wards, with caring personnel (who may be staff physicians, physician's assistants, family nurse practitioners, or best, a combination) and superb nurses would be better.

Most medical students begin their careers with interest, enthusiasm, and energy. It is our job as teachers and physicians to make certain that these qualities are not only preserved but also heightened and transmitted to the care of patients. Each patient should legitimately feel, as should his or her physician, that he or she is a "great case."

FAITH FITZGERALD, M.D.
University of California, Davis,
Sacramento, CA 95817 Medical Center

Dr. Levinsky replies:

To the Editor: As Dr. Shurin indicates, nurse practitioners and physician's assistants will have increasingly important roles in the delivery of primary care. They will not, however, replace primary care physicians. My article dealt with means to recruit adequate numbers of such physicians.

I agree with Dr. Fine that professional satisfaction in primary care comes from relating to people, not from treating "interesting" diseases. (Indeed, I used quotation marks around "uninteresting" in my article to separate myself from the implications often attached to that word in this context.) It takes time to talk to patients and to understand them as people. I believe that a restructuring of the economics of primary care is needed. Otherwise, the time allotted to an office visit will continue to be too short for developing and maintaining the personal relationship necessary for both patient and practitioner.

Dr. Siwek believes that altering the criteria for admission to medical schools will greatly affect the percentage of U.S. medical graduates who choose primary care. The experience at Jefferson Medical College is instructive in this regard.[1] Graduates of a special program combining a selective admissions policy with a special educational program are far more likely to practice primary care than their classmates in the regular program at Jefferson. Over the past decade, however, the percentage of available places filled in the special program has decreased to 33 percent. As I stated in my article, I believe that we will not recruit adequate numbers of generalists by alterations in selection criteria and educational reform alone.

Contrary to Dr. Kieliszek's impression, the Department of Medicine at Boston University, which is responsible for patient care both at University Hospital and Boston City Hospital, prides itself on training physicians for the practice of general internal medicine, as well as for subspecialty practice or an academic career. In fact, our primary care residency is the largest federally funded primary care residency program in the United States and one of the most successful.[2] His impression that Boston University considers training at Boston City Hospital somehow uninteresting is mistaken. The integrated Boston University medical residency includes both Boston City Hospital and University Hospital as major and equal partners.

NORMAN G. LEVINSKY, M.D.
Boston, MA 02118 Boston University Medical Center

1. Rabinowitz HK. Recruitment, retention, and follow-up of graduates of a program to increase the number of family physicians in rural and underserved areas. N Engl J Med 1993;328:934-9.
2. Goldenberg DL, Pozen JT, Cohen AS. The effect of a primary-care pathway on internal medicine residents' career plans. Ann Intern Med 1979;91: 271-4.

SHATTUCK LECTURE — MISCONDUCT IN MEDICAL RESEARCH

To the Editor: In his Shattuck Lecture as published in the *Journal* (June 3 issue),[1] Congressman John Dingell says that the Subcommittee on Oversight and Investigations of the U.S. House of Representatives, which he chairs, has "looked only at clear-cut cases involving fabrication, falsification, or plagiarism." He then includes among these cases the investigation by his subcommittee of a 1986 paper published in *Cell,* by Dr. Thereza Imanishi-Kari and others, including myself.[2] Congressman Dingell's lecture is replete with suggestions that it is an established fact that fabrication was involved in the writing of the paper. He is incorrect, as shown by the published record as well as the statements of the U.S. Attorney for Maryland.

It has been seven years since the paper was published, during which time numerous papers have supported and extended the original findings.[3-10] Many outside the immunologic community will be surprised to learn that the science in the *Cell* paper was essentially correct, because for the past three years members of the media and Congressman Dingell have claimed that there were serious flaws in the paper. Dingell's charge that the paper "relied in large part on data that were falsified" is not only unproved but extremely unlikely to be true.

In his Addendum to the lecture, Congressman Dingell notes that even though he sent the information he had accumulated to the U.S. Attorney in Baltimore, after a yearlong investigation the U.S. Attorney declined to prosecute. What he does not say is that a central reason for the lack of prosecution was the invalidation by an independent forensic investigator of the evidence suggesting that Dr. Imanishi-Kari had produced data fraudulently (quoted in Hilts[11]). Mr. Albert H. Lyter found that the Secret Service analyses of her notes from the study were "erroneous." If the science has stood the test of reproducibility and the evidence of fraudulent data production does not hold up, there is simply no case against Dr. Imanishi-Kari.

