The Klausner Revolution

In his first year as head of the National Cancer Institute, cell biologist Richard Klausner has shaken up the cancer establishment and begun to change the culture of the place. What's next?

For the past year, one of the biggest, oldest, and—some would say—most inward-looking biomedical establishments in the world has been under the command of a rank outsider. Richard Klausner, who had previously managed nothing larger than a cell biology lab, took charge of the $2.2 billion National Cancer Institute (NCI) in August 1995. From the day he arrived, he began talking about trying to "change the culture" of the place. Klausner vowed to set clear strategic goals, open the institute to outsiders, promote new ideas, and establish a flat administrative structure (*Science*, 18 August 1995 p. 912). A year later, NCI is experiencing a whirlwind.

Klausner quickly reorganized the administrative structure of NCI, consolidating all basic science and making a clear separation between extramural and intramural programs. He also surgically removed a middle layer of management, giving lab chiefs more direct control of their own budgets. That internal shake-up is now done except for some "fine-tuning," says his administrative deputy, MaryAnn Guerra. Klausner has shifted funds from NCI's own programs into the extramural, academic research community, and he has brought in outside scientists as advisers to help him run the place. He is moving to make cancer genetics a major focus of NCI's work. He has set in motion top-to-bottom reviews of clinical research supported by NCI and of the 55 cancer centers it funds across the nation; Klausner has said he expects it will result in "a very significant overhauling." All this, he acknowledged in a recent interview with *Science* (see p. 1329), has taken more work and time than he expected. But that doesn't surprise people familiar with NCI, who are watching the progress of the Klausner revolution with interest. Says one longtime NCI consultant: "It will take megatons to move the bureaucracy of NCI."

What is already clear, however, as an intramural scientist with decades of experience at NCI says, is that the new director has been "a breath of fresh air." This lab chief, requesting anonymity, says, "This is the first time I've experienced such sweeping change" at NCI, although he worries a bit about the side effects. "People tend to lose their individuality" in times of turmoil and avoid taking chances. This might inhibit risk-taking. "Suddenly, everything I am accustomed to has changed," the scientist said.

Klausner is the first NCI director since 1980 who didn't rise from within NCI's ranks. And he is only the second among the last seven directors, going back to 1960, to come from outside. (The other exception was Arthur Upton, who came from Oak Ridge National Laboratory to head NCI from 1977 to 1980.) A molecular biologist at the National Institute of Diabetes and Digestive and Kidney Diseases with an interest in gene discovery, Klausner brought an active scientist's perspective to the job. And as the chair of a 1992 in-house review of the National Institutes of Health's (NIH's) entire intramural program, he had definite ideas about how a large federal research program should be run. High on his agenda, he told *Science*, was to send a message to young scientists that "it's not suicide" to stay in basic science. He delivered it by moving money from intramural programs to extramural grants.

The shift occurred after Klausner had revamped the institute's executive committee, converting it to what he describes as a broad-based "governing board." He invited outsiders—including clinical researchers such as Martin Abeloff of Johns Hopkins University and David Livingston of the Dana-Farber Cancer Institute in Boston—to sit as regular members and help shape NCI's central policies. Klausner says these visitors "kept us honest" about supporting extramural research. One result: The committee voted to significantly raise investigator grant support, increasing the proportion of approved applications receiving funds from 15% in 1995 to 23% in 1996. This shift in the "pay line" cost roughly $40 million, most of it financed by a 6% increase in the congressional appropriation and the rest by a decision to decrease spending on contracts and targeted research. Now NCI's goal is to raise the figure to about 30%.

NCI also adopted a rule that any applicant with a proposal whose merit rating fell within four percentage points of the funding cutoff could appeal to the executive committee for an immediate hearing. Proposals involving patients in research got a better break: If they score within 10 points of the cutoff, they are eligible for a quick appeal. "The idea," says NCI's director of extramural affairs, Marvin Kalt, "is to not waste time on amended grants ... and not wait another 9 months for the next cycle" of formal reviews to get a clear decision on a researcher's idea. Applicants who appeal get one shot, though; if they fail, there is no further appeal. This year, NCI has funded 56 grants that failed to meet the pay line. It is no surprise that, as Kalt says, the "response from grantees has been positive."

