

THE ASSAULT ON DAVID BALTIMORE

Congress and the media hailed the case of a whistle-blower at M.I.T. who brought down the Nobel Prize-winning biologist and his colleague. But what if they were wrong? A new ruling due this month may invoke a more complex view of the way science works.

BY DANIEL J. KEVLES

DAVID BALTIMORE won the Nobel Prize in Medicine in 1975, when he was a thirty-seven-year-old professor of biology at M.I.T. Thirty-seven is young for a Nobel, but Baltimore had been known among biologists as a wunderkind for some time. The work for which he shared his prize, a study of how a special class of viruses reproduce themselves (the AIDS virus was later shown to be one of them), ran contrary to most beliefs on the subject at the time. After receiving the Nobel, he continued doing research, but he also began to take a leading role in public debates about genetic engineering, the AIDS epidemic, and other issues over which science and public policy meet. He brought to whatever he did a degree of self-confidence that some of his colleagues thought was arrogance but that was integral to his achievements. In 1990, when he was fifty-two, he became president of Rockefeller University, one of the world's distinguished centers of teaching and research.

Less than a year and a half after he went to Rockefeller, David Baltimore fell from grace. Citing pressure from his colleagues and the personal toll of fighting a long battle over what was alleged to be a fraudulent paper he had collaborated on when he was at M.I.T., he resigned on December 2, 1991. A front-page article in the *Times* noted that the "spectacle" of Baltimore's downfall made it seem "larger than life, with an effect greater than any case of scientific fraud in memory."

David Baltimore was never suspected of faking anything himself, but he had stubbornly defended the work of someone who was—a biomedical scientist at M.I.T. named Thereza Imanishi-Kari, who was one of six coauthors of the disputed paper, which was published in the journal *Cell* in 1986. Baltimore's support of her work was perceived to be unprofessional and unwise, if not irresponsible.

From the beginning, some people said that Baltimore and Imanishi-Kari were being unfairly pursued by witch-hunting zealots who didn't understand the way science works, but others—and often they seemed to be in the majority—said that it was high time that scientists were held accountable to the public that in large part pays their bills. The Baltimore case touched deep-seated doubts about the scientific enterprise. It has now dragged on for a decade, leaving wrecked careers in its wake, pitting congressmen against scientists, and producing both martyrs and tormentors.

Scientists in this country have long been part of an opulent establishment—recipients of large sums of public money who have been granted a remarkable degree of autonomy in deciding how to use them. But in recent years they have come under siege from creationists, New Agers, animal-rights activists, and critics of genetic engineering, as well as cost-conscious officials. They see their power slipping, most seriously in Washington. Fear of diminished funding was a common, if sotto voce, theme in the professional assessment of Baltimore's behavior. Among those who were in favor of his stepping down as president of Rockefeller University were many who wanted to avert reductions in government research money by demonstrating that scientists could take care of their own problems.

Today, David Baltimore is back at M.I.T., where he is again a professor of biology. He continues to do brilliant work, but he is dishonored as a public figure. "I enjoy doing science," he told me once, "and I'm going to try very hard to prevent people from taking science away from me." His standing may soon be restored. Thereza Imanishi-Kari appealed the findings against her, and hearings were held last summer which permitted

her, at last, a full and fair day in court. A ruling on her appeal is expected at the end of this month. She has mounted a powerful case that she is innocent, and if that is so—and I am persuaded that the evidence supports her—then a great injustice has been done in the name of scientific integrity and the public trust.

ALL three of the principal figures in the Baltimore case live and work within a few miles of one another in the Boston-Cambridge area: Baltimore, Imanishi-Kari, and a scientist named Margot O'Toole, who blew the whistle on the other two. There would have been no Baltimore case without O'Toole, a postdoctoral fellow whom Imanishi-Kari had hired to work in her lab at M.I.T. in the summer of 1985. She was asked to do experiments that would extend the work described in the *Cell* paper, and her frustration and embarrassment at not being able to get the results she sought led to the first complaint about Imanishi-Kari's data. O'Toole's dogged insistence that she was right and her boss was wrong has been at the heart of the affair. She has become a symbol of the heroic young scientist who takes a stand against the system and prevails over powerful figures like David Baltimore.

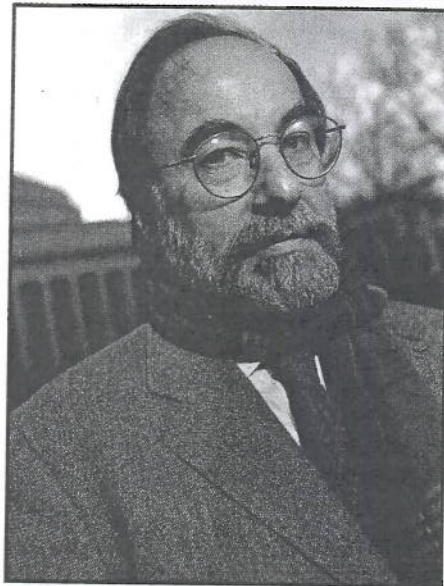
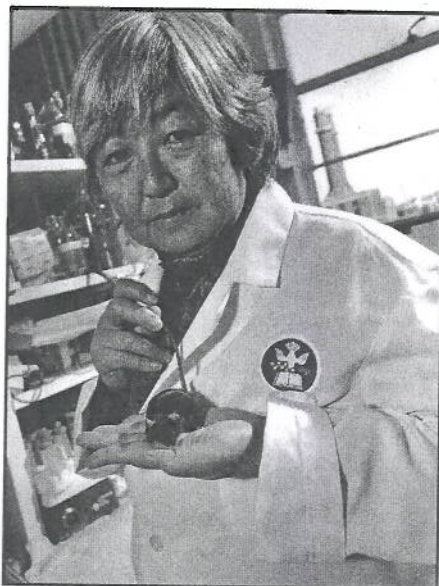
Margot O'Toole is now on the research staff of the Genetics Institute, a biotechnology company in Cambridge, but her reputation as a scientist rests almost entirely on her adversarial role in the dispute with Baltimore and Imanishi-Kari. She is the recipient of several awards emanating from her actions, among them the Humanist of the Year Award from the Ethical Society of Boston, and the Ethics Award of the American Institute of Chemists. Now in her early forties, O'Toole has an open Irish face and a manner that prompted a congressional investigator to say, "The first time you meet her, she just

reeks with integrity and credibility." I first met her one day a few years ago in Cambridge, when I picked her up for lunch. She is a compelling storyteller, and her tale of the Baltimore case held me in thrall for hours.

O'Toole had been brought up in a strong Catholic household in Dublin and spent two years in a convent school. Her father was an engineer for the Electricity Supply Board and was also a playwright. He wrote of "speaking out in the workplace, not going along," O'Toole says, and one of his plays, "Man Alive," which satirizes the bureaucratic complacency of a giant utility company, uncannily foreshadows key elements in the Baltimore case. The central character is an outspoken engineer named Tim O'Malley, who is told to keep his dissident thoughts to himself. He is declared an incompetent troublemaker, but he refuses to quit, pledging at the end of the play that "as long as I stay I'll be a thorn in their backside, and every time they sit on anyone again they'll think of me."

In 1966, when O'Toole was fourteen, the family moved to Boston, where her father eventually directed a program in science writing at Boston University. She received her doctorate at Tufts University School of Medicine, in Boston, in 1979, and spent almost five years as a postdoctoral fellow at the Fox Chase Cancer Center, in Philadelphia. She returned to Boston in early 1985, when her husband, Peter Brodeur, was appointed to an assistant professorship in the Tufts department where they had both done their graduate work. Her thesis adviser, Henry Wortis, helped get her a place in a lab there. She had been his first doctoral student—her husband had been his third—and Wortis found her capable and engaging. Even now, he keeps a photograph of her tacked to his bulletin board—a snapshot of a smiling, attractive young woman, her hair wet from rain and her eyes alight with mischief. That spring, Wortis invited O'Toole to a party at his home, where she met Thereza Imanishi-Kari, who was then forty-one, almost nine years older than O'Toole. On the spot, she offered O'Toole a one-year postdoctoral fellowship. O'Toole's research money was about to run out, and the offer was a godsend.

THEREZA IMANISHI-KARI now works in a laboratory in the Pathology Department of the Tufts medical school. Because of the Baltimore case, she was denied funds from government grants



*Duelling scientists, from top:
Thereza Imanishi-Kari, Margot O'Toole,
and David Baltimore.*

from the National Institutes of Health, although she has continued to receive support for her research from private agencies, such as the American Cancer Society. I met with her in a small office just off her laboratory, a bright, open room containing several working credenzas laden with glassware, chemicals, and cultures. The lab occupies the top floor of an old brick building with an elevator that stranded me between floors until I pressed the emergency button. Imanishi-Kari is a short woman in her early fifties with a flat, high-cheekboned face. She was born into an immigrant Japanese family in Brazil, and she speaks seven languages, but her English, which is even now sometimes difficult to understand, was especially poor ten years ago, when the disputed research was published.