Should there be any doubt about this interpretation, one need only look at the U.S. Attorney's press release announcing his decision.[12] He noted that his office "will prosecute appropriate cases" and, after emphasizing the care taken in his investigation, said that "prosecuting a criminal case on such debatable grounds would not be in the interests of justice." He explicitly said that the "central issue" was "the fundamental validity of her scientific work" and that it was an issue to be decided in the scientific community.

I must also protest Congressman Dingell's implication that I was under investigation by the U.S. Attorney; I was told explicitly that I was not.

Congressman Dingell introduces his rendition of the facts by saying that Dr. Margot O'Toole was "vilified and effectively driven from her profession" because she was the whistle-blower in this case. In fact, Dr. Imanishi-Kari and I have been careful to treat her with respect, even when we totally disagreed with her, because we recognized the right of one scientist to question the work of others. It has been documented that she was not driven from her profession but instead chose to leave it.[13] For an extended period she made no known effort to return to science, and when she applied for a position, she gained one at the Genetics Institute. In fact, it is Dr. Imanishi-Kari who has been vilified, and were it not for the support of Tufts University she would have been driven from her profession. Even today it is not clear

whether she will be able to continue as the important contributor to modern immunology that she has been. Dr. Imanishi-Kari's federal grants were cut off, although no determination of her guilt has been made. Recently, she has been allowed to reapply, but the grant she previously received was not returned to her. To my mind, Congressman Dingell should be apologizing to Dr. Imanishi-Kari, the real victim in this case, and not repeating inaccurate information about Dr. O'Toole.

Congressman Dingell holds himself up as the guardian of the integrity of the scientific process. If that is the role of his subcommittee, then I believe that the subcommittee should be investigating the most egregious miscarriage of justice in this case — the leaking of the 1992 draft report by the National Institutes of Health (NIH) that charged Dr. Imanishi-Kari with falsification. To this day, that report has never been officially completed or released, and it contained a strong dissent by two of the five members of the scientific panel. The leaking of the report, which led to its treatment as an established fact in the media, was in my view an illegal act that should be explained by the subcommittee.

DAVID BALTIMORE, PH.D.
New York, NY 10021 The Rockefeller University

1. Dingell JD. Misconduct in medical research. N Engl J Med 1993;328:1610-5.
2. Weaver D, Reis MH, Albanese C, Costantini F, Baltimore D, Imanishi-Kari T. Altered repertoire of endogenous immunoglobulin gene expression in transgenic mice containing a rearranged mu heavy chain gene. Cell 1986;45:247-59.
3. Grandien A, Coutinho A, Andersson J. Selective peripheral expansion and activation of B cells expressing endogenous immunoglobulin in μ-transgenic mice. Eur J Immunol 1990;20:991-8.
4. Costa TE, Suh H, Nussenzweig MC. Chromosomal position of rearranging gene segments influences allelic exclusion in transgenic mice. Proc Natl Acad Sci U S A 1992;89:2205-8.
5. Iacomini J, Yannoutsos N, Bandyopadhay S, Imanishi-Kari T. Endogenous immunoglobulin expression in mu transgenic mice. Int Immunol 1991; 3:185-96.
6. Holmberg D. High connectivity, natural antibodies preferentially use 7183 and QUPC 52 V_H families. Eur J Immunol 1987;17:399-403.
7. Cooke R. "False" now judged true. Newsday. May 18, 1993:12.
8. Lam K-P, Herzenberg LA, Stall AM. A high frequency of hybridomas from M54 mu heavy chain transgenic mice initially co-express transgenic and rearranged endogenous mu genes. Int Immunol (in press).
9. Imanishi-Kari T, Bandyopadhay S, Busto P, Huang CA. Endogenous Ig production in mu transgenic mice. I. Allelic exclusion at the level of expression. J Immunol 1993;150:3311-26.
10. Imanishi-Kari T, Huang CA, Iacomini J, Yannoutsos N. Endogenous Ig production in mu transgenic mice. II. Anti-Ig reactivity and apparent double allotype expression. J Immunol 1993;150:3327-46.
11. Hilts PJ. Researcher accused of fraud in her data will not be indicted. New York Times. July 14, 1992.
12. Bennett RD. Press release. July 13, 1992.
13. Davis B. Dingell's witness for the persecution. Wall Street Journal. July 22, 1991.

To the Editor: Congressman John Dingell states that the public deserves science of the highest quality, free of fraud, plagiarism, and deceit. What is at issue is whether in pursuing this aim he has failed to meet his own standards.

