIDS

How Varmus Got the Job

Shortly after taking over the Department of Health and Human Services, Donna Shalala asked her friend Howard Temin to suggest possible candidates to be director of the National Institutes of Health (NIH). Temin, a Nobel laureate at the University of Wisconsin—the university Shalala presided over for 5 years—came up with three or four names, but he warned that one was a longshot: fellow Nobelist Harold Varmus of the University of California, San Francisco (UCSF). "He gave me Varmus' name and said I couldn't get him," Shalala laughs. Indeed, "Lots of people said I couldn't get a bench scientist of the first rank," Shalala told *Science*.

Shalala thrives on challenges, but she didn't pick Varmus simply because Temin said she couldn't get him. With the help of assistant secretary of health Philip Lee and deputy assistant secretary D.A. Henderson, Shalala persuaded UCSF biochemist Bruce Alberts, who now heads the National Academy of Sciences, to chair a six-member search committee, which included two women and one African-American.* "I wanted a well-represented committee that the scientific community thought was competent," says Shalala. The committee began work in early April and, except for one face-to-face meeting on 28 April, it did all its work by telephone conference calls and faxes.

One of the first items of business was to decide what kind of person they were looking for. The number one concern, says committee member James Wyche, associate provost at Brown University, was that "the person's research credentials had to be impeccable." The White House made it clear that being female or a minority would be an added attraction, though committee member Samuel Thier, president of Brandeis University and former president of the Institute of Medicine, stresses that "we were never pressured to do anything." Shalala adds that Vice President Al Gore simply advised her to "find an outstanding scientist."

The committee made a master list of names, says Thier, with each member suggesting a handful of people. Names were added from letters sent to the committee, suggestions made by Shalala's office and Congress, and individuals who had applied for the job. Not surprisingly, the list soon swelled to more than 50 names. The committee ranked the candidates, placing about 15 in the top category. The White House personnel office then weighed in with its own list of 60 or so people, who, says Alberts, were "of very mixed quality." Mixed or not, more than a dozen names on the White House list—including Varmus'—were also on the committee's master list.

The committee members, says Wyche, wanted to "look at candidates beyond resumes." So, with Lee's blessing, on 28 April, they began interviewing the dozen top candidates by telephone. One minority candidate made it to this stage but did not make the final cut. "The committee and I personally felt disappointed about not being able to advance a minority," says Wyche, who is black. And, as Shalala was warned, many top candidates bowed out along the way. "About half the people we were interested in weren't interested," said Alberts.

From the outset, Shalala made it clear to the committee that she wanted to know the pros and cons of the top candidates. "I've run enough search committees to not ask for a first choice, because you get cornered if you don't like it." So the committee offered her four names on 19 May: Varmus; Yale provost Judith Rodin, a behavioral scientist; Patricia Donahoe, a pediatrician at Massachusetts General Hospital and Harvard; and William Danforth, chancellor of Washington University. Shalala herself then began interviewing the candidates, and, she says, "a couple of them pulled themselves out." Shalala adds that "some of the other candidates urged me to get Varmus if I could get him."

Varmus wasn't immediately convinced that he wanted the job. "He came in loaded for bear," says Shalala of her interview with Varmus. "But I'm fairly sophisticated at the care and feeding of first-rank scientists." Part of that nurturing included allowing Varmus to run his own lab at NIH.

On 23 June, Shalala transmitted her choice to the White House. According to a source who has seen the letter, she "strongly recommended" Varmus and "mentioned" Rodin and some other names whom the source declined to divulge. Shalala says "the president didn't take very long at all" to settle on Varmus, although it took until 3 August to announce his decision.

As for her friend Temin, Shalala jests that she intends to hold him responsible for Varmus' performance.