KLAUSNER'S FIRST YEAR

- Reorganized the entire NCI structure
- Intramural labs get increased authority for hiring, procurement
- Negotiated Mideast cancer research agreement among hostile partners
- Raised single-investigator grant pay line from 15% to 23%
- Set rapid appeals process for rejected grants near pay line
- Began independent reviews of all cancer centers and clinical trials
- Called summit of *BRCA1* researchers to resolve data inconsistencies
- With Pentagon, funded clinical trials through federal health insurance
- Reshaped "bypass budget" into a glossy strategic plan
- Began closing clinical section of Frederick cancer center
- Started work on an electronic "cancer genetics network"
- Planned "genome anatomy project" for early cancer diagnostics
- Created a new special populations office on ethnicity and disease
- Formed an independent cancer council at the National Academy of Sciences

Strategic planning

These money decisions, while important, are really only tactical, says James Armitage, an oncologist at the University of Nebraska who chairs a panel that has undertaken a broad review of NCI-funded clinical research. More important, Armitage sees a "strategic change" taking shape at NCI. Klausner is saying that "what we're here for is to discover new knowledge, and all our efforts should be judged in that light," says Armitage. By avoiding specific disease targets, such as prom-

ising to defeat cancer in a decade—the kind of pledge that typified the original war on cancer—Armitage thinks NCI may become "more productive ... less affected by political issues and less vulnerable to disease-of-the-day [lobbying]."

The NCI's most visible planning effort under Klausner has been the preparation of a strategic plan—normally anathema to biomedical scientists. When former NIH director Bernadine Healy tried to write one for NIH in the early 1990s, she met with scorn from researchers who complained that biomedical research can't be planned like a NASA mission. But Klausner says he felt he had to take on the "paradoxical challenge of planning for science." Over several months in late 1995 and early 1996, he consulted a select group of scientists and NCI leaders to set specific goals and timetables for the next 5 years. The result is a rewrite of what has come to be called the "bypass budget," a document mandated by the 1971 National Cancer Act, which asks NCI to jump over departmental bosses and submit its funding recommendations straight to the president. It had become NCI's wish list, a 5-centimeter-thick "phonebook" describing everything in progress or in prospect that might be done to fight cancer. The old version gave little sign of what should take precedence. Klausner's version is not so reticent.

Released in May, the new bypass budget lays out in a slick, 80-page booklet a 5-year road map for the institute. Replete with glossy photos and anecdotes of families coping with cancer, it gives a terse account of ongoing programs, then launches into the core of Klausner's strategy. It has some explicit goals, such as: "Identify within 5 years every major human gene predisposing to cancer." Its theme reflects Klausner's view that cancer is "a disease of genetic instability," and it indicates that he intends to push NCI to the forefront of gene-based diagnostics and medicine.

Klausner's operating style is evident in the way he is implementing this strategic plan. He has established five new "mini–think tanks," including both intramural and extramural scientists, to develop detailed strategies. At least two of them will focus on genetics. One group—led by geneticists Alfred Knudson, an NCI adviser formerly at the Fox Chase Cancer Center in Philadelphia, and Barbara Weber of the University of Pennsylvania—is considering how to create a "cancer genetics network." Klausner describes this embryonic network as a group of expert centers that will share a common protocol and the use of an electronic network and database. The aim, he says, is to build an infrastructure and accumulate data that will

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SCIENCE INTERVIEW

NCI: A Lab Scientist's View, From the Director's Office

A year after he was appointed director of the National Cancer Institute (NCI), Richard Klausner met with Science *editors and reporters for a broad-ranging discussion of the cancer program. The following is a transcript of the meeting, edited by* Science *for brevity.*

SAM KITTNER

Q: When you took over NCI, did you think about where you wanted to go with NCI in 4 or 5 years and stage the changes?

A: Well, yes and no. I'm actually a fairly impatient person. I felt I've worked very hard the first year to try to transform the place as quickly as possible. And there was a reason for that. ... I really felt that it was time for a cultural change, a change of spirit, a change of approach. I did not think that there was a need to phase in a set of principles. I thought those principles needed to be articulated immediately—day one—and acted on immediately. And so we restructured quite profoundly—one of the largest restructurings in the department's history. Those restructurings were built ... [on a fundamental test]: Is it furthering science?