What his lecture lacks is an appreciation of the value of evidence. None of the several panels of scientists (including ourselves) that reviewed the original allegations found sufficient evidence to negate the conclusions of the *Cell* paper* or to demonstrate that fraud had been committed. Those allegations and hypotheses were concerned with the interpretation of experiments and involved issues such as whether valid control mice were used and whether a monoclonal antibody had the appropriate specificity. The issue of falsification was raised years later, in 1988 and early 1989, after the Secret Service, at the request of Congressman Dingell's subcommittee, had begun a forensic examination of the original laboratory records. As we have since learned, the forensic evidence that was used to damn Dr. Imanishi-Kari and colleagues could not withstand scrutiny. The belief (the hope?) of a U.S. Attorney, or of Mr. Dingell, that it would do so does not substitute for the deed.

Claims that senior scientists at Tufts University and the Massachusetts Institute of Technology had agreed that the paper was fundamentally flawed but should not be corrected are absolutely untrue, as we have testified, along with Dr. Baltimore, Dr. Herman Eisen, Dr. Imanishi-Kari, and others. Other than Dr. O'Toole, every person with direct knowledge of the discussions in May and June of 1986 has denied that there was any understanding that the paper was so flawed that it deserved retraction. At a meeting two of us attended, Dr. Imanishi-Kari told Dr. O'Toole that she was free to differ in her interpretations of the data in the *Cell* paper. Dr. O'Toole replied that she was satisfied by this statement and offered to shake hands. By no stretch of the imagination can this interchange be construed as an agreement to retract.

There is no evidence that Dr. O'Toole was vilified and virtually driven from science. Although she has stated that she did not think she would be given references or hired for a job in science, there is no evidence in the public record that her job applications were refused or her requests for recommendation denied. Collectively, we have received only a single request for a recommendation, which was given, and this was for the job that she now has.

In science, ideas, hypotheses, and hopes are only the beginning. The proof lies in the experiments. The evidence in this case is not well known by the public and the findings are still pending, yet Congressman Dingell treats his hypothesis as proved. If, like him, we could all guarantee the certitude of our hypotheses, we would be relieved of the need to perform experiments. Substituting advocacy for evidence confuses the practices of Salem with those of science.

HENRY H. WORTIS, M.D.
BRIGITTE HUBER, PH.D.
Boston, MA 02111 Tufts University School of Medicine

ROBERT WOODLAND, PH.D.
University of Massachusetts
Worcester, MA 01655 Medical School

*Weaver D, Reis MH, Albanese C, Costantini F, Baltimore D, Imanishi-Kari T. Altered repertoire of endogenous immunoglobulin gene expression in transgenic mice containing a rearranged mu heavy chain gene. Cell 1986;45:247-59.

To the Editor: The *Journal* is not the appropriate forum for a point-by-point rebuttal of the spurious charges against Dr. Gallo that Congressman Dingell repeated in his Shattuck Lecture. I would simply like to highlight some of the omissions from the lecture.

The lecture fails to note that in 1984 Dr. Gallo and his colleagues demonstrated that a new retrovirus was the cause of AIDS and thereby paved the way for all subsequent epidemiologic and research efforts and for the development of a blood test that has saved countless thousands of lives. The importance of this accomplishment is not diminished by the fact that the isolate used for the blood test apparently had been contaminated accidentally by a sample sent to Dr. Gallo's laboratory from the Institut Pasteur. Contamination

by the French isolate occurred in laboratories throughout the world, most notably the Institut Pasteur itself. Scientists understand that accidental contaminations are inevitable in virology; they are neither sinister nor suspicious. Furthermore, Dr. Gallo's laboratory had another isolate that could have been used for the blood test, an isolate now widely used for research purposes, as well as several other isolates.

What is most lacking in the Shattuck Lecture is any sense of perspective. Certainly, scientific misconduct is deplorable and should be combated. But we must take care that the cure does not become worse than the disease. If, as has happened in Dr. Gallo's case, the crusade against scientific misconduct becomes an excuse for the endless rehashing of unfounded charges, society will be the loser.

Dr. Gallo's own perspective is honed by the knowledge that AIDS and cancer now threaten to kill hundreds of millions of people. The controversies of the past seem trivial as compared with that reality, and efforts to rekindle them in the name of uncovering scientific misconduct serve only to retard scientific progress. The scientific community, fortunately, has its priorities in order; French researchers, for example, are cooperating with Dr. Gallo's laboratory on a range of important projects. It is past time for other communities to reevaluate their priorities.

JOSEPH N. ONEK
Counsel for Dr. Robert Gallo
Washington, DC 20004 Crowell & Moring

Editor's note: Because Dr. Gallo's appeal of the Office of Research Integrity report is pending, he requested that his counsel respond to Mr. Dingell's Shattuck Lecture.

To the Editor: It would be preferable for Congressman Dingell to defend the work of his subcommittee without voicing his opinion on the details of ongoing investigations. By discussing the specifics of the ongoing cases involving Dr. Baltimore and Dr. Gallo, he denies the accused the right to respond, question, or cross-examine their accusers. The congressman holds all the cards and is not accountable to any known rule book. How does one answer public accusations by a powerful congressman who controls the very committee managing the investigation?

Dingell's first accusation against Gallo amounts to little more than guilt by association. Two people in Gallo's laboratory, among the hundreds who worked there over a 25-year period, were convicted of governmental "crimes." In finding Gallo at fault, Dingell ignores the fact that the discovery of these actions required subpoena power and the ability to examine private bank accounts — powers not afforded an NIH laboratory chief. Describing the affair involving Dr. Daniel Zagury, he says that Gallo himself "failed to report [two] deaths." Gallo was only one author in this multi-institutional study in the *Lancet*, serving primarily as a source of supply — he was not a principal author or investigator who would be expected to know clinical details that changed between the date of submission and the publication date. Dingell also fails to mention that Zagury was exonerated of all allegations by French authorities.

As for the AIDS blood test, Dingell's suspicions defy logic. If Gallo had something to hide, why would he himself first publish the sequence of his "IIIB" strain (one of the isolates referenced in the pivotal 1984 papers and the blood-test patent)? Were he guilty of deliberate misappropriation, his interests would have been better served by doing the opposite. Sequencing revealed a difference of 1.3 percent in the genome between the French and the U.S. strains, leading him to suspect nothing unusual since this was typical of the differences between the isolates of the only other human retroviruses known at the time. Only in later years was wider mutation shown to be a defining characteristic of the human immunodeficiency virus. Hindsight also shows that neither Gallo's "IIIB" nor the original French "BRU" strain used for comparison was what either laboratory thought it was; instead, both were contaminants of the later, more aggressive French strain, "LAI," which contaminated several other laboratories around the world. By what fair rules of science, law, or logic should we conclude that this evidence suggests wrongdoing on Gallo's part?

Dingell has at most uncovered two instances of ambiguity in the Gallo affair, not a smoking gun. The implied pattern of wrongdoing seems little more than a consequence of an intensive, years-long fishing expedition, a process that would no doubt find a string of small sins in anyone's life. What other scientists, politicians, or reporters could stand up to such scrutiny? Are not Gallo and Baltimore, with their undeniable contributions to humanity, entitled to the same presumption of innocence that is offered even the most vicious criminals? Instead, they have been speculatively tried and convicted in everything but the legal forums, without once being afforded the normal constitutional protections. Should this be the price of working in science?

Most people with AIDS are less concerned with congressional self-justification than they are with finding a cure. To whom is Dingell accountable for diverting two of our most productive scientists from that goal?

MARTIN DELANEY
San Francisco, CA 94103 Project Inform

Editor's note: Congressman Dingell will be given an opportunity to respond to these letters and to Dr. Healy's Sounding Board essay (in this issue of the *Journal*) in a subsequent issue.

2-CHLORODEOXYADENOSINE TO TREAT REFRACTORY HISTIOCYTOSIS X

To the Editor: Treatment of histiocytosis X is palliative at best. It includes corticosteroids, alkylating agents, antimetabolites, vinca alkaloids, and irradiation.[1] Since 2-chlorodeoxyadenosine, a purine substrate analogue active against lymphoid cancers,[2] is toxic to monocytes in vitro,[3] and since tissue histiocytes are derived from circulating monocytes as they move from the intravascular space to soft tissues, we administered 2-chlorodeoxyadenosine to a patient with histiocytosis X.

A 33-year-old woman had presented at the age of 15 years with polyuria and polydipsia due to diabetes insipidus. Two years later vesiculopustular lesions developed on her gingiva, scalp, and vagina that were histologically consistent with a diagnosis of histiocytosis X. High-dose steroid therapy was administered, with improvement. The cutaneous lesions were treated with vinblastine; they responded at first but later became refractory. Oral etoposide, vincristine, cyclophosphamide, and methotrexate were administered, without benefit.

Before treatment with 2-chlorodeoxyadenosine, the patient had numerous vesiculopustular lesions of 3 to 4 mm and shallow ulcers of her scalp, oral mucosa, vagina, and external auditory canals. Liver function was normal, the white-cