# Is NIH's Crown Jewel Losing Luster?

*Science* examines the NIH intramural program and finds intramural and extramural researchers agreeing that strenuous efforts must be made if excellence is to be sustained


Can Harold Varmus fix the intramural program at the National Institutes of Health (NIH)? Some researchers would say that's an outrageous question. After all, they argue, the intramural program, boasting 4500 researchers in 25 institutes, centers, and divisions, doesn't need fixing by the newly nominated NIH director—or by anyone else, for that matter. It's one of the jewels in the crown of U.S. biomedical research, they say. Reasons for enthusiasm about the $1 billion-a-year program in Bethesda aren't hard to find. From the program have come four Nobel laureates: Julius Axelrod (in 1970 for helping discover neurotransmitters), Marshall Nirenberg (1968, for his part in cracking the genetic code), Carleton Gajdusek (1976, for his pathbreaking work on slow viruses), and Christian Anfinsen (1972, for elucidating how the enzyme ribonuclease assumes its full three-dimensional shape).

One level down from the Nobelists, there's also plenty to shout about. The lab of Robert Gallo isolated the first human retrovirus, in addition to the growth factor interleukin-2, and proved that HIV causes AIDS. Ronald Crystal, W. French Anderson, Michael Blaese, and Steven Rosenberg led the way to gene therapy trials in humans. Less visible in the lay press, but highly regarded by their peers are NIH researchers such as Earl and Thressa Stadtman, who pioneered the field of enzyme regulation, Gary Felsenfeld, who studies gene regulation, and Igor Dawid, a leading developmental biologist.

And yet some top researchers and scientific managers, though deeply loyal to NIH, say the intramural program is losing some of its luster. "This has, in its time, been the success story of the United States when it demonstrated the range of basic and applied research, and it made clinical medicine what it is," says Donald Fredrickson, NIH director from 1975-81. But, he adds, "there are serious problems on the campus."

Fredrickson's worries find echoes in others. Samuel Thier, president of Brandeis University and former head of the Institute of Medicine, who got early training at NIH, says he has "a sense that there is an aging in place. They're not as competitive." C. Thomas Caskey,

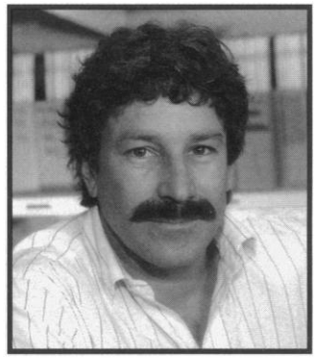
## THE QUALITY OF RESEARCH

For the extramural community of U.S. biomedical scientists, spread through research universities across the nation, the peer-review process that determines who gets funded guarantees the quality of research. It's a straightforward, though not always kind, Darwinian mechanism: The stronger the research, the more likely it is to be funded.

That's an excellent model for encouraging basic research, but the intramural program wasn't set up just to encourage basic science; it was designed to provide a setting for applying basic research to clinical problems. As former NIH director Fredrickson puts it, the intramural program at NIH "is responsible to the most important, basic anxieties of everybody—health and disease." To meet that responsibility, Congress has added one disease-specific institute after another over the past 106 years. And within these institutes, researchers are all but guaranteed funding, never having to apply for grants.

That safety net has benefits for research. It frees intramural investigators to do high-risk investigations and direct their efforts at disease, spending no time competing for grants. Proponents of the program point to the Nobel Prize–winning work—and its near cousins—as proofs that this method breeds success. Yet even some of NIH's closest friends are concerned that the quality of research is not as high, overall, as it was two decades ago, during the so-called Yellow Beret era, when an appointment at NIH offered a safe haven from Vietnam and lab chiefs could choose from the nation's most promising young researchers. Klausner himself says, "I think NIH intramurally has slipped," but adds, "it could be resuscitated."

Specifically, critics point to the fact that many of NIH's stars have left. In the past few years, W. French Anderson and Ronald Crystal, who helped make the National Heart, Lung, and Blood Institute (NHLBI) a leader in gene therapy, departed. So did NHLBI's Arthur Nienhuis, a leading stem cell biologist. The National Cancer Institute (NCI) will soon lose Peter Howley, chief of tumor virus biology, and Stuart Aaronson, head of the laboratory of cellular and molecular biology. These researchers decided to leave to take on challenges ranging from running a university department to running a biotech company; they won't be easy to replace.



**"I THINK NIH INTRAMURALLY HAS SLIPPED [BUT] IT COULD BE RESUSCITATED."**

**RICK KLAUSNER**

"You measure the quality of research by the number of figures gone and how they've been replaced," says former director Fredrickson. He says the intramural program's "output is still very high, but it's suffering a hemorrhage that's not being stemmed."

There are still plenty of top-flight researchers in the program. But the critics contend that as a result of the turnover, the variability of quality in the program has increased and there are more pockets of less than absolutely first-rate work than there were 20 years ago. A respected NIH veteran who left for a research university compared the campus to the most highly touted academic research centers, such as the University of California, San Francisco (UCSF). "Generally, you think of UCSF and get a very good impression all around. It probably isn't true, but you think it's uniformly excellent. The same is not true for NIH." And though this former NIH star says there are the makings of "10 extraordinary departments" in the

chair of Baylor's Institute for Molecular Genetics, concurs: "Almost anyone you talk to will tell you this thing is spending one hell of a lot of money and it needs to be tuned up."

These sentiments suggest that the intramural program is at a crossroads. Before and during the stormy tenure of former director Bernadine Healy, the program suffered profound blows, from within and without. Internally, there has been an exodus of some of the program's top scientists. From the external world, there have been harsh (though largely private) attacks by scientists in the extramural community who believe intramural scientists have an easier time because they do not compete for grants. And with Congress becoming increasingly desperate about stemming budget growth, the intramural program is beginning to receive microscopic scrutiny on Capitol Hill.

In the face of these pressures, which road will the new leadership of NIH take? Will they continue the methods and policies that have prevailed for the past decade? If they take that path, it will mean they have decided the claims of the critics—that the crown jewel is losing its luster—are exaggerated. On the other hand, they may conclude that the critics are right: Things aren't quite what they used to be on the Bethesda campus and a strenuous effort to revitalize the program, while retaining what is best in the present system, is in order.

With choices like that confronting the new leadership of NIH, *Science* launched an inquiry into the intramural program's strengths and weaknesses. Our investigation lasted 6 months and included interviews with more than 100 scientists at every level—including four who have run NIH. As we made our way through this landscape, one very useful map came from NIH itself: the "Klausner report," commissioned by former NIH director Bernadine Healy after complaints from bench-level scientists that they were being left out of critical administrative decisions. Named for Richard Klausner, head of the Cell Biology and Metabolism branch at the National Institute of Child Health and Human Development (NICHD), the report was written by a panel of 18 distinguished intramural scientists (for a list, see page 1126). The report reached Bernadine Healy's desk in April 1992, but it has received little publicity.

The Klausner report, very penetrating for an institutional self-analysis, helped set the agenda for *Science*'s questioning. Among the subjects raised by the report, four were key topics:

- The quality of research in the intramural program (which some researchers interviewed by *Science* suggest has become less uniform than it once was).
- The traditional style of management in the program (which many describe as rigid, "top down," and confining).
- The hierarchy within some laboratories (run on old-fashioned "Herr Professor" lines that inhibit young researchers' independence).
- The program's difficulties in recruiting and retaining top-notch scientists at all levels.
- In examining these issues, it became clear that a fifth topic may soon overshadow all the rest. This issue was not addressed directly in the Klausner report, but it was brought up by most of those close to the intramural program: the increasingly severe funding constraints on the program, which some feel will force existing programs to be cut to provide resources for growth.

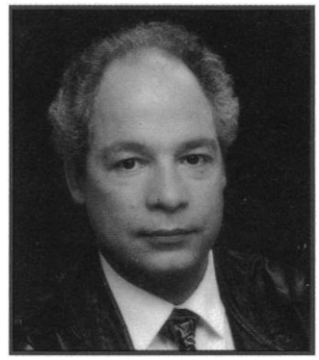
None of these issues is simple. All are complex, and since they are interrelated, they must be dealt with simultaneously. How the new leadership of NIH deals with them will determine the health of the intramural program for years to come. In Part I of our NIH inquiry, *Science* examines each of these key issues in turn. In Part II, which will be published shortly, we will examine the equally important question of who sets the research agenda for NIH—and how it is set.

intramural program, he says that, on average, "it's not as attractive as it once was."

Top administrators of the program, however, say this view is wrong. "There's a lot of good evidence that we have excellent research here," says Lance Liotta, NIH deputy director for intramural research and himself a lab chief. James Wyngaarden, NIH director from 1982 to 1989, says "the quality's enormously high." More to the point, these advocates say, overall quality is not going down. On the contrary, says Liotta, the excellence of research in the program is "generally increasing." Liotta does acknowledge that not all intramural research is of stellar quality, but that, he says, is simply a fact of life: "In any organization there are stars and people who can be improved."

Turnover, says Liotta, is actually a positive process that is part of NIH's mission. "One of the purposes of NIH is to create an environment where talented people shine—and then they're recruited. We're really a stopping place for our scientists, and we maintain a core of mentors to train scientists for the extramural community." NCI director Samuel Broder also sees great benefit in the turnover of talent. "Most people who leave NIH don't leave the planet," says Broder, explaining that they spread good science to other institutions, something he thinks is part of the mission of NIH, and, what's more, is good for it, since "biological systems need renewal."

There is no conclusive way to tell who is right—the program's critics or its defenders. Yet there are indicators that could be used for an assessment. One is citation data from the Philadelphia-based Institute for Scientific Information (ISI). Liotta is quick to point out that NHLBI was recently ranked first in "citation impact" (average number of citations per paper) in a ranking of institutions doing work on cardiovascular and respiratory medicine. In a similar ranking for recent AIDS research (1988-92), four NIH institutes were among the top 20: Allergy and Infectious Diseases (NIAID) (5), Dental Research (10), Neurological Disorders and Stroke (11), and NCI (17).



**THE QUALITY OF INTRAMURAL RESEARCH IS "ENORMOUSLY HIGH" AND "INCREASING."**

**LANCE LIOTTA**

Another insider at NIH pointed to ISI's 1992 list of the 100 most cited scientists in the world during the 1980s (which measures only the total number of citations, not citations per paper). Of the 75 or so U.S. researchers on the list, 16 were in the NIH intramural program for much of the decade. Yet the same researcher conceded that six of those scientists had left the campus for other posts; another is now leaving.

And other citation data don't paint quite as rosy a picture as the one Liotta offers. In a recent citation analysis of "high-impact institutions in molecular biology and genetics" from 1988-92, the highest rated NIH institute, NICHD, came in 16th, and only one other—NCI—was ranked in the top 25. A listing of the top 25 individual researchers in the same field included only one from NIH: Richard Klausner. (Francis Collins, recently recruited to become director of the National Center for Human Genome Research, NCHGR, made the list, but for work done at the University of Michigan.) One researcher who was listed among the top 25 and insisted on anonymity called it "amazing" that Klausner is the only researcher whose work at NIH puts him in the top 25 in the key field of molecular biology and genetics.

Although the loyal critics and the staunch defenders of the intramural program are far apart in their assessment of the program's current quality, both sides agree

on one thing: The mechanisms for maintaining quality could be sharpened.