–Jon Cohen

* The three committee members not mentioned in the story were: Elizabeth Neufeld, chair of the biological chemistry department at the University of California, Los Angeles, who spent 21 years at NIH; William Richardson, president of Johns Hopkins University; and Linda Wilson, president of Radcliffe College.

activist Martin Delaney of Project Inform in San Francisco raised what he claims are widespread but not widely proclaimed concerns—about Varmus' lack of experience as an administrator, his lack of involvement with the AIDS community, and his aversion to political influence in the setting of research goals (*Science*, 9 July, p. 156). Some AIDS activists are particularly nervous about Varmus' opposition last year to a proposal to expand the power of NIH's Office of AIDS Research. Varmus and his colleague Marc Kirschner, now chairman of cell biology at Harvard, lobbied against it as a potential threat to peer-reviewed research. In an effort to mend fences, Varmus met last week with a delegation of AIDS activists led by Mark Harrington, leader of the Treatment Action Group. All Varmus will say is that "I enjoyed our conversation; I learned a lot about their position," and "I don't see any major conflicts."

Some of the issues raised by Delaney may surface at Varmus' confirmation hearing, and Varmus is reluctant to discuss policy matters until then. He is, however, already on the record on several issues affecting NIH, thanks to a manifesto he co-authored with Bishop and Kirschner in *Science* (22 January, p. 444). The trio made a pitch for increasing the NIH budget by 15% a year, funding 30% of all approved extramural grants (some institutes have had a funding rate as low as 15%), splitting the agency off from the Department of Health and Human Services (HHS), strengthening the "authority of the director over the individual institutes," involving outside scientists more in the direction of NIH, developing new ways to transfer science to biotech companies, and shielding basic research from political mandates.

Varmus already seems to have dropped the idea of an independent NIH, however: He says he's no longer worried about fighting his way through layers of bureaucracy at HHS because he's on very good terms with "the two people above me in the hierarchy, Phil Lee [the assistant secretary for health], who has become a friend of mine and is very accessible, and Donna [Shalala, secretary of HHS]." Their openness and compatibility "made the whole thing seem like a much more attractive job," he says.

A public scientist

Even if he isn't concerned about his relations with HHS, Varmus faces a big challenge in mastering the political side of NIH and the

leadership skills required to manage a big institution on a wide public stage. Although he has never done anything like this before, he has handled some hot research policy issues and enjoys the limelight.

In the mid-1980s, for example, Varmus mediated a wrangle over the naming of the AIDS virus, chairing a committee that settled on human immunodeficiency virus, or HIV. A colleague at UCSF, Jay Levy, says Varmus handled the negotiations so adeptly that committee members were able to do all their business by fax and phone, without wasting time on travel. With Kirschner, he's helped organize symposiums for a group in Congress called the Biomedical Caucus. Staffers and members of Congress get together about once a month to meet big-name researchers and hear their views on current topics. And along with William Richardson, the president of Johns Hopkins University, Varmus breathed life into a group called the New Delegation on Biomedical Research and hammered out a common position endorsed by both scientists and university officials on how the government should deal with indirect cost reimbursement for grants. This show of consensus paid off when White House budget officials revised the guidelines on indirect costs (circular A-21) in 1992 and 1993 and incorporated some of the New Delegation's proposals in the new rules. Richardson, who later served on the search committee that chose Varmus for the NIH job, says he was impressed with Varmus' skills as a natural consensus builder and leader.

Finally, in the last year, Varmus has became directly involved in one of the thorniest issues to hit cancer research in a long time—the Senate's earmarking of $210 million for breast cancer studies funded through the U.S. Army. Varmus sat on an Institute of Medicine panel that drew up a set of recommendations for how the money should be spent. The process introduced him to the breast cancer activists, a familiarity that may help him in the coming months as he meets "a lot more...people who are interested in specific diseases."

The next stop for Varmus is the Senate's Labor and Human Resources Committee. The committee is waiting for the FBI to complete its check and for a separate "background check." When these are done, the paperwork will be sent to the Senate, which will send yet another investigator to quiz Varmus. The nominee will then meet privately with committee members, and after that, he will undergo a public hearing. Committee aides say this won't take place before the end of September. Then comes a vote in the Senate. It all takes time. But with solid support in the biomedical community and scant political opposition, his nomination seems headed for pretty smooth sailing.