Thereza Imanishi grew up in Indaia-tuba, a town near São Paulo, where her parents were first tenant farmers and then the owners of a small trucking business. She and her sisters fought to get an education, and after her older sister left home over the battle the parents permitted Thereza to go to high school and then university in São Paulo. Her grandfather wanted her to learn about her family's culture, and in 1968 she went to Kyoto University to do graduate work in biology. She says that there were hardly any women studying science in Kyoto, so she hung out with the men, perfecting her child's Japanese into the male, rather than the female, version of the language.

Kyoto University was in a state of upheaval in 1968, like most universities at that time, with fights constantly breaking out on the campus. She repaired to cafés with other students, where they studied immunology and talked about the tendency of Japanese scientists to rely on research systems developed in other countries. She resolved that for her experiments she would invent and rely on her own research system, which is what she did while she was completing her graduate work—at the University of Helsinki, in Finland. She had gone there in 1971, because she felt that the continual disruptions in Kyoto made it impossible for her to do serious work. Using a chemical called NP, she developed a method of tracking immune responses in mice.

In 1974, she obtained her doctorate and married a Finnish architect named

Markku Tapani Kari. She spent several years in the laboratory of Klaus Rajewsky, in Cologne, where her work brought her to the attention of David Baltimore. In 1980, when she got an offer from M.I.T., she asked Rajewsky for his advice. He replied, "Well, M.I.T. is a very competitive place. It's like a sea full of sharks, and they eat the little ones very fast." She went anyway. "That was the beginning of my nightmare," she says.

Imanishi-Kari joined the faculty as an assistant professor and moved into a laboratory at M.I.T.'s Center for Cancer Research, on Ames Street. She had brought with her from Germany a freezerful of valuable NP research materials. She was smart, competent, and vivacious. Even Margot O'Toole says that initially she found Imanishi-Kari "very unusual and quite charming." By M.I.T.'s standards, though, she published too few scientific papers, and part of what she published struck others as being a narrow extension of her earlier work with the NP system. However, she was enlarging her repertoire of expertise by learning how to use some of the techniques of molecular biology, and, after she began collaborating with David Baltimore on a study of the pro-

duction of antibodies in 1984, her tracking system led to some surprising and peculiar results. The findings didn't make any difference to her future at M.I.T., since she had been told that she would not be put up for tenure, and in August of 1988 she received a tentative offer, which she said she would accept when it became final, of an assistant professorship at Tufts.

ONE way the body protects itself is by producing antibodies that latch on to and destroy an invading agent such as a virus or a bacterium. The variety of infectious agents that invade the body is enormous, and the most striking feature of the immune system is that it is capable of generating a comparably enormous range of antibodies. Antibody production is largely controlled by genes active in white blood cells. How and why these genes produce sufficient custom-tailored antibodies to ward off particular infectious agents is one of the great puzzles in science. Imanishi-Kari's NP system provided a way of getting at some of the details of the process. Mice injected with NP would produce distinctive antibodies with a distinctive chemical re-

gion, or signature—called an idiotyp—on their surface.

For their experiments at M.I.T., Baltimore and Imanishi-Kari used a breed of "transgenic" mice that a biologist at Columbia University had developed by inserting the gene for an antibody to NP, with its distinctive idiotyp, into the newly fertilized eggs of a normal mouse, which would have produced few, if any, antibodies of this type. The eggs were introduced into the wombs of surrogate-mother mice, and some of the eggs developed into the transgenic mice—mice that carried a foreign gene for the antibody to NP. What was startling about Baltimore and Imanishi-Kari's experiments was that in many of the cells they took from the transgenic mice antibodies with these idiotypes seemed to have been produced not by the transgene but by genes native to normal mice. Imanishi-Kari speculated that, through a process called idiotypic mimicry, the foreign gene had stimulated the abundant production of the antibodies that the mouse would have otherwise produced infrequently or not at all. The phenomenon seemed significant for both the science of immunology and, potentially, for medicine. It

promised to illuminate further how genes produce antibodies, and suggested that antibody production might be varied in inventive ways.

A separate approach to the experiment was pursued by David Baltimore's postdoctoral fellow David Weaver, another of the *Cell* paper's coauthors. His molecular analysis of the genes of the mice complemented the accumulating data Imanishi-Kari was getting. Baltimore and Imanishi-Kari had different ideas about the mechanism that accounted for these results, but, whatever Baltimore's interpretative disagreements with her, he was convinced that the observations to be reported in the *Cell* paper in the spring of 1986 were genuine: two



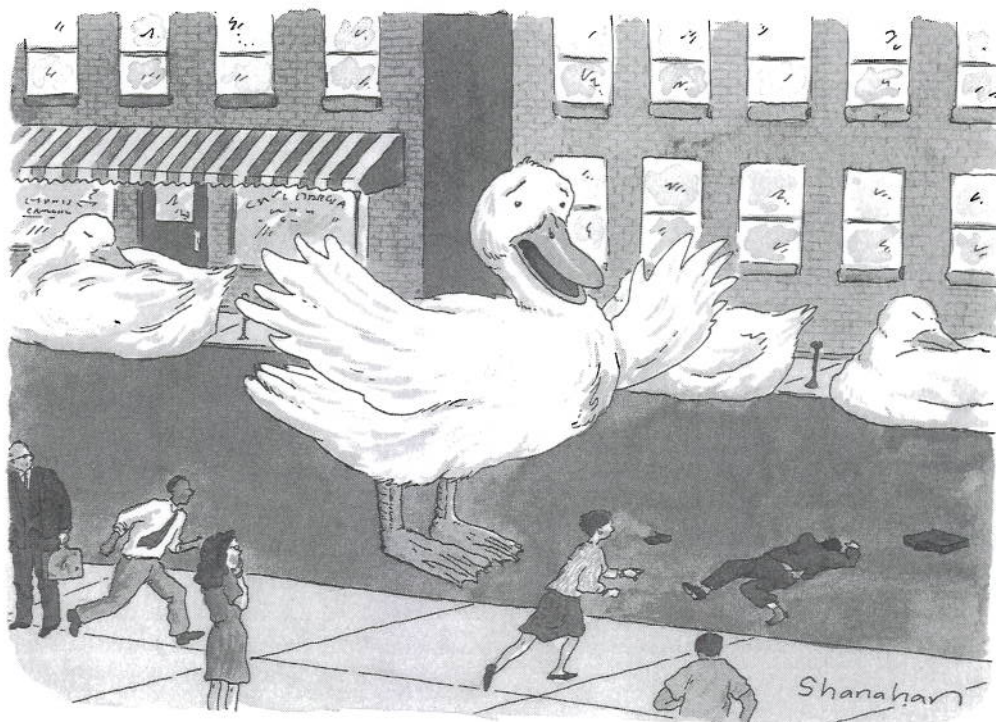
"Never, ever do that again!"

independent lines of analysis had led to the same conclusion.

ON June 1, 1985, Imanishi-Kari welcomed Margot O'Toole to her laboratory and put her to work addressing the question of whether idiotypic mimicry might be provoked by interactions between cells. To that end, O'Toole's assignment was to isolate two types of white blood cells—T cells containing the transgene and normal B cells—and then to transfer a mixture of the two into a mouse whose immune system had been destroyed by radiation. O'Toole, who had experience with this procedure, was to test whether the normal B cells produced antibodies that displayed the NP idiotypic. She worked with a woman named Moema Reis, a visiting scientist from Brazil, who was another of the collaborators on the research that led to the *Cell* paper. Reis, an expert in mouse genetics, was in charge of breeding mice for the various experiments under way in the laboratory.

In September, when enough mice were available, O'Toole started on the cell-transfer experiment. Her initial results were arresting. Using the same reagents—that is, chemical sensors—that Imanishi-Kari had employed, she detected antibodies with the telltale idiotypic that appeared to come from the normal cells circulating in the mouse. "I was *sure* that I was onto something hot. I was on cloud nine. I thought this was the most important scientific thing that I had ever done," O'Toole says. She planned to publish three articles as a consequence of her work at M.I.T. "It was a very big deal in my life," she says now. "I was going to be able to be a scientist, which was a very iffy proposition at that point. I was really excited and delighted about the whole thing."

The delight was short-lived. O'Toole had to obtain confirmation of the cell-transfer experiment before it could be published, and, despite repeated attempts, she was unable to reproduce her original results. She believed that her problem centered on a particular reagent called Bet-1. Imanishi-Kari held that Bet-1 would discriminate between antibodies produced by the transgene and those pro-



"You saw him, didn't you? Crazy guy stepped right in front of me! No way could I stop!"

duced by the mouse's native genes. (Bet-1 was used to recognize the antibody produced by the transgene, and AF-6-78, another reagent, was used to recognize the antibody produced by the native gene.) A graph in the *Cell* paper, identified as "Figure 1," summarized the sensory characteristics of both reagents. But in O'Toole's hands Bet-1 did not behave in conformity with the figure. She spent months struggling to make it work. "Bet-1 became absolutely an obsession with me," she says. Frustrated, she began to grow suspicious of Imanishi-Kari's data.

Imanishi-Kari, for her part, soon became irritated and dissatisfied with the younger scientist's work. "I kept telling her, 'You have to put on all these controls,'" Imanishi-Kari says. But she found it difficult to tell O'Toole what to do. "She was supposed to know more than I did in adoptive cell transfer."

IMANISHI-KARI had informed O'Toole at the outset that she had only enough grant money available to employ her for a year. She says that she repeatedly urged her to apply for grants but that O'Toole did not seek any. O'Toole recalls Imanishi-Kari's urging her to apply for grants to pursue the cell-transfer research but also screaming at her to publish the prelimi-

nary results of another experiment, whose results O'Toole also doubted. O'Toole says that Imanishi-Kari berated her constantly, saying, "You'll never amount to anything. You'll never get a job. You'll be just one of those women the husband has to support."

Imanishi-Kari had been separated from her husband for four years, was in the process of getting a divorce, and was raising her daughter, who was then ten. She knew all about the conflicts that women scientists face. "You have to work very late," she says. "You have to work Saturday and Sunday without any distractions, let alone when you have distractions." She wondered whether O'Toole, who had had a son while working in Philadelphia, had the tenacity and the devotion to survive professionally. She says that during that year O'Toole often had to be away from the laboratory to take care of her child, and that she "was trying very hard to get another child and was having a lot of difficulties."

By early spring of 1986, the two scientists were barely speaking to each other. In April, around the time the *Cell* paper was published, Imanishi-Kari told O'Toole to confine herself to the care and breeding of the mice and do no more experiments. She says she didn't want

O'Toole to use expensive laboratory resources to no productive purpose. Imanishi-Kari began conducting the cell-transfer experiments herself, and O'Toole says that shortly thereafter Imanishi-Kari called her in and said, "Margot, look. There's really something here," showing her data that suggested the results O'Toole had been unable to get. Then Imanishi-Kari, sitting at her desk, went over the data with a pen. To O'Toole, who was looking over her shoulder, she appeared to be crossing out high measurements in mouse groups that she wanted to be low, and low measurements in those that she wanted to be high. "See, there's a real trend here," O'Toole recalls her saying. "She was really happy and perky. I was just astonished.

"Until that moment," O'Toole says, "I was frantic trying to make myself get the data. I was frantic trying to understand why I am not able to be a scientist. Watching her, I just had this utter feeling of tranquillity that I was not partaking because I would not partake." O'Toole adds, "She said, 'Bring me your data.' And then she went through my data and made them conform. She turned around to me and she said, 'So, what do you think?' Then she turned back. And this word came out of my mouth, spontaneous and genuine. It just escaped in a whisper out of my lips: 'Fascinating.' And she turned around to me and she looked in my eyes, and her eyes were smiling at me. And she liked me. And she pitied me. And she welcomed me back into the fold."

Imanishi-Kari says that she has no specific recollection of the encounter that O'Toole found so significant. "What I recall is that I went through her data myself, and then I made an ordered sheet of her own data, keeping order my way. I did not change her data." Nor, she said, did she ask O'Toole to manipulate her data.

O'Toole continued to brood over her failed cell-transfer experiments. "I just couldn't let go of trying to figure out what it was that I couldn't figure out. So one day—despite my absolute determination to keep the peace, and not rock the boat, and get out with my tail in one piece—without even thinking about it, I said to her, 'Well, Thereza, why do you think that Bet-1 worked for you and it didn't work for me?' And she laughed and she said, 'It works the same for us as it does for you.'" Imanishi-Kari says that the re-

mark, if she made it, was likely an offhand declaration that Bet-1 was working for her and that it was working for O'Toole, too—if she would only handle it properly. O'Toole, however, heard it as an admission that the reagent did not work at all.

ON Wednesday, May 7, 1986, O'Toole opened one of Moema Reis's notebooks to look up some mouse-breeding data and stumbled on a cluster of pages—seventeen of them—that looked like a record of some of the key experiments that had been published in the *Cell* paper. She says that by then she knew the paper by heart: "I had studied this better than



I had studied anything before in my life. I would weep over this, saying, 'Why can't I get the same result?' When she saw the columns of numbers on the seventeen pages, the thought flashed into her mind that Bet-1 did not do the job that Figure 1 said it did. The numbers did not support certain experimental results reported in Table 2 and Table 3 in the *Cell* paper, and the discrepancies suggested to her that the paper's central findings might be flawed.

On May 9th, O'Toole told Brigitte Huber, a friend and one of her mentors at Tufts, about the seventeen pages and the problems they raised. Huber decided to pursue the matter with Henry Wortis and Robert Woodland, an immunologist at the University of Massachusetts Medical Center, in Worcester. O'Toole hadn't charged that the paper was fraudulent—only that it was marked by serious errors. She told me that she had been "bending over backwards to be accommodating, to be responsible, to be nonconfrontational," and she added, "I was definitely sure she"—Imanishi-Kari—"was guilty of self-deceit. But is that fraud? I certainly didn't think that I was supposed to be the one to make that call."

In two meetings in Imanishi-Kari's laboratory during the next two weeks—the first without O'Toole, the second with her—Wortis and his colleagues examined the *Cell* paper's claims. O'Toole said at the second meeting that she now had an alternative explanation—one different from idiotypic mimicry—of how the transgenic mice produced NP-specific antibodies. Imanishi-Kari told O'Toole that if she wanted to believe in her interpretation of what happened in the transgenic mice she was free to do so. O'Toole stood, said that

she was satisfied, and offered to shake hands with Imanishi-Kari. But Imanishi-Kari refused.

As far as Wortis, Woodland, and Huber were concerned, Imanishi-Kari had responded satisfactorily. They had discovered two errors: the *Cell* paper somewhat overstated the ability of Bet-1 to discriminate between antibodies produced by the transgene and those produced by native genes in the transgenic mouse, and it mistakenly reported that a certain test had been done on the mouse cells from Table 2 that in fact had been done on other cells. O'Toole wanted the errors corrected publicly, but the investigators felt that correction was unnecessary, since they were minor and neither error determined the central claim of the paper; in fact, when Bet-1 erred, it did so by mistakenly identifying antibodies produced by the native genes as having come from a transgene, thus overestimating the production of antibodies by the transgene, which was the opposite of the result Imanishi-Kari was looking for. She would have had no reason to overstate Bet-1's discriminatory power.

O'Toole, dissatisfied that no correction would be published, obtained another hearing on her criticisms—this one at M.I.T., under the guidance of Herman Eisen, a respected senior immunologist. Baltimore, Imanishi-Kari, O'Toole, and David Weaver explored O'Toole's complaints for two hours late in the afternoon of June 16th. Weaver says that the air was tense but that Baltimore and Eisen were solicitous of O'Toole, recognizing that it was no doubt difficult for her to press her quarrels with the paper on its two most senior authors, one of whom was a Nobel laureate. Baltimore says that he came to the meeting unfamiliar with the antibody tests that Imanishi-Kari had done at the level of detail at which O'Toole analyzed them. "It was the kind of work I didn't know how to do, had never done, and I had collaborated with Imanishi-Kari for that reason." Baltimore was troubled to learn about the problems with Bet-1 but concluded that the reagent worked well enough for the experiment. The discussion revealed that the misstatement about Table 2 had occurred because Baltimore had got some general information about transgenic mouse cells from Imanishi-Kari and had mistakenly thought it referred to the specific cells in Table 2.

Baltimore thought that the data in the seventeen pages were inconclusive with

regard to O'Toole's view of the *Cell* paper: they represented only a small part of the data from Imanishi-Kari's lab, and, in any case, as with much experimental data, the use and interpretation of the over-all body of results demanded what science often requires—the exercise of judgment and imagination. "I was satisfied that what we knew up to that point was appropriately represented in the paper," Baltimore says. "Maybe someday it was going to turn out that there was a wrong interpretation on the basis that Margot was suggesting, and maybe not. But you weren't going to answer the questions by arguing about them. You could only answer them with further research." Baltimore suggested that O'Toole pursue the normal means of airing scientific disputes by writing a letter to *Cell* that outlined her views. He also suggested further experiments that might be done to test her theory. O'Toole said later that she thought that Baltimore's expression of opposition to her ideas would prevent a letter being published in *Cell*.

O'Toole, her one-year appointment in Imanishi-Kari's lab now at an end, had in mind working with her husband at Tufts, but Henry Wortis recalls telling Brodeur, "Anyone who thinks that Thereza and Margot could coexist in the same department without fireworks would have to be crazy." She was now pregnant with her second child, and she went to work for her brother, who ran a business called the Gentle Giant Moving Company. There she set up a computerized-dispatching system for him. While awaiting the birth, she remained in touch with Brigitte Huber, the friend at Tufts who had alerted Henry Wortis to O'Toole's complaints. Huber had participated in the subsequent investigation, and it was she who had conveyed to O'Toole the news that no correction would be published. Her two children were close in age to O'Toole's son, and she remembers that on a visit to the Museum of Science in Boston that fall, with their children in tow, O'Toole "blasted me for what I had done to her career. I felt attacked by her continuously."

O'TOOLE had also talked to another scientist, Charles Mapletorpe, about her doubts about the *Cell* paper's data. Mapletorpe had spent several bitter years at M.I.T. working on his Ph.D. under the supervision of Thereza Imanishi-Kari and had finally received it the preceding sum-

AN OPENING IN THE LARGEST CITY

The lovers look perfectly natural
next to these atrocious paintings
of the Sea of Okhotsk and the Sea of Marmara:
I'm the one who needs a prop,
an invitation or just a wineglass.
I've worked all my life on this mask
of fascinated suffering, still a guard
might arrive at any minute and whisper,
and I'd have to nod, summoned.

Occasionally a distinguished guest
pauses to peer in a gilt frame
and whisper: *Extraordinary*.

All these seas are dead.
I can see my face reflected
in the terribly thick patina,
and the arc of her cigarette:
the trick is not to focus
on the foreground, the linseed scumble,
the knowing brushstrokes that convey
order, chaos, a misty shore
and the attraction of irresistible winds.

—D. NURKSE

mer. It was said that he hated her. He had read an article in the *Times* about two scientists at the National Institutes of Health, Ned Feder and Walter W. Stewart, who had written a controversial paper, as yet unpublished, on a case of scientific misbehavior. Without telling O'Toole, who had asked him to keep her doubts about the *Cell* paper in confidence, he telephoned Feder.

In the mid-sixties, Walter Stewart was a brilliant undergraduate in physics and chemistry at Harvard, where he met Ned Feder, who, seventeen years his senior, was then a member of the biology faculty. In 1968, after trying graduate work for a year, Stewart found a niche in Feder's laboratory at the N.I.H. Three years later, he began to referee papers submitted to *Nature*, and he scrutinized one submission closely enough to determine that its claim—which was that learned behavior could be transferred from the brain of one animal to another through a chemical called scotophobin—had not been demonstrated by the experiments its authors had done. He scored something of a coup when *Nature* published his rebuttal alongside the article. He was only twenty-seven.

"The model of science is supposed to be free and open debate"—the phrase is a rallying cry for Stewart and Feder—"but there's much too little debate," he says.

At the N.I.H., Stewart developed useful dyes for the study of cell structure. Over a number of years, he and Feder filled hundreds of notebooks with data on the nerve cells of thousands of inbred snails, but they kept what they learned pretty much to themselves. Their output was low by N.I.H. standards, but in the mid-eighties they began to capture attention—in what was a kind of return to Stewart's scotophobin triumph—for an early version of the paper that would earn them the *Times* story that Charles Mapletorpe read.

Stewart and Feder had investigated the work of John R. Darsee, a young researcher in cardiology who had been found guilty of scientific fraud in 1982. He had published over a hundred papers, with forty-seven coauthors. Stewart and Feder concluded that many of the coauthors had known, or should have known, that Darsee's data were false, and they suggested that a systematic study of the scientific literature was in order. John

Maddox, the editor of *Nature*, told the *Times* that, while he thought Darsec's coauthors had been "careless" rather than "dishonest in any active sense," Stewart and Feder's analysis contained "enough horrors to make people sit up on the edge of their chairs." (In January, 1987, Maddox published the paper in *Nature*, but included a critique from one of the coauthors and noted editorially that Stewart and Feder "have not understood that the unfettered right to publish scientific data does not equate with a right to denigrate others' character.") In fact, people were sitting up enough to make the two N.I.H. scientists see a future in fraud busting. Many of their colleagues thought that this sort of thing was inappropriate for research scientists, but Stewart and Feder had got authorization to proceed nevertheless. Eventually, they threw out their snails.

In the summer of 1986, after Mapletorpe's talk with Feder, Stewart called O'Toole and asked if she was satisfied with what had been decided in her meetings with the scientists from Tufts and M.I.T. She said no, and he told her that he and Feder wanted a copy of the seventeen notebook pages, so that they could analyze the data themselves. O'Toole, worried that reopening the matter would jeopardize her husband's career at Tufts, refused to provide them. Stewart and Feder kept after her for weeks, telling her that she had a professional obligation to come forward if she possessed unique information showing that a published paper was probably wrong. In September, O'Toole finally mailed Stewart and Feder a copy of the seventeen pages.

O'Toole says that Stewart went about mastering the arcana of the *Cell*-paper experiments "like a tiger," calling her at home and at the Gentle Giant Moving Company for advice and guidance. He and Feder soon concluded, for much the same reasons as O'Toole, that the *Cell* paper's "experimental results not only failed to support [the] main conclusions, but in many cases actually contradicted these conclusions." On December 18th, they wrote to the coauthors, saying that they had conducted "a partial internal audit" of the *Cell* paper using copies of seemingly relevant laboratory records they had obtained from "a scientist," that the paper seemed problematic by this reckoning, and that they wished access to more of the records so as to "perform a more thorough analysis."

Baltimore, who had thought that the matter of the *Cell* paper was closed, assumed that O'Toole had reopened it. As the coauthors' spokesman, he replied to Stewart and Feder that he saw no point in cooperating with them, because he was satisfied that the data fell "within the norms of scientific evidence" despite the questions raised about them by "a discontented postdoctoral fellow."

For months, Stewart and Feder bombarded the coauthors with letters and calls, asking, unsuccessfully, for data and documents. During this time, Baltimore apparently lost his temper in a telephone conversation with Stewart. According to Stewart, he characterized O'Toole as pursuing a "personal vendetta," accused Stewart and Feder of having written a "vicious" manuscript, and said that he might sue both of them for "harassment and libel."

In mid-March, in a letter to J. Edward Rall, the N.I.H.'s Deputy Director for Intramural Research, Baltimore suggested a course of action which he had urged on Stewart during their tempestuous telephone conversation—that Rall appoint "a couple of immunologists" to examine Stewart and Feder's assessments, on the understanding that if the *Cell* paper passed muster again Stewart and Feder would apologize and henceforth shut up about the subject. On April 1st, senior officials at the N.I.H. asked the agency's misconduct office to handle the case. While they declined to muzzle Stewart and Feder forever, they forbade them to submit their analysis of the *Cell* paper to any scientific journal until the matter was resolved.

Stewart and Feder fought back, broadcasting the details of their investigation to scientists across the country. In mid-July, the American Civil Liberties Union successfully intervened on Stewart and Feder's behalf. Stewart and Feder took to airing their report on the *Cell* paper in talks on college campuses. They were permitted to submit a revised version of their analysis to *Cell*, but *Cell* turned it down. *Science* also rejected it. Meanwhile, the N.I.H. formed an investigative panel to assess the *Cell* paper.

AT this point, the stakes in the Baltimore case went up: Congress got involved. Early in 1988, Stewart and Feder discussed the case with Peter Stockton and Bruce Chafin, who worked un-

der Representative John D. Dingell, a Democrat from Michigan. He chaired the Energy and Commerce committee, which had jurisdiction over the budget for the National Institutes of Health. (In 1988, this was more than six billion dollars and rising.) Dingell was an aggressive pursuer of people he thought were wrongly benefitting from their access to taxpayers' money. He used the Subcommittee on Oversight and Investigations to go after extravagant defense contractors, corrupt bureaucrats, and illegal influence peddlers with ferocious and, usually, successful tenacity. Congressional insiders liked to say that he inspected the front seats after a hearing to see how much sweat the witnesses had left.

Dingell and his aides, Stockton and Chafin, had been looking for an unresolved case of a research institution covering up scientific misdeeds, and after talking to Stewart and Feder they scheduled a hearing for April 12th on fraud in N.I.H. grant programs. The witnesses were to include several officials from the institutes and also Stewart, Feder, Charles Mapletorpe, and Margot O'Toole.

David Baltimore heard about the imminent hearing from reporters who called him for comments even before Stockton and Chafin talked with him about it. On April 10th, he opened his Boston *Sunday Globe* and was mortified to find an article that prominently displayed both his picture and an opinion about the *Cell* paper from Stockton: "It's hard to tell if it's error or fraud. At certain times, it appears to be fraud and other times, misrepresentation." By now, Dingell's staff had met Margot O'Toole, and they thought that they had an exemplary case of a coverup of scientific misdeeds. "Here was someone chewed up by the system," Chafin says. "Here was a perfect object lesson."

At the subcommittee hearing on April 12th, O'Toole said that she was reluctant to testify. She said later that she had been scared, and she was doubtless worried about endangering her husband's career at Tufts. She told the subcommittee that during the inquiries in 1986 her "assertions that the data did not support the published claims were completely confirmed"—although both investigative bodies had decided that the data she disputed were more than adequate. Stewart





"I'm sending you to summer camp."

and Feder entered their analysis of the *Cell* paper into the record of the hearing, thus achieving a kind of publication of that analysis, and selectively summarized their findings, testifying that "in a number of crucial cases" the paper gave "an inaccurate and, in fact, misleading picture of the underlying data"; that the reports of the investigations at Tufts and M.I.T. were "seriously defective," with certain issues "ignored or treated evasively"; and that when they had tried to discuss O'Toole's allegations with Baltimore he "attacked her character and motives," and went on to assail them "personally" and threaten them with legal action.

THE Dingell subcommittee's behavior touched sensitive nerves in Baltimore which had a great deal to do with his personal history and his political sensibilities. His parents, the children of poor Jewish immigrants to New York, had prospered enough from his father's work in the garment district to move to Great Neck, Long Island. Politics and public affairs were a staple of family conversation. Both his parents had strong left-wing sympathies, Baltimore says, but "they were both proud of the fact that they had not involved themselves in the Communist Party in the thirties." While neither they nor their friends had thought of themselves as likely targets of McCarthyism in the fifties, they'd seen the McCar-

thy hearings as an attack on left-leaning people like themselves.

Baltimore became passionately interested in biology in high school. Upon going on to Swarthmore, he taught himself molecular biology there, for it was a new field and the college offered no courses in it. He whizzed to a doctorate at Rockefeller University in 1964, at age twenty-six, and then went to work at the Salk Institute, in La Jolla, California. He says that he liked the outdoor life there but found the political conservatism increasingly irritating. With the escalation of the war in Vietnam, he became politically active, and in 1967 when he got an offer to join the M.I.T. faculty he took it.

By 1970, Baltimore had accomplished the work for which he would win the Nobel. He remained politically engaged, supporting civil rights and women's rights. He encouraged young women scientists, and a number of those he has trained now hold academic positions in universities across the country. One of them is his wife, Alice Huang. She was his postdoctoral student at Salk, became a full professor at the Harvard Medical School, and is now Dean for Science at New York University.

The Dingell subcommittee's attack on Imanishi-Kari, a foreigner who lacked the connections and the fluency in English to defend herself effectively, offended Baltimore deeply. In mid-May of 1988, he

sent a lengthy letter to some four hundred colleagues around the country defending the *Cell* paper and lambasting Stewart and Feder, not least for drawing sweeping conclusions about the paper on the basis of seventeen pages out of the thousand or so that had been produced for it. Baltimore explained that, besides wanting to clear his name and the names of his co-authors, he felt compelled to warn the scientific community that "a small group of outsiders" threatened to use "this once-small, normal scientific dispute" to "cripple American science."

Baltimore believed that the outsiders had a distorted idea of how science really works. No honest scientist fabricates or falsifies data, but it is naïve to think that some unsought truth will leap out, clearly and unambiguously, from the data. Insight and creative evaluation are needed. Studies have indicated that, in arriving at his laws of heredity, Gregor Mendel exercised selective judgment and that the American physicist Robert A. Millikan, in the research on the electron for which he won the 1923 Nobel Prize in Physics, did, too. If they had been wrong, they would have paid the price in their reputations. Some analysts have, indeed, found Mendel and Millikan candidates for fraud charges, and perhaps Representative Dingell, if he had been given the chance, would have gone further.

Margot O'Toole felt that Imanishi-Kari's belief in idiotypic mimicry led her to overlook data that raised difficulties. But in fact O'Toole's initial charge that the *Cell* paper misrepresented its experimental undergirdings called Imanishi-Kari to account partly because she simply decided that those ambiguities were not of consequence. She had solid analytical reasons for doing so, but O'Toole didn't acknowledge this. Dingell was in any case interested only in the fact that the paper contained errors. He seemed not to know that errors vary in their scientific significance, that evaluating their meaning involves critical judgment, and that discrimination in the use of data is a feature of scientific inquiry. In his letter to his colleagues, Baltimore warned that new laws and regulations could have a chilling effect on intellectual life. He saw "this affair as symptomatic, warn-

ing us to be vigilant to such threats, because our research community is fragile, easily attacked, difficult to defend, easily undermined."

IN the succeeding months, reactions from scientists spilled into the press, and tended to favor Baltimore. Representative Dingell and his staff were widely accused of scientific McCarthyism. Stewart and Feder were decried as off-the-wall vigilantes. After the congressional hearing, they had been detailed to Dingell's subcommittee, and the principal co-authors of the *Cell* paper were asked to send in documents relating to the case. Dingell subpoenaed everything they might have that was even remotely related—original data, calculations and notes, laboratory notebooks, correspondence, and copies of grant applications. Baltimore and Weaver sent in their materials promptly, but Imanishi-Kari was dilatory in sending in hers, partly because they were a disorderly hodgepodge of file folders and spiral notebooks which she had collected in a box, and partly because she needed them to respond to the N.I.H. investigation. Baltimore's lawyer advised her to organize her materials, and she arranged a lot of her data in a single notebook and sent the notebook with the rest to Washington in July.

In mid-November, Baltimore, Imanishi-Kari, Weaver, and O'Toole received a draft of the N.I.H.'s report on the *Cell* paper. The judgment was unambiguous: "No evidence of fraud, conscious misrepresentation, or manipulation of data was found." The report did say that "significant errors of misstatement and omission, as well as lapses in scientific judgment and interlaboratory communication," had been discovered, by which were meant the overstatement concerning the specificity of Bet-1, an ambiguity in the description of what had been measured in Table 2, and the misstatement concerning the test on the mouse cells in Table 2. Baltimore and three of his coauthors had already published a letter in *Cell* clarifying their statements about Bet-1 and Table 2. The N.I.H. wanted them to publish further clarification, along with additional data, including a report of corroborating data that Imanishi-Kari said she had taken in June of 1985—later termed the "June subcloning data"—to replace the Table 2 results. They did so, although they got permission to include the June subcloning

data as a supplement to Table 2 rather than as a replacement for it. When the final N.I.H. report was released, on January 31, 1989, Baltimore told reporters that he felt "vindicated."

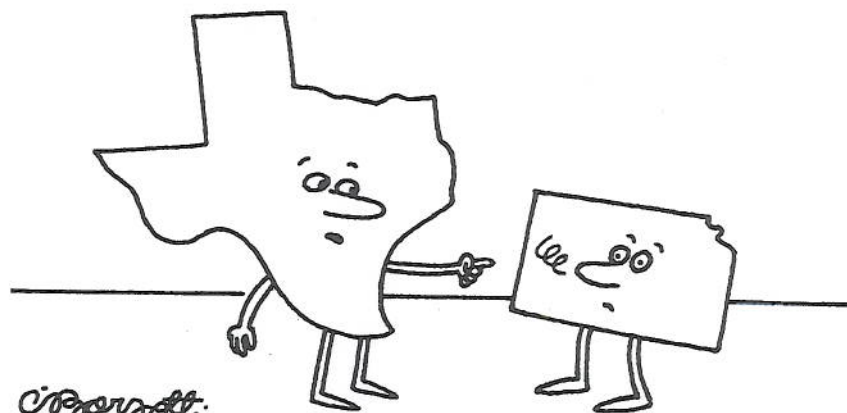
To Representative Dingell and his staff, however, the N.I.H. report was far from the final word. To show that the handling of fraud and misconduct by the scientific community was unsatisfactory, they would have to demonstrate that the inquiries at Tufts and M.I.T. into O'Toole's challenges and also the N.I.H. investigation had been inadequate—to prove, in short, that O'Toole was right. At Cold Spring Harbor, New York, that January, during a meeting of scientists and congressional staffers convened to discuss scientific fraud, Stewart outraged many in the audience by writing "Holocaust" on the blackboard and saying, in so many words, that people who stood by while misconduct occurred and whistle-blowers suffered were tantamount to Good Germans. An official at the N.I.H. told me that he went to Capitol Hill to talk things over with Stockton and several other members of Dingell's staff. "I felt that if they could have dropped an atom bomb on M.I.T. . . . they would have done it," he said. "They were on a mission. They didn't have any perspective. They wanted to get somebody, and they wanted to make a big hit."

STEWART says that at about this time it dawned on him that the three principal coauthors at M.I.T., the three scientists at Tufts, and Herman Eisen must have decided to "lie about the facts"—that "seven people had conspired to conceal a really important thing, to the enormous detriment of O'Toole." He says that when he finally sorted through all the

documents he knew "instantly" that something was funny about them. He says he told the staff that he "thought this stuff was forged, and they said, 'Figure out a way of proving it.'" He pursued his task assiduously, obtaining considerable help from O'Toole, with whom he spoke for hours on the telephone. He says that in four or five months he managed "to construct really tight arguments" to prove his case, but that the arguments were all scientific, too arcane to sell to the public.

Dingell's staff decided to call in the Secret Service for help. The Secret Service has considerable experience in the detection of falsified documents, since its duties include the enforcement of laws against counterfeiting cash, identification documents, and food stamps. But the agency rarely did this sort of work for Congress or dealt with the type of material that was in the notebooks in this case.

By April of 1989, the Secret Service seemed to have come up with the kind of evidence that Dingell's people were looking for. Its representatives reported to the subcommittee that some of the notes on experiments were misdated and out of sequence, and that other dates had been changed. Dingell called a hearing for early May, and invited Baltimore, Imanishi-Kari, and David Weaver to Washington so they could be briefed beforehand. During their briefings, they were given a short memo outlining the Secret Service findings, but the complex forensic analyses were only presented orally, making them difficult to follow. Under these circumstances, the coauthors decided not to respond until they had more opportunity to study the findings. Several days later, in a meeting with Baltimore, Weaver, some people from N.I.H., and several lawyers, Imanishi-Kari was asked by Baltimore if



"Ooh, you have a tornado right there."

she realized what Dingell had been getting at: that she had not only misrepresented experiments but had made them up out of whole cloth. Indeed, the term "fakery" had been used during the briefing. Imanishi-Kari answered that she knew "exactly how these experiments were done, and I know how much fucking shitwork I did for this. Right? And if I like to fake, I would do a better job than this. There are easier ways to do this."