It isn't that intramural scientists are not held accountable for quality. Once every 4 years a group of outside investigators known as the board of scientific counselors reviews each lab's work, researcher by researcher. Some of those familiar with this process, however, argue that it lacks teeth and that it is not a truly independent review.

A high-ranking NIH administrator who demanded anonymity says, "These reviews are never independent, because the institute director or the scientific director influences who is selected for the board of scientific counselors." She adds that when a negative review is submitted, there isn't any way to make sure it's translated into action. "If the director doesn't like it, he can just say the guy [doing the review] had a bad hair day," she quips. "No one has to see [the report]." Indeed, NIH told *Science* that these reports are not available for public review.

Other senior NIH insiders agree that the recommendations by the board of scientific counselors, which go to the scientific directors who run the intramural programs at each institute, are not always followed. A highly respected lab chief says that in spite of the review process, the scientific director at his institute—which he insisted not be named—has failed to clean house. "There are three lab chiefs and maybe four that should step down or scale back their labs," says this researcher, whose institute has fewer than a dozen labs.

Other top NIH researchers, however, bristle at the idea that the review process is toothless. "I've closed three labs during the last 5 years because our board of scientific counselors felt these labs should be shut down," says Irwin Kopin, scientific director at the National Institute of Neurological Disorders and Stroke (NINDS).

Nevertheless, the Klausner committee was concerned enough about the problem to recommend that the scientific directors should be required to respond—formally—to the recommendations in each review. Liotta concedes that this level of accountability was not uniformly practiced in the intramural program when he took over as deputy director in August 1992, but he says "that's exactly" the policy now being put in place. "It's improving, and we're making it more uniform with new policies," he says. "I can assure you it's a rigorous review across all institutes."

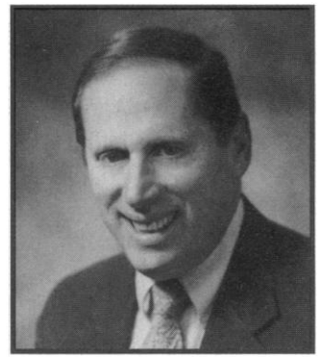
Yet some insiders don't think the Klausner committee's recommendation goes far enough. A lab chief who demanded that his comments be off the record suggests one solution that would preserve the advantages of the current system while adding an extra measure of quality: giving intramural researchers rolling contracts that would be renewed following a good review, like the system used by the Howard Hughes Medical Institute. "Nobody who's good and productive would be afraid of that," he says. Liotta counters that this solution isn't practical since NIH, with its government hiring rules, is "not as flexible" as Hughes and couldn't easily remove those who didn't get good reviews.

Constraints like this one—along with the special nature of the intramural program itself—dictate that the task of assessing and, if need be, improving the quality of NIH intramural research will be a thorny and difficult one. Nonetheless, it is a task Harold Varmus will find looming in his inbox from the day he arrives in his Bethesda office.

## 'TOP DOWN' MANAGEMENT

If the quality of research is a hot button in the debate over NIH's intramural future, it is no more controversial than the dialogue taking place over the style of management in the program—and how it differs from the style of the extramural community. In contrast to university research departments, which generally have a loose, collegial structure, NIH units frequently have a "top down" style, in which the voices of individual investigators are muffled. Says William Paul, head of the laboratory of immunology at NIAID, co-chair of the Klausner committee, and one of the most respected researchers in the intramural program: "Many of my senior colleagues don't feel they have a voice in recruitment, fund allocation, space allocation, or where NIH is going."

If individual investigators don't have much say in where their institute is going, who does? The answer, generally, is the institute's scientific director. Each of the 21 scientific directors (see table on page 1126) reports directly to the institute director and has authority over budgets and space for every lab in the institute. (The exception is NCI, which has four scientific directors.) The directors are a well-entrenched group: They are appointed for indefinite terms, and the 13 who have held their jobs for 5 years or more control more than 75% of the total intramural budget.



**"MANY OF MY SENIOR COLLEAGUES DON'T FEEL THEY HAVE A VOICE IN WHERE NIH IS GOING."**

**BILL PAUL**

"The scientific director, as long as he has the confidence of the institute director, has enormous power," says Paul. Former NIH director Healy puts it even more strongly. "The scientific directors," she says, "often feel they don't have to even answer to the institute director. They are their own show."

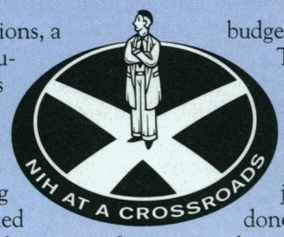
Such power was designed to direct research down fruitful avenues, and, in the past, this method produced success. But as hierarchies become more entrenched, the top down system has become sclerotic and incapable of tough decision making, according to many of those interviewed by *Science*. "Where I'd fault some of the scientific directors is when budget constraints come in, they'll apply cuts across the board and not ask what should get eliminated," says Peter Howley, a Klausner committee member and an NCI lab chief who is leaving after 20 years to chair the pathology department at Harvard University.

The failure to make tough choices can have direct consequences on researchers at the bench level. Take Joseph Bolen. In the early 1980s, Bolen, a staff fellow at NCI, couldn't wait to get to work. By the time his car reached Wisconsin Avenue, the tree-lined street leading to NIH, Bolen recalls, "My blood really started pumping." His young colleagues were a talented bunch; NIH "was an exciting place to be"; and Bolen's research on the enzymes called tyrosine kinases and the role they play in cellular signal transduction was going well. As his research star rose, NCI gave Bolen tenure, along with a prestigious Award of Merit for Research, and made him the head of a lab with 10 people under him.

Yet, over time, Bolen's enthusiasm for NIH waned. It wasn't just his government salary, which started looking small as his kids came closer to college; it was also the fact that there was no room for his lab to grow. To get more space, he says, his managers would have had to trim other labs that weren't doing as well. And that was something the scientific directors either weren't willing or weren't able to do.

In Bolen's view, some NIH scientific directors aren't in close enough touch with cutting-edge science to decide which labs should be cut. "There are labs [at NIH] that wouldn't be competitive at a university setting," says Bolen. "That tells you that perhaps people at the top don't have the power or the knowl-

# How Much Is Enough? NIH's Best-Funded Labs




Although the subject provokes sharply divided opinions, a substantial group of researchers think the NIH intramural program needs to increase its efficiency and its quality. While it's difficult to measure things such as efficiency and quality at a program as big and diverse as the intramural program, there are some obvious places to look, and two of those are measures of funding and lab space. As part of our investigation, *Science* asked NIH to provide us with a list of the 10 best-funded intramural researchers and the square footage in their labs (see table below).

Although funding in the intramural program is handled differently than it is in the extramural program, *Science* made every effort to obtain figures comparable to those for extramural researchers. Thus the figures in the table include salaries, services and supplies, animals, travel and equipment, and research support contracts, and they exclude indirect costs and funds spent on clinical support. The list also excludes lab chiefs who simply pass money along to independent investigators.

When Lance Liotta, NIH deputy director for intramural research, was asked whether the figures in the table could be compared with grant support for extramural researchers, he noted that "virtually all of these funds come from the intramural budget. On the outside, investigators only get a portion of their support from R01 grants or contracts. They can also use funds from a practice plan, clinical support, and endowments. That's an important distinction." Liotta notes that the funds listed here cover costs for animal research; extramural grants sometimes do not.

Liotta also noted that "in terms of productivity and accomplishments, may of those [on the list] are stars." Indeed, several on the list have made major accomplishments by doing just what the intramural program is supposed to do, pushing quickly into risky terrain with high clinical payoffs. Crystal helped pioneer gene therapy; Gallo's lab developed the first marketed blood test for antibodies to HIV; Gajdusek helped lay the foundation for the field of slow viruses.

Furthermore, as Igor Dawid, head of the laboratory of molecular genetics at the National Institute of Child Health and Human Development, points out, the list does not mean all labs in the intramural program are very large—looking at the entire picture could lead to different conclusions. "This list could create the view that NIH is massively overfunded," says Dawid. In fact, Dawid says, "there's almost a question of whether many labs at NIH are too small to be effective." For example, he says, genome sequencing is not effective with four people. "There's probably a need for big and small labs," he concludes.

Nevertheless, the table produced a dramatic effect on extramural researchers. After explaining what is included in these figures and what isn't, *Science* showed the list to a group of well-funded, highly regarded researchers at academic and private research institutions. Few investigators were willing to be quoted by name, but most were startled. "It's appalling," says one researcher at Rockefeller University, whose lab has less than a $500,000 budget and 2000 square feet. "I'm glad I'm sitting down. There's nobody's budget [at Rockefeller] that even matches the bottom person on this list."

A frequently cited investigator at another West Coast research institution who is familiar with the work of four of the 10 labs says their output does not justify the resources allocated to them. "What's being done in these labs is certainly not much better and is even worse than what's being done on the outside," asserts this researcher, who has a $700,000 budget and 1200 square feet.

Though Bruce Alberts, new head of the National Academy of Sciences, did not know enough about the 10 to comment on their work, he says he's "very dubious" about whether, in general, labs of this size are a good idea. "My philosophy's completely different," says Alberts, who recently left an $800,000 a year lab with 2000 square feet at the University of California, San Francisco. "In biology, we don't want a factory production, we want creative ideas. And we get creative ideas by giving money to young people." Alberts, whose own lab had 12 postdocs, contends larger labs tend not to get the best researchers, since the most dynamic and creative young researchers "want to publish without senior researchers and get credit for their own work."

Alberts says he would like to see a study comparing funds spent by intramural labs against labs doing similar work in the extramural community. "There are imaginative ways to get at this," Alberts says. Liotta says he welcomes direct comparisons between intramural and extramural researchers. What is more, he says, the "institute directors learned a lot [from creating the list at *Science*'s request] and so did the scientific directors." The question remains: Would they learn still more from a direct comparison of extramural and intramural funding?

–J.C.

**BIG TEN: TOP-FUNDED NIH INVESTIGATORS**

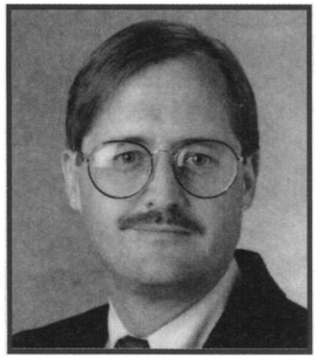
| Investigator | [1]Staff | [2]Budget (in millions) | Square ft. | [3]Publications 1990-92 |
|---|---|---|---|---|
| 1. Ronald Crystal, MD Pulmonary Branch, NHLBI | 34 Doctoral | 4.400 | 5755 | 87 |
| 2. Michael Sporn, MD Lab of Chemoprevention, NCI | 20 Doctoral | 2.881 | 7291 | 31 (1992) |
| 3. Carleton Gajdusek, MD Lab of Central Nerv System Stud, NINDS | 17 Doctoral | 2.606 | 7685 | 115 |
| 4. Robert Gallo, MD, Lab of Tumor Cell Biology, NCI | 19 Doctoral | 2.606 | 6845 | 42 (1992) |
| 5. Stuart Aaronson, MD, Lab of Cell & Molecular Biology, NCI | 16 Doctoral | 2.595 | 4456 | 35 (1992) |
| 6. Stanley Rapoport, MD, Lab of Neurosciences, NIA | 17 Doctoral | 2.534 | 3391 | 104 |
| 7. Louis Sokoloff, MD, Lab of Cerebral Metabolism, NIMH | 12 Doctoral | 2.359 | 4672 | 26 |
| 8. Arthur Nienhuis, MD, Clinical Hematology Branch, NHLBI | 11 Doctoral | 2.199 | 3450 | 35 |
| 9. Daniel Weinberger, MD, Clinical Brain Disorders Branch, NIMH | 18 Doctoral | 2.007 | 3848 | 63 |
| 10. Dennis Murphy, MD, Lab of Clinical Science, NIMH | 7 Doctoral | 1.845 | 2002 | 75 |

1. Staff (as of end of FY 1992)
2. Budget (FY 1992): Includes personnel, services and supplies, travel and equipment; includes costs for purchase of animals and research support contracts, but does not include Management Fund Expenditures or research patient support contracts.
3. Publications: Except where noted, these are publications signed by the investigator in 1990, 1991, and 1992.

SOURCE: NATIONAL INSTITUTES OF HEALTH

edge to alter the situation." And Bolen further charges that critical suggestions by the board of scientific counselors often do not lead scientific directors to make significant changes. "It just doesn't happen," asserts Bolen. "Most commonly, labs are dissolved when lab chiefs die."

For Joe Bolen, the result was the search for an exit. By 1990, he had departed for Bristol-Myers Squibb, where he has 20 people working under him, 10 times the lab space he had at NCI, and a salary "several-fold" higher than his government compensation. Bolen's flight wasn't solo. "My peers, the group I hung out with who were all tenured and poised to take the next step—no one's left" at NIH, he says.



**"THERE ARE LABS [AT NIH] THAT WOULDN'T BE COMPETITIVE AT A UNIVERSITY SETTING."**

**JOE BOLEN**

Bolen's story suggests that part of the answer to keeping talented young researchers lies in making difficult decisions about allocating lab space and funding. In the extramural program, those decisions are made automatically through peer review. Should the intramural program adopt that model? Because its mission is different from that of the extramural program, few argue that the top down style ought to be jettisoned altogether. What the critics do say is that in order for the top down system to work, those at the top—the scientific directors—must themselves be first rate and in contact with the scientific cutting edge.

And there's the rub, because the scientific directors have traditionally received little regular review. In fact, until a 1988 Institute of Medicine report called for regular performance reviews for scientific directors, there was no system of regular performance appraisals for these key administrators. Since then, only three scientific directors have been reviewed, according to Lance Liotta.

The Klausner committee concluded that it is "critical" for scientific directors to be evaluated regularly. The report recommends a procedure for reviewing the directors' performance, including interviews with the scientific staff that reports to each director. Some members of the extramural group that reviewed the Klausner report went further, suggesting that rather than being appointed indefinitely, scientific directors be given 5- or 6-year terms, renewable after good performance reviews.

Liotta agrees that scientific directors need to be regularly evaluated—and he says NIH is taking steps to do just that. Though he concedes "we could be moving faster" in reviewing the scientific directors, Liotta says five reviews are under way and the rest should be scheduled, if not completed, by next year. Completing those reviews will be a start, but it will certainly not resolve the complex issue of just how the intramural program ought to be organized and managed.

## 'HERR PROFESSOR' LABS

The top down style that endows an institute's scientific director with so much power is mirrored by an arrangement within many NIH labs that gives the lab chief tremendous authority over his younger colleagues. At a major research university, a young researcher sinks or swims depending almost exclusively on how much grant support he or she can wrest from the NIH competitive extramural system. In the intramural program, however, a young researcher can succeed scientifically and yet be stymied by the senior scientist who runs the lab and doesn't cherish independence on the part of young subordinates.

Consider the lot of one young NIH researcher, who, for fear of further antagonizing his boss, insisted on remaining unnamed. The researcher is highly regarded, a fact confirmed by interviews with many in his area of expertise as well as by his excellent publication record. Yet his lab chief is "squeezing him" to collaborate, he claims, and because he has resisted that pressure, his chief has essentially frozen his level of research funding over the last 4 years. "I can't tell you how many ideas I've offered up that have never gone anywhere," he says. He adds that he has even looked for outside funding, which caused problems, since his managers consider going outside for funds "an embarrassment."

This young researcher says discussions with the scientific director who oversees his lab chief didn't help. The scientific director "doesn't appreciate young talent and potential, and he doesn't think in long-term goals," the young investigator asserts. Even more frustrating, he says, is the fact that his scientific director doesn't seem to have a firm scientific understanding of the young investigator's work. Rather than judging the work himself, the scientific director's "set of reference points are other sources, like [my lab chief]."

The result is that this investigator, who has tenure at NIH, is seriously considering leaving for a university setting. "I'm very frustrated where I am," he says. Yet he says leaving the intramural program would be painful, since he thinks that when the system works, it encourages risk-taking in a way that is extremely beneficial for science. "If there's anyone who appreciates the opportunity here, it's me. I never thought I'd outgrow such a beautiful system for research, but I've outgrown it."

This young researcher is discontented, but according to his peers, he's far from being a congenital malcontent. Furthermore, he is not alone in his concern. The Klausner committee also wrestled with the problem of what one NIH researcher dubs the "Herr Professor" labs. In this model, which mimics old-fashioned European research groups, all investigators work for the lab chief, include his or her name on their papers, and have little say about funding or space. There are no good estimates of how many NIH labs are organized along these lines, but it is at least a significant minority.

The Klausner committee's report was unequivocal about this problem. They recommended that, rather than creating any new labs on this model, NIH should establish tenure-track positions. The report urges that the bright young researchers occupying those tenure-track positions be guaranteed "an independent position with independent resources." In addition to revitalizing the research program, such a policy change would be an important recruiting tool, the authors of the report argue, helping make the intramural program "one of the most attractive institutions in which to begin a career in biomedical research."

The structure of the Herr Professor labs is an issue on which even the most loyal defenders of the intramural program acknowledge the need for change. And indeed, insiders say that even before the Klausner committee was formed, the NIH scientific directors were considering a tenure-track policy. Though Liotta stresses that many Herr Professor labs have been very productive, he quickly put the tenure-track policy into place after assuming the directorship last year. "Our new tenure-track policy will move us toward fewer monolithic labs in the future," says Liotta. "And that's especially good for recruitment of minorities and women."

Certainly, offering academic-style, tenure-track positions could make NIH more attractive to creative young researchers starting out in science. But there's no move afoot to dismantle the existing monolithic labs, and because NIH lab chiefs tend to stick around for many years, the Herr Professor labs, with their legacy of European research tradition, may be an issue at NIH for years to come.

## RECRUITING THE BEST

As the Klausner report pointed out, phasing out the Herr Professor labs was important not just to refresh the existing research program but also to provide an environment that would draw the best and brightest—something NIH once had no trouble doing. It has such trouble now, though, as Thomas Caskey, who knew the institution from the inside during the "Yellow Beret" days of the late 1960s and early 1970s, is well aware.

From 1965 to 1972, Caskey was an investigator at the NHLBI, and in that period, he says, those who got into the intramural program "competed very hard for those positions." The result was an exciting group, including, down the hall from Caskey, Joseph Goldstein and Michael Brown, who later shared the Nobel Prize for their work on cholesterol metabolism and how it might contribute to heart disease.

Two decades later, Caskey, who runs an MD/Ph.D. program at Baylor, has a less sanguine point of view on intramural recruiting. Few of his top students, he says, are inclined to head for the intramural program. "The number's been quite low for a long time," says Caskey. The reason, he adds, is that NIH doesn't appear to these superior students to be in the very highest ranks of scientific excitement. "I don't think NIH has had the productivity or breakthroughs in science that have occurred at Harvard, Washington University in St. Louis, UCSF, or Baylor."

And it isn't just Caskey's best students who aren't drawn to NIH the way they used to be—the phenomenon appears to be widespread. "We don't have as many brilliant young people now," says Joseph Rall, an investigator who has worked at NIH for 38 years and formerly headed the intramural program. "I'm more worried now than I have been in a long time."

The Klausner report concurred with these anecdotal reports, concluding that the overall quality of current intramural post-docs is "more varied" than it was previously. And this uneven quality in the ranks of the young researchers led the committee to concerns about refilling the ranks of their senior colleagues. The Klausner report says that on the campus it is "the current perception that the recruitment mechanism that worked so effectively in the past, largely based on choosing staff from the pool of intramural research program postdoctoral fellows, is no longer sufficient for the institution's needs."

If the cadre of young researchers at NIH is

## 'Power to the People'—Research Style

Are senatorial ambitions the answer to some of the problems in NIH's vast intramural program? No, we're not talking about Bernadine Healy's interest in a Senate seat from Ohio. We are talking about an innovative proposal offered last year by the Klausner committee, a blue-ribbon group of NIH researchers that conducted a critical review of NIH's intramural program (see main story).


The Klausner committee concluded that one crucial problem at the NIH intramural program was a top-down style of management that shuts many senior scientists out of the decision-making process on the Bethesda campus. As former director Healy puts it: "In the extramural community, everything is coming from the bottom. In the intramural community, it's all top down. It's positively dictatorial. And I think a lot of the morale problem is that it is so top down." To address that problem, the Klausner report calls for a novel idea: giving bench-level researchers a voice in management by establishing a "faculty senate" modeled on those at universities.

**"IN THE EXTRAMURAL COMMUNITY, EVERYTHING IS COMING FROM THE BOTTOM. IN THE INTRAMURAL COMMUNITY, IT'S ALL TOP DOWN."**

**BERNADINE HEALY**

If the report's recommendation were implemented, there would be eight newly organized NIH "faculties," constructed according to the boundaries of scientific disciplines rather than along the lines of disease-oriented institutes, as the program now is. Those faculties would send representatives to a senate that would provide a forum for intramural scientists to hash out problems and arrive at consensus solutions. Those solutions, in turn, would be passed on to the scientific directors, the 21 key scientific administrators who set the research agendas for their institutes. The report suggests that the faculty senate advise scientific directors on tenure decisions, appointment of lab chiefs, and on which outside scientists to select for the site visits the intramural program uses to review its labs.

To someone from the academic community this may not seem like a particularly radical proposal. But Healy, who established the Klausner committee, sees it as revolutionary. The idea of a faculty senate at the NIH, she says, represents "power to the people"—a prospect she says she's delighted with.

The scientific directors, however, are reportedly not thrilled at the notion of having their power diluted. They did give nominal approval to the notion of a faculty senate in their review of the Klausner report, completed on 10 March. At least that's what they said for the record. Off the record, NIH insiders say, the scientific directors—who suggested that the senate be called a "scientific advisory group"—were none too happy with the idea of even modest power-sharing.

"The scientific directors are pretty upset that Klausner and the other scientists who have no authority over the scientific directors did that report," says Healy, who, before she left office in June, heard a rising volume of complaints about these proposals. "It really erodes the power base of the scientific directors because they're no longer calling the shots."

In the face of internal opposition, it isn't clear whether the notion of a senate could ever be implemented. And *Science*'s investigation found that even if a faculty senate were established, some bench-level scientists, frustrated by the current system, have little faith that it would do more than add another layer of politics and bureaucracy to an already politicized, bureaucratic institution.

Those in favor of the idea counter that the payoff could be high—bringing the best scientists into the decision-making loop. "Many of our most able scientists are not lab chiefs," says William Paul, chief of the immunology lab at NIAID, and co-chair of the Klausner group. Under the current system, says Paul, those who are not lab chiefs must "push the system" in order to be heard. "It's very hierarchical and it's hard for them. Although there's no power in a faculty senate—their powers are by moral suasion—the scientists would have a mechanism where their voices can be heard." And making those voices from the bottom heard by those at the top seems to be one thing many agree is needed in the NIH intramural program.

–J.C.

no longer adequate for replenishing these losses, where will the fresh supply of outstanding researchers come from? Some insiders think the recruitment of Francis Collins as director of NCHGR, replacing James Watson, is a model for how the intramural program might draw talent from the external research community to renew itself.

To get Collins from the University of Michigan, where he was established as a major player in the field of human genetics, NIH pulled out every possible stop. Collins was allowed to bring seven people from his lab to NCHGR and to recruit a dozen other investigators from outside NIH. These terms were personally guaranteed by figures no less than Bernadine Healy and Health and Human Services Secretary Donna Shalala. Such high-powered salesmanship helped persuade Collins to accept the very real cost of moving to NIH: a reduction in salary and cuts amounting to half his research staff and half his lab space.

Many of those in the intramural program cheer Collins' arrival as a much-needed shot in the arm. Michael Gottesman, acting scientific director of NCHGR, calls Collins' arrival a "vote of confidence" for the Bethesda campus. But the benefits of recruiting Collins were associated with significant costs, according to some insiders. "Lots of resources are going to the Genome Project from our budgets," says one institute director who insisted on anonymity; the same director expressed fear that the quality of NIH research across the board will suffer as a result. Even more painful to this director is the fact that Collins has the funding and space to recruit people away from the director's institute: "I cannot compete with that. It's a terrible thing that's happening."

Collins counters that he is conscious of this problem and that he has been careful not to raid other institutes. The three senior postdocs he hired from within NIH, he says, were recruited to keep them on campus; they had offers from other institutions and, without his proposal, "all three of these people would have left NIH." Yet, in spite of Francis Collins' best efforts to reduce the discomfort caused by his arrival, it is clear that even the most successful strategies for solving problems in the NIH intramural program carry a price.

**NIH INTRAMURAL SCIENTIFIC DIRECTORS**

| Scientific Director | Research Institute | FY92 Budget (millions) | Years in Job |
|---|---|---|---|
| Richard Adamson | National Cancer Institute, Division of Cancer Etiology | 71.9 | 13 |
| Bruce Chabner | National Cancer Institute, Division of Cancer Treatment | 101.2 | 11 |
| Alan S. Rabson | National Cancer Institute, Division of Cancer Biology, Diagnosis and Centers | 61.5 | 18 |
| Peter Greenwald | National Cancer Institute, Division of Cancer Prevention and Control | 3.2 | 12 |
| John Gallin | National Institute of Allergy and Infectious Diseases | 119.9 | 8 |
| Irwin Kopin | National Institute of Neurological Disorders and Stroke | 75.7 | 10 |
| Arthur Levine | National Institute of Child Health and Human Development | 68.3 | 11 |
| David Lim | National Institute of Deafness and Other Communication Disorders | 8.2 | 1 |
| Markku Linnoila | National Institute of Alcohol Abuse and Alcoholism | 19.8 | 2 |
| George Martin | National Institute on Aging | 37.4 | 5 |
| John McLachlan | National Institute of Environmental Health Sciences | 70.9 | 5 |
| Henry Metzger | National Institute of Arthritis and Musculoskeletal and Skin Diseases | 15.6 | 6 |
| Stephen Mergenhagen* | National Institute of Dental Research | 31.3 | <1 |
| Robert Nussenblatt | National Eye Institute | 29.4 | 1 |
| Darrell G. Kirch* | National Institute of Mental Health | 92.6 | <1 |
| Allen M. Spiegel | National Institute of Diabetes and Digestive and Kidney Diseases | 80.4 | 3 |
| Roy Pickens | National Institute on Drug Abuse | 24.0 | 4 |
| Edward Korn | National Heart, Lung, and Blood Institute | 97.1 | 5 |
| Ada Sue Hinshaw* | National Institute of Nursing Research | .7 | 3 |
| Michael Gottesman* | National Center for Human Genome Research | 0 | <1 |
| David Lipman | National Library of Medicine, National Center for Biotechnology Information | 6.0 | 5 |

* Acting

The 18 intramural scientists who served as task force members on the Klausner report were: Richard Klausner, NICHD; William Paul, NIAID; Igor Dawid, NICHD; Peter Howley, NCI; Claude Klee, NCI; Arthur Nienhuis, NHLBI; Robert Balaban, NHLBI; Michael Brownstein, NIMH; Gary Felsenfeld, National Institute of Diabetes and Digestive and Kidney Diseases; Harold Gainer, NINDS; Lynn Gerber, Clinical Center; Michael Gottesman, NCI; W. Marston Linehan, NCI; Malcolm Martin, NIAID; Bernard Moss, NIAID; Howard Nash, NIMH; Thressa Stadtman, NHLBI; Thomas Waldmann, NCI.

The extramural advisory group that reviewed the Klausner report was chaired by Michael Brown of the University of Texas, Southwestern Medical Center (UTSMC) and included: C. Thomas Caskey, Baylor University School of Medicine; Alfred Gilman, UTSMC; Marian Koshland, University of California, Berkeley; Philip Leder, Harvard Medical School; Samuel Thier, Brandeis University; Harold Varmus, UCSF.

## CUTTING FOR GROWTH

If the NIH intramural program could keep growing as rapidly as it has over the past decade, the choices it faces wouldn't be quite so difficult. When an institution's resource base is expanding quickly, there is sometimes enough wherewithal to keep funding less-than-stellar projects and still invest new funds for the future in creative projects and younger players.

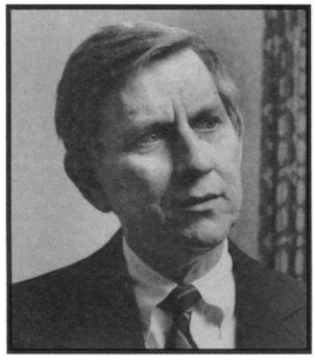
Until now, that's how the program has worked. During the 1980s, Congress kept the intramural program growing at the same pace as the extramural program. As a result, since the early 1980s, the intramural program has consistently received about 11% of the total NIH budget, which itself was rapidly increasing (see table on this page).

Now, however, members of key congressional committees are beginning to ask whether that situation must prevail forever. A 24 June report from the House Committee on Appropriations notes that "as a central part of the fiscal year 1995 budget planning cycle, the committee expects the new director of NIH to review carefully the role, size, and cost of the intramural program. The committee is concerned that the composition of this research is not based on a well thought out division of labor between the extramural and intramural programs."

One congressional staffer, who insisted on anonymity, said the central question that must be addressed is: Why should a given research project be carried out in the intramural program rather than somewhere else? "NIH is going to be forced to answer this because of constrained growth," the staffer says. "They've managed themselves in ways that depended on geometric growth. They now must deal with limitations both on space and dollars."

In the past, NIH has been able to meet whatever budget constraints arose in individual programs with a cut here and a cut there—but in the near future the constraints could be considerably tighter. To meet them, while at the same time putting together packages that can attract people of the caliber of Francis Collins, it may be necessary to go beyond thinking about scattered cuts and consider the possibility of eliminating entire programs to free resources for future growth.

In fact, some former NIH insiders are already thinking along these lines. Vincent DeVita Jr., director of NCI for 9 years and now head of Yale's Comprehensive Cancer Center, says he thinks it's time to weigh whether whole programs—even entire institutes—are justifying their existence in a rapidly changing scientific landscape. As an example, he cites NCI's Frederick Cancer Research Facility. "I had a lot to do with making Frederick," says DeVita. "We did that because molecular biology needed a home. Now everyone and his brother does molecular biology."



BAYLOR COLLEGE OF MEDICINE

**"ALMOST ANYONE YOU TALK TO WILL TELL YOU THIS THING IS SPENDING ONE HELL OF A LOT OF MONEY AND IT NEEDS TO BE TUNED UP."**

**TOM CASKEY**

A prominent academic AIDS researcher, who would speak only on condition of anonymity, says the NIH Clinical Center, which houses 540 beds, more than half the clinical research beds in the country, is another unit whose mission needs careful examination. The Clinical Center, this NIH alumnus argues, is too often used for studies that could be done at any university hospital. "The Clinical Center is not unique because you have someone there who can give AZT and ddI in a certain combination," he says. Instead, he argues, the Clinical Center should be a place for cutting-edge clinical techniques like gene therapy. "With unique resources," he adds, researchers there "should be doing unique work." Former NIH director Wyngaarden also wishes the Clinical Center housed more ambitious, unique work that does not duplicate research done elsewhere. "There's pretty much unexciting stuff at the Clinical Center," he says, citing, for example, the fact that "there's far too much drug testing."

The same issue—the need for NIH units to avoid overlap with other research centers and do unique work—is being raised by members of the intramural community. "We ought to be doing work that has more risk and more potential," says an NIH lab chief who requested anonymity. "We ought to be trying to hit the ball out of the park or produce reagents that others need. We shouldn't do what others do. If what we're trying to do is novelty, then half of the basic labs in my institute are passing the test and the other half are overfunded."

Yet following up this kind of thinking with action is not going to be easy, especially if the action involves reducing funding for individual labs, or cutting back whole programs. Vince DeVita knows firsthand just how bruising it is to close a program. "It's like closing military bases," DeVita says. "We closed a program in the Cancer Institute—Organ Systems—and it was fought fiercely. People who ran that program still won't speak to me. They hate me."

Of course, no one wants to be hated, and so it's easy to understand why the top scientific managers at NIH might be tempted to make small cuts, spread evenly over their entire domains, rather than confronting the pain of zeroing out a program. But if Harold Varmus and his colleagues at the top of NIH want the sustained excellence that produces Nobel Prizes, clinical advances, and influential basic science, they may not have the luxury of a cautious, piecemeal approach. Preserving what is best in the intramural program while continuing the highest level of excellence will mean tough choices, deep cuts, and agonizing decisions. It would be all too easy for defenders of the intramural program to circle the wagons and attempt to repel any efforts by Congress to insist on those tough choices. And yet when researchers—intramural and extramural—of the stature of those quoted here raise their voices to say change is needed, they can hardly be ignored.

–Jon Cohen

**NIH FUNDING TRENDS 1983-1993**

| Year | Intramural (IM) | Total NIH | IM as % of Total |
|---|---|---|---|
| 1983 | 560,993 | 4,309,421 | 13.0 |
| 1984 | 604,568 | 4,827,757 | 12.5 |
| 1985 | 639,451 | 5,497,098 | 11.6 |
| 1986 | 640,177 | 5,688,749 | 11.3 |
| 1987 | 748,637 | 6,685,506 | 11.2 |
| 1988 | 805,417 | 7,186,959 | 11.2 |
| 1989 | 882,417 | 7,893,586 | 11.2 |
| 1990 | 975,871 | 8,505,256 | 11.5 |
| 1991 | 1,048,834 | 9,217,940 | 11.4 |
| 1992 | 1,132,183 | 10,060,390 | 11.3 |
| 1993 | 1,167,445 | 10,326,604 | 11.3 |

NOTE: All figures are in millions and include the former ADAMHA Institutes: NIMH, NIDA, and NIAAA.