–Eliot Marshall

SUPERCONDUCTING SUPER COLLIDER

DOE Pulls Plug on SSC Contractor

From the start, the Superconducting Super Collider (SSC) has been an academic project in every sense: designed, built, and eventually to be operated by companies and researchers working under a consortium of 79 universities called Universities Research Association (URA). No longer. Last week, Energy Secretary Hazel O'Leary took the job of building the $11 billion accelerator away from URA and announced plans to give it to a company more experienced with large construction projects. Clinton Administration officials hope that the change, which followed highly publicized investigations into URA's accounting and management procedures, will help convince the Senate to vote next month to preserve the accelerator and the House of Representatives to reverse its earlier vote to kill the project.

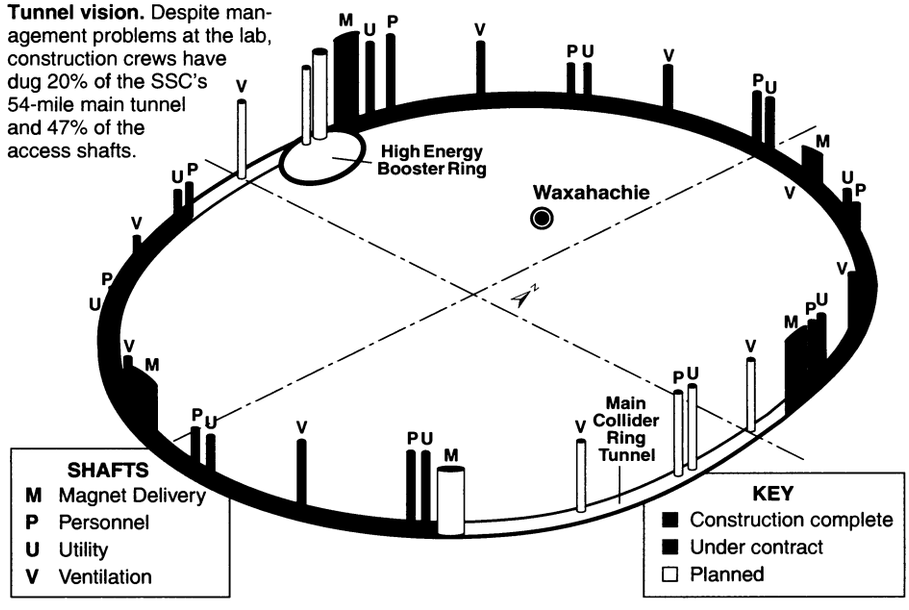
URA, which was formed in 1965 to build and operate the Fermilab particle accelerator, will still have a role in the project, overseeing the design of the SSC and managing its operation as a scientific laboratory. But overseeing actual construction of the 54-mile ring—a task that has been the source of most of the management complaints and is now about 20% completed—will go to a new contractor, yet to be named. "URA is retained to do what it does best: research and development, scientific design, and management and operations of scientific facilities," O'Leary testified last week at a Senate hearing on the project.

O'Leary said that a 30-day review by the Department of Energy (DOE) confirmed what SSC officials have long insisted, that the project was on time and on budget. But the review also found lapses, including the fact that an approved accounting system to control cost and schedule overruns is more than a year overdue and still deficient, that baseline costs and schedules have been "inconsistent," and that the lab has done a poor job of anticipating labor shortages. Alarmed by the absence of solid accounting to show that the lab is within budget, auditors such as the congressional General Accounting Office have predicted large cost overruns. But O'Leary said that the DOE review turned up no such budget problems.

"In general, URA has fallen short of providing the level of managerial oversight necessary," O'Leary testified. But she told Congress that the SSC, which 6 months ago she confessed failed to excite her "passion," was now indispensable. "The project must go forward," she said.

DOE officials hope to select a new lead contractor this fall and are looking for a company with experience in large construction projects. Two possible candidates are Bechtel Corp. and Martin Marietta Corp., both current subcontractors for portions of the SSC construction. DOE and URA officials expect that the transition will not take more than a few months, a delay that would be absorbed by the 3-year project extension that President Bill Clinton imposed earlier this year to improve the chance of finding foreign partners. The cost of the change, O'Leary said, would be "de minimus" compared to the overall project cost and should be recouped in future management savings.

Speaking last month to his staff, laboratory director Roy Schwitters hinted at the DOE decision when he reassured employees



Tunnel vision. Despite management problems at the lab, construction crews have dug 20% of the SSC's 54-mile main tunnel and 47% of the access shafts.