At the Dingell-subcommittee hearing, on May 4th, the Tufts, M.I.T., and N.I.H. investigators all defended their findings that the *Cell* paper was scientifically reputable. Imanishi-Kari accounted for the out-of-sequence ordering of the data in her notebook by explaining that she was often too busy in her laboratory to record original data—often consisting of tapes printed out by radiation counters—in her notebooks until sometimes months after she had done an experiment. She simply filed the data or left them lying around for a while. She said that the Secret Service analyses made "no sense," that they seemed to be claiming merely "that I am not a neat person," which, she added, was true. She emphasized that, although her notes might seem "messy," she knew "where they are and how to read them," and "that's what's important." She also pointed out that the pages whose dating the Secret Service called into question appeared to contain no data that had been published in the *Cell* paper—a surmise that later proved largely correct.

David Baltimore said during the hearings that he understood the subcommittee's right to "demand accountability for government funding of scientific research," but he attacked its press leaks and its "prosecutorial style." He denounced Walter Stewart's "pernicious" data audits and censured him for "the loathsome comparison of scientific fraud, of which he accuses me, to the Nazi Holocaust."

Around 7 P.M., after nine hours of testimony, Dingell, beginning to sum up, chided the *Cell* paper's principal coauthors for not cooperating and, in particular, for refusing to respond to the findings of the Secret Service prior to the hearing. He chastised Baltimore for his "rather ringing attack upon this committee," pointing to Baltimore's claim that he had been charged with fraud—a claim that Dingell said was "untrue"—and to his "allegation"

that "some of the persons involved in these matters were behaving in a fashion worthy of Hitler." Subcommittee watchers say that Dingell arranges to have the last word, with closing statements that are intended to be unanswerable and unanswered. However, as Dingell raised his gavel to end the proceedings, Baltimore asked for a chance to respond. "I was charged with fraud," he said, passing up to Dingell a copy of the *Boston Globe* story with its headline on the 1988 hearing and its quotation from Stockton. He picked up an article from *Science* that described Stewart's behavior and read it aloud, his voice low and shaking with fury. Stewart's comparison of scientific fraud to the Holocaust and his likening of scientists who looked the other way to Good Germans were, the journal noted, "not the best analogy to use before an audience of scientists, where more than a few are Jewish." Dingell soon closed the hearing and left.

MEANWHILE, owing both to Dingell's continued pressure and Margot O'Toole's tenacity, the Baltimore case was being reopened at the N.I.H. When O'Toole saw the draft of the N.I.H. report exonerating Imanishi-Kari of misconduct in November of 1988, she had protested that it was "wholly inadequate." She claimed that the June subcloning had not been done, and asked to see the original data for Figure 1 herself. The N.I.H. supplied most of what she wanted, except for certain raw data for the figure, which Moema Reis said had been entered directly on the original figure in her notebook. Around this time, just before the Dingell-subcommittee hearing on May 4, 1989, the Secret Service briefed the N.I.H. on its findings that Imanishi-Kari's notebooks might have been faked. The N.I.H. found their allegations, coupled with O'Toole's attack on their own report, unsettling. At the end of April, N.I.H. officials told Dingell's staff that it was initiating a detailed audit of all Imanishi-Kari's data, and was placing special emphasis on forensic analysis of the notebooks.

Bruce Singal, Imanishi-Kari's lawyer, had pointed out earlier that, even though she had often transcribed her data into her notebooks long after she did an experiment, the radiation-counter tapes had been generated at the time the experiment was performed. Dingell instructed the Se-

SHOWCASE BY CHRIS CALLIS

TOUGH ACT

WHEN she wants to turn up the volume, Lindsay Duncan, one of England's most popular leading ladies, can roar with the best of them, as she did in her rowdy "Merry Wives of Windsor" during a 1986 stint with the Royal Shakespeare Company. Here, as "proud Titania" (she doubles as Hippolyta) in the R.S.C.'s vivacious "A Midsummer Night's Dream," at the Lunt-Fontanne until May 26th, the fair-skinned, fine-boned Duncan is captured in a moment of wide-eyed operatic anger. But in fact Duncan's defining dramatic quality is something less vulgar and more delicate; she has a distinctively elegant English reserve. "I'm a slow cooker," she says of her deliberate, mulling-it-over way of working on her characters. "I'm not a very aggressive performer. I tend to come to the boil rather slowly."

Duncan doesn't shirk the darker sides of her characters. She turned in a terrifying performance as an emotionally abusive mother in David Mamet's brilliant "The Cryptogram," in the West End last year: the character's steely detachment played well against Duncan's seraphic looks. She makes an audience come to her, and this gives her performances a sense of mystery. It also makes her very sexy onstage—a quality she has exploited to award-winning effect as the lethal, manipulative Mme. de Merteuil in "Les Liaisons Dangereuses," on Broadway and in the West End ("I'll never get over my good fortune at meeting that part"), and as the stiff-necked, nervy Maggie in "Cat on a Hot Tin Roof," at the Royal National Theatre. In the fall, Duncan will appear opposite Stephen Rea in Harold Pinter's new full-length play, "Ashes to Ashes," in London.

"You feel you're part of something, not on the sidelines turning over words and effects," she says of her work in groundbreaking plays like the Mamet and the Pinter. "You're in touch with something important. It's thrilling. You can't coast." Not that she would. Duncan's gift is for going deep, not for staying on the surface.

—JOHN LAHR

Lindsay Duncan,
New York City, May 2, 1996.

cret Service to try to determine whether what Singal said was true.

The N.I.H. had recently established an Office of Scientific Integrity, to prove that the agency could handle issues of fraud without Dingell. In June, Margot O'Toole wrote to Brian Kimes, the acting director of the O.S.I., that evidence she had been sent by the N.I.H. revealed "that the experimental findings shown in Figure 1 of the *Cell* paper have been falsified." Kimes decided during the summer that the O.S.I. investigation would include O'Toole's charge that the June subcloning had never been done. He also decided that the O.S.I. should, in its investigation, obtain the assistance of O'Toole herself.

BRIAN KIMES is a forthright, level-headed, boyishly handsome man, a biochemist by training, who loves science and the N.I.H., where he has been a research administrator in the National Cancer Institute for some twenty years. He took the temporary job of setting up the O.S.I. reluctantly, and remembers telling James B. Wyngaarden, the director of the N.I.H., that "it was not my ambition to send scientists up the river." He recalls that at the beginning the professional staff was tiny, just two scientists and an administrator. They were overburdened with a

backlog of scores of cases and didn't have much of a sense of how the office should operate. Suzanne Hadley, a research psychologist who was a veteran of scientific-misconduct investigations elsewhere at the N.I.H., quickly assumed a major role. "She would dig into the case like a detective," Kimes says. "I felt that she was obsessed a little bit with it, and she was not keeping her balance and perspective at the time."

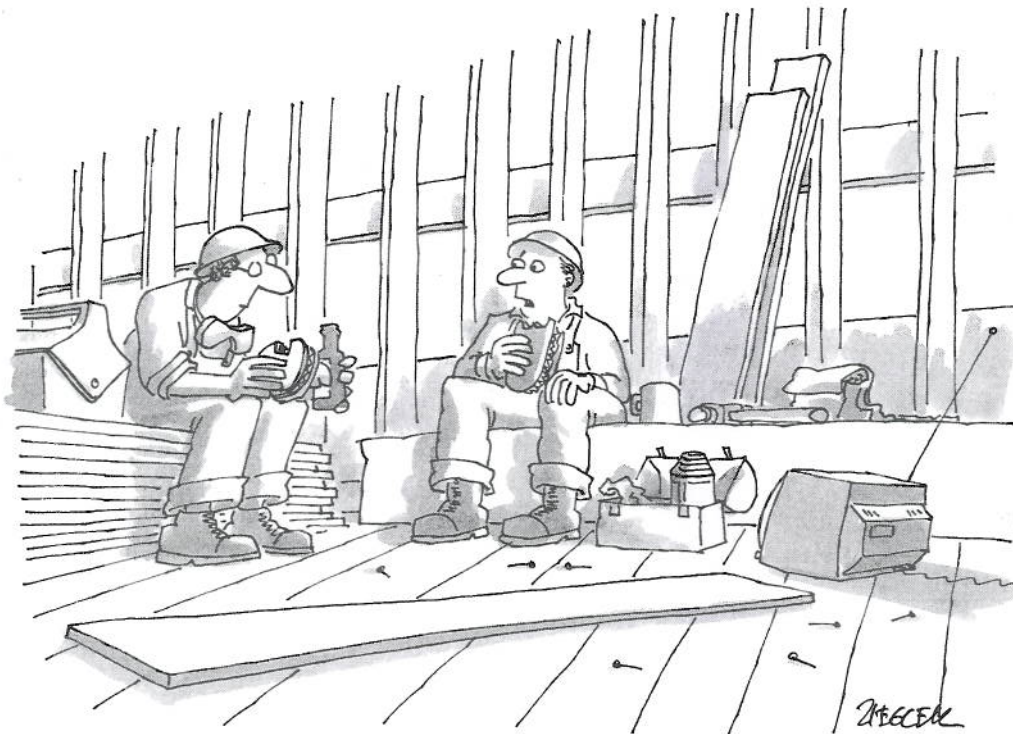
N.I.H. officials were concerned that the agency not appear remiss in the Baltimore case. "We were taking a lot of hits from Dingell on this with the public," Kimes says. "Wyngaarden was extremely worried about the politics of it, because those are things that could impact all of the N.I.H. It was a very uncomfortable situation." He recalls that the O.S.I. staff was "always under the watch of Dingell." He "could subpoena anything. He could get anything from our office any time he wanted," and his staff leaked material to the press, including "very confidential, private information" about people who, like Imanishi-Kari, were merely under investigation. "They were totally unethical," he says.

Kimes's office had agreed to let Margot O'Toole share the materials that the O.S.I. accumulated, and he asked her to

draw up a written list of allegations concerning them, even though "at the time she felt she had been messed around with so much that there was very little way that you could get a totally rational discussion out of her." He thought that she would understand the data, although "we weren't relying on her comments." He says that the case was "so political" that "to try to exclude her from everything would have made us look like bad guys." Early in November, 1989, she submitted eighteen allegations, declaring that the notebooks "do now contain records which purport to substantiate the claims I challenge, but these records are totally fabricated in some instances, and significantly falsified in others. I have therefore made a charge of fraud."

O'Toole's lengthy conversations with Stewart and her sense of having been "messed around with" formed the background for her move from accusations of error to allegations of fraud. She believed that her efforts to get the *Cell* paper corrected had earned her only alienation and injury. At the hearing held by Dingell's subcommittee in 1988, she said that she had broken with "many people I have admired . . . and some who were my friends," and that the dispute had "halted my career, disrupted my social milieu, and had a devastating effect on my life." Henry Wortis says that even now O'Toole never comes to social events in the Tufts pathology department, where her husband works. Under ordinary circumstances, the department would be a sustaining part of her professional family, and Wortis, as her doctoral adviser, would be a professional paterfamilias. But the bitter circumstances of the Baltimore case have cut her off from what would have been natural relationships, and had very likely put the dispute at the emotional center of her life.

O'Toole's cluster of resentments had expanded far beyond her belief that she had been professionally betrayed by the overstated claims for Bet-1. It was now much too late to remedy that slight. If Baltimore and the others had shown in the beginning that they took her seriously by publishing a correction for Bet-1, Stockton told me, "They could have been out of the whole



*"We begin the day hammering. Then there's Regis and Kathie Lee.'
Then we do some more hammering, followed by lunch and 'Days of Our Lives,'
more hammering, 'Oprah,' and, finally, home."*

fucking thing. Absolutely nobody would have ever heard of this. They could have made O'Toole probably happier than shit." But now O'Toole felt personally insulted by Baltimore's angry private characterization of her to Stewart and by a report from Stewart that Eisen had called some of her objections to the *Cell* paper "pretty incoherent." What appeared to bother her even more was a conviction that she had been professionally smeared. In December of 1986, shortly after Stewart and Feder approached the coauthors for access to their data, Eisen had written a report of the M.I.T. inquiry in which he stated that O'Toole's "allegations of misrepresentation" raised issues that for the most part turned on "matters of judgment" and revealed no evidence of fraud or misconduct. O'Toole eventually obtained a copy of the report and read it to mean that she had levelled an unfounded charge of fraud against Imanishi-Kari, even though she had scrupulously confined her initial challenge to error. She told the Dingell subcommittee that she had been portrayed as "a person who had raised ridiculous and trivial and unsubstantiated allegations against my supervisor for vindictive reasons." O'Toole's correspondence with N.I.H. officials was laced with similar complaints, including the claim that the N.I.H. panel report was "damaging" to her and that senior scientists had been "campaigning" against her and saying that she "was not telling the truth." Her allegations were embedded in an account of the dispute that was thoroughly self-justifying. She says that she was fighting for her reputation, her sense of who she was.

BEGINNING in the summer of 1989, the O.S.I. invited Imanishi-Kari to cooperate in the investigation, asking her to index her notebooks and to provide certain other information. She recently told me that she had been reluctant to do so, since the supplemental material she had given to the N.I.H.—notably the June subcloning data—was being used as the basis for fraud charges. Bruce Singal, her lawyer, had told the O.S.I. several times that his client would not respond unless she was provided with a specific list of the charges against her and the evidence supporting them. He was unable to get a full list from the O.S.I., even after April 11, 1990, when the N.I.H. terminated one of Imanishi-Kari's research

grants—a rare event at the agency—without explanation other than an allusion to the evidence that the O.S.I. was accumulating against her. The Secret Service reported to Dingell that Imanishi-Kari's radiation-counter tapes were not consistent with the putative dates of her experiments. All told, the information she was given about the investigation was vague and incomplete. In July and October, 1990, Singal nevertheless permitted Imanishi-Kari to respond to the O.S.I., because, he said, she wanted to defend her reputation.

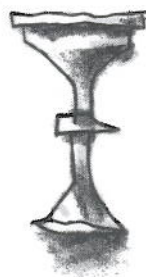
Imanishi-Kari was, to all intents and purposes, prevented from mounting a genuine defense. The O.S.I. combined the duties of investigator, prosecutor, judge, and jury, and pursued them all in the manner of the Star Chamber. Both during and after the investigation, Imanishi-Kari was denied the right to see the evidence, the right to learn what witnesses said, and the right to cross-examine them. The burden of proof was on the accused rather than on the accuser.

The Office of Scientific Integrity, Orwellian in name, justified its procedures with an Orwellian logic. The reason that those under investigation could not be given access to their original data was that they might alter it. The reason they could not confront witnesses against them was that their doing so might discourage whistle-blowers. And in this case the whistle-blower had, in effect, become part of the prosecution. O'Toole was asked to provide an assessment of new evidence when it was received. She was given information from the Secret Service reports and had detailed knowledge of the notebooks, which she used during the investigation to bolster her allegations of fraud.

Suzanne Hadley had taken over the investigation after Brian Kimes returned to the National Cancer Institute. He thinks that, once the balance he had provided was gone, Hadley's obsession with misconduct began dominating the O.S.I. Hadley "identified with whistle-blowers in general," Kimes says, especially those she thought had been mistreated, and she was "very involved with O'Toole," as they all were—"more . . . than we should have been." Hadley and O'Toole seemed inherently compatible in their view of how science should be practiced. O'Toole felt that Imanishi-Kari had used her data with inappropriate selectiveness, and Hadley

believed that "the phenomenon is always right," as she put it later in a lecture on biomedical ethics at the University of California at San Diego. Analysts of science call such a view "naïve inductivism."

LATE in March of 1991, a two-hundred-page draft of an O.S.I. report, stamped "Confidential," was leaked to major American news organizations. The doc-



ument unceremoniously discredited Baltimore, whose persistent defense of Imanishi-Kari it called "difficult to comprehend," and vindicated O'Toole, calling her actions "heroic." It also declared Imanishi-Kari to be guilty of fraud.

The leaked report fixed the impression of the case in the public mind. In a column in *Time*, the commentator Barbara Ehrenreich captured the over-all response: "Baltimore pooh-poohed O'Toole's evidence and stood by while she lost her job. Then, as the feds closed in, he launched a bold, misguided defense of the sanctity of science." She added, "What he lost sight of, in the smugness of success, is that truth is no respecter of hierarchy or fame. It can come out of the mouths of mere underlings, like the valiant O'Toole."

Under pressure from all sides, Baltimore reluctantly retracted his coauthorship of the *Cell* paper pending final resolution of the case, and, in a statement in *Nature*, with equal reluctance declared a mea culpa. "I now recognize that I was too willing to accept Imanishi-Kari's explanations, and to excuse discrepancies as mere sloppiness," he said. O'Toole rejoined that he had much more to regret, whereupon Baltimore called into question her account of events in a way that seemed to undercut his contrition. Several members of the Rockefeller University faculty said that the best interests of the institution required that he quit its presidency. While driving with his wife to Thanksgiving dinner, he decided to resign.

Imanishi-Kari refused to retract the *Cell* paper. Since its publication, scientists in other laboratories had worked to extend the paper, obtaining support for some of its features while asking questions about some of its interpretations, and Imanishi-Kari herself was engaged in further research to pin down what happened to the transgenic-mouse cells. In a letter to *Nature* at the end of June, a hundred and thirty-five biomedical scientists protested

that the Office of Scientific Integrity had produced its report in "a politically charged atmosphere under intense pressure from Congress," and that, as a leaked draft to which Imanishi-Kari had not yet had a chance to respond, the report formed a poor basis for judgment.

The year before, Dingell had directed his staff to share the forensic evidence with the United States Attorney for the District of Maryland, the home of the N.I.H., and it was through the attorney's office that Imanishi-Kari, who was now facing the possibility of prosecution, saw her original notebooks again and also, finally, the full Secret Service reports. A forensic expert retained by her lawyers analyzed the Secret Service findings and original material and reported that it was in fact impossible through the techniques employed by the agency to draw any conclusions about when the radiation-counter tapes had been generated. Nor could the sequence of the experiments be verified. In July of 1992, the United States Attorney's office announced that it would not seek an indictment, and Baltimore withdrew his retraction of the *Cell* paper.

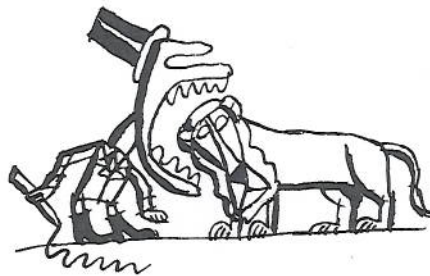
In June, in response to outcries against its Star Chamber aspects and procedural lapses, the Office of Scientific Integrity had been taken away from the N.I.H. and reconstituted as the Office of Research Integrity, within the office of the Assistant Secretary for Health. Scientists who were tentatively found guilty of fraud or misconduct would henceforth have the right to take their cases to an appeals board, which would report directly to the Secretary of Health and Human Services, and which would afford them all the rights of due process, including the right to call and cross-examine witnesses and scrutinize the evidence against them. In October of 1994, more than eight years after Imanishi-Kari was first brought under suspicion by O'Toole, the O.R.I. issued a final report: it upheld the preliminary finding of guilt. It proposed to bar Imanishi-Kari from eligibility for government grants for ten years, although the normal penalty in fraud cases is three to five years. Thereza Imanishi-Kari immediately filed an appeal.

IMANISHI-KARI'S appeal, which was heard last summer, and on which a ruling is imminent, addressed nineteen charges levelled against her. The hear-

ing was held in a small room in the Hubert H. Humphrey Building, in downtown Washington, under the auspices of a three-member panel empowered by the Department of Health and Human Services. Some of the charges struck at her tendency not to practice science in the mechanical way that Suzanne Hadley, for one, seems to think that it ought to be practiced, and part of them rested on the claim that materials on roughly a third of the pages in the main notebook that Imanishi-Kari had compiled and sent to the Dingell subcommittee in 1988 were fabricated or falsified. The key materials were the radiation-counter tapes—they resemble adding-machine tapes—and handwritten records of numbers taken from similar tapes that had, purportedly, been discarded. The O.R.I. use Secret Service reports to demonstrate that Imanishi-Kari had falsified the tapes, and it employed a statistical technique to show that she had fabricated the handwritten numbers.

In human affairs, as in science, truth is inseparable from the standards and processes employed in determining it. The O.R.I.'s rules do not require that it prove its case on any point beyond a reasonable doubt; it need only show that the charges are supported by a "preponderance of evidence." Under a reasonable-doubt standard, the O.R.I. would very likely have had no case, but even under the looser standard none of the O.R.I.'s arguments appeared preponderant against Imanishi-Kari's rebuttals. The statistical techniques, for example, revealed only how Imanishi-Kari handled numbers, not whether she made them up. Even one of the O.R.I.'s own expert witnesses conceded that the statistical analysis, by itself, was not "enough for me to say it's fabrication."

"You can't blame the Secret Service," Joseph Onek, Imanishi-Kari's principal appeal lawyer, says. "It was all Greek to them." If they had been better able to interpret the material, they would have rec-



ognized that some of the allegedly fabricated notebook pages were not used in the *Cell* paper. They would have seen, as Onek pointed out in a brief, that the notebook "contains many examples of data which undermine [her] scientific position or fail to support it adequately or which are bizarre or seemingly impossible." Precisely that point had bothered Cecelia Sparks Ford, who presided over the panel. On the last day of testimony, she asked O.R.I.'s chief scientific witness, "If you were going to set out to fabricate data of this sort, why would you fabricate data that can be described as not the best data to support what you are about? . . . Why wouldn't you fabricate the best possible set of data, all of which was related to what you purported in the paper?" The O.R.I. official responded, "That's a hard one."

The O.R.I. had a difficult time explaining any of Imanishi-Kari's motives for the multiple misdeeds she was alleged to have committed, especially with regard to Bet-1, the reagent that stymied O'Toole and led to the original complaint. The O.R.I. claimed that Imanishi-Kari was at serious fault for overstating the reagent's discriminatory powers, that she was responsible for misrepresenting the characteristics of Bet-1, and that she had an obligation to report her discrepant results. Onek replied that the O.R.I. ignored much of the data showing that Bet-1 worked, that Imanishi-Kari had simply taken Figure 1 from Moema Reis's notebook, and that it was standard practice in Imanishi-Kari's field not to report isolated discrepant results that are not serious. "With this charge," Onek said, "O.R.I. has gone beyond manufacturing evidence of a crime. O.R.I. has manufactured the crime itself." Onek added that everyone who uses Bet-1 knows that it is temperamental. O.R.I. found no evidence that Imanishi-Kari intended to deceive with Bet-1. She had no reason to. As the original investigating panel at Tufts had recognized, to have exaggerated the discriminatory powers of Bet-1 would have worked against the central claim of the paper.

As to the charges about Table 2 and the June subcloning data that Imanishi-Kari had offered in support of it, the O.R.I. surmised that she fabricated the data after the fact, once there was an investigation of the *Cell* paper. Accord-

ing to their scenario, she quickly made up results to bolster the published data. But, again, the June subcloning data was not the sort of thing that anyone in that position would create to save herself. She noted at the time that some of it was "bizarre," and even the O.R.I. could not explain why she would have invented it. Early in his brief, Onek pointed out that Imanishi-Kari's notebooks expressed "all the inconsistencies and surprises that one would expect in the laboratory notebook of a real bench scientist engaged in cutting-edge research"—sometimes supporting her theories and sometimes not. Making sense of such data demanded judgment, insight, and imagination.

It is now ten years since O'Toole first raised her questions against Imanishi-Kari. At the close of his brief, Onek took note of the anniversary, declaring that the "ensuing decade of staged hearings, leaked documents, ever-changing charges, and inaccurate reports shattered her scientific career." To date, the O.R.I. has lost almost all of its high-profile cases on appeal. It should be no surprise if it loses this one, too.

THE Office of Research Integrity, which now has about forty employees, continues to investigate scientific-fraud-and-misconduct cases and to oversee investigations of charges at institutions receiving grants from the N.I.H. But a question arises as to how much, if any, special machinery to enforce scientific integrity should be operating. Brian Kimes says that most of the cases that came to the O.S.I. on his watch were "trivial." No reliable data exist on the incidence of scientific misconduct, but it is likely that the serious form of it—fabrication and falsification of data—is rare.

David Baltimore committed several errors of judgment in the course of his case, and some scientists say that turning the dispute over the *Cell* paper into a battle about the vitality of American science was both arrogant and foolish. But he was right about the most important issues. Joint research published by Alan Stall at Columbia University and Leonore A. Herzenberg at Stanford in 1993 confirmed the *Cell* paper's observation that the transgenic-mouse cells produced a high level of native antibodies, a point that corroborated Imanishi-Kari's own

further work, which had been published a few months earlier. The Stanford-Columbia team did not attribute the phenomenon to the kind of idiotic mimicry postulated in the *Cell* paper—new evidence had made that interpretation questionable—and they differed with Imanishi-Kari over the mechanisms that were at work in the cells. But Herzenberg, the geneticist at Stanford, told a reporter that the *Cell* paper "showed that the antibodies these mice made were abnormal, and our current paper confirms that absolutely."

Baltimore was neither foolish nor arrogant in contesting John Dingell and being dismissive of Stewart and Feder. Dingell's idea of science threatened to quash the kind of creative reading of experiments that had made recognition of the abnormal behavior of the mouse cells possible. The congressman and his staff pursued Imanishi-Kari relentlessly, in effect prosecuting her. She has had to resort to legal services valued at roughly a million dollars. Friends paid some of the costs; her lawyers and expert

witnesses provided the majority of the rest pro bono.

John Dingell lost his committee chairmanship in 1994, when the Republicans took control of the House. Stockton and Chafin soon left, and both are now in private business.

In February of 1993, Stewart and Feder sent a fourteen-hundred-page document to the American Historical Association alleging that the historian Stephen Oates, the author of biographies of Abraham Lincoln, Martin Luther King, Jr., and William Faulkner, had lifted many passages in these works from other sources without attribution. The A.H.A. had already cleared Oates of charges of plagiarism in the Lincoln book; he was a private citizen; biographies of Lincoln, King, and Faulkner had nothing to do with science; and examination of the passages that Stewart and Feder fingered suggested to many observers that the pair knew little, if anything, about what constituted plagiarism. Soon after, the N.I.H. abolished their laboratory and assigned them to separate jobs. Stewart immediately went on a hunger strike. ♦



"Hank, when you're finished firing this gentleman I have some rather unfortunate news for you as well."