Q: Could you give an example of how the culture of NCI has changed?

A: [Researchers brought in from the extramural community] sit weekly on the governing board that makes decisions about things like setting the pay line [the percentage of extramural grant applications that get funded, which rose from 15% to 23% this year]. ... To have those voices in the room ... forces us to be able to act on what we said we believed. And in fact that's why we were able to so dramatically change the pay line. There were two reasons. One, we got a good budget. But, in fact, even before we had that budget, we had been able to raise the pay line significantly. ... We looked at everything we were doing: the intramural program, contracts, everything. We went through them and asked tough questions. ... Everything was put on the table. ... The message it sends to the community is ... that staying in this enterprise is worth doing. It's not suicide. That had to be our first priority. We could have articulated that, but having at the decision-making table people like [Edward] Harlow and [David] Livingston and [Martin] Abeloff and [Alfred] Knudson just kept us honest.

Q: Congress is now considering $250 million in special appropriations for breast and prostate cancer research that would go to the Pentagon and not the Cancer Institute. What do you think about that?

A: That's fine. ... It's good if the money will be spent well, and I don't see any reason that the Department of Defense cannot engage in peer review just as well. The breast cancer money [appropriated to Defense in the past] has been spent through a peer-review process, and that peer-review process is going to be reviewed. I happen to think from what I've seen that it looks excellent. In fact, I think there are aspects of it that we can learn from. I don't feel proprietary about where the money comes from. ... I think it's fantastic.

Q: NCI was criticized for using AIDS money for research that really didn't have much to do with AIDS. What changes have you made?

A: I sat down last August [with other National Institutes of Health (NIH) leaders] to work out what we thought was an intellectually useable, useful, and defensible [definition] for AIDS and AIDS-related work. ... We have an obligation to make sure the monies are spent in a way that we believe and we can defend as contributing to the AIDS program. We did not shut down research. ... [But] we have reduced the intramural AIDS funding from about $102 million to about $66 million. We did that in a number of ways. We cut down programs, because at the same time, we were doing very intensive reviews. ... The majority of intramural labs had their budgets reduced just by establishing cost-management principles. When those reductions were in AIDS money, we took it and we put it into the extramural pool. ... We now have a working group that is advising us on priorities in AIDS malignancies, and we have already established

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yield information about the prevalence of genetic mutations and the results of therapy that might otherwise be missed.

Another mini–think tank—led by Eric Lander of the Whitehead Center/Massachusetts Institute of Technology Center for Genome Research and Arnold Levine of Princeton University—is already drawing up plans for a new NCI investment in cancer diagnostic methods based on gene sequencing. Klausner told *Science* that this investment in what he calls the "cancer genome anatomy project" will be aimed at creating equipment that might "read in real time from a single cell the complete genome," using novel electronic sensors. Several biotech companies are investing in such technology (Lander and Levine are associated with two of them), and Klausner has invited staffers from these firms to meet with his planning group.

Klausner would like to put substantial resources into this area. The bypass budget proposes spending $79 million in 1998 on "developmental diagnostics," including $50 million to establish 10 labs to support technology-oriented R&D. Klausner says one of the first tasks will be to create high-quality libraries of full-length cDNA sequences from well-characterized human tissues, something that has never been done. NCI will soon be asking for bids to develop such libraries, he says, and he plans to use the NCI facility in Frederick, Maryland, as a "national resource center" for cDNA library production.

Klausner also used this consensus-building method to good effect last spring, nipping what might have become an embarrassing scientific disagreement in the bud. Aware that studies of the mechanism of the breast cancer gene *BRCA1* were reporting inconsistent results on expressed proteins, Klausner called for a summit of the involved scientists in his office in Bethesda, Maryland, along with NIH director Harold Varmus and others (*Science*, 10 May, p. 799). "A whole bunch of us sat for a day and talked about it," Klausner recalls. "After some initial anxiety, people really opened up ... and agreed to exchange reagents, and they agreed on a whole set of experiments that needed to be done." Klausner says that they asked to be invited back to review the results later, and he plans to issue invitations this fall.

On a wider scope, Klausner and the National Academy of Sciences last month agreed to create a new council based at the academy to debate policy and make recommendations for cancer policy affecting the nation, particularly controversial topics like how to control smoking. This independent body, Klausner has said, will include people representing "all the stakeholders in the national cancer program, be chosen by the academy, and establish its own agenda."

The new NCI director certainly cannot be faulted for a lack of new ideas. But all the new activity may be confusing to some observers. Commenting on the proliferation of expert consultants and cancer advisory committees under Klausner, one patient advocate said that people may begin to wonder "what does one group do that all the others don't do?" The answer to that question may become clear. But it's not an issue that seems to trouble Klausner. From his viewpoint, when it comes to planning the NCI's future, there's no such thing as too much advice.

–Eliot Marshall

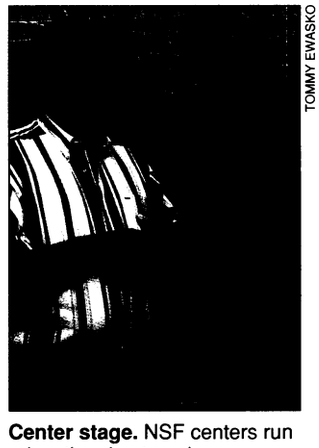
ASSESSING RESEARCH

Pilot Study Teaches NSF Costly Lesson

When a panel of the National Academy of Sciences issued an assessment last month of one of the most visible research programs at the National Science Foundation, the outcome was music to NSF's ears. The Committee on Science, Engineering, and Public Policy (COSEPUP) gave a strong endorsement to NSF's Science and Technology Centers (STCs) program—a $60-million-a-year effort launched in 1989—and recommended that it be continued (*Science*, 16 August, p. 866). Although NSF officials were pleased with the result, the review process itself pleased virtually nobody. Indeed, the assessment turned out to be a $727,000 lesson in how not to measure the value to society of basic research.

NSF officials had hoped the review would do double duty. They needed a top-to-bottom assessment of the STCs to help them decide whether to renew the program before the first centers complete their 11-year funding cycle in 2000. But they also wanted to make the review a model for how to assess the NSF's entire $3 billion research and education portfolio. NSF and every other federal agency will soon be required to make such sweeping evaluations under the 1993 Government Performance and Results Act (GPRA), which directs agencies to justify their budgets based on the value of what they accomplish (*Science*, 6 January 1995, p. 20).

NSF's original plans called for one organization to conduct a 2-year study in two steps: a thorough evaluation of the STC program, which would feed information to an expert panel that would offer advice on the future of the program. But center directors were worried that a contractor might not be able to assemble the necessary talent for a blue-ribbon assessment of their programs. "This program was created out of an academy panel [the so-called 1987 Zare report], and we felt there should be an equally distinguished panel looking at its future," says Ken Kennedy, director of the Center for Research on Parallel Computation based at Rice University. So last summer NSF divvied up the job, awarding COSEPUP $184,000 to assemble the expert panel and giving a $543,000 contract to Abt Associates Inc. of Cambridge, Massachusetts, to collect information on the program. (Abt's four-volume report was submitted to NSF in June.)



TOMMY EWASKO

Center stage. NSF centers run educational outreach programs like this one involving Rice's Richard Tapia and student Pamela Williams.

The academy hoped its expert panel would be able to shape Abt's effort to gather a mass of information on how well the centers were meeting their triple mission of pursuing frontier research, improving science education, and transferring knowledge to industry. Unfortunately, Abt had already developed its survey and begun to collect data by the time the academy panel was formed. In addition to the different paces of the two organizations, NSF was forced to push up Abt's deadline because it needed to submit the findings this summer to another advisory panel, which was preparing a final recommendation to the National Science Board. The board, NSF's oversight body, is expected to make a decision in November.

The result was a procedural nightmare. "The panel strongly recommends against NSF's use of a process like the one used in the STC program evaluation as a model for future evaluations," COSEPUP concluded in its report. "We need to recognize that this was an approach that didn't work even though [NSF] spent huge amounts of money on it," says William Brinkman, vice president for physical sciences at Bell Laboratories and chair of the COSEPUP panel. "The fundamental structure was wrong."

And the price was most definitely not right. "We realized, in retrospect, that there was no way we could afford to do this across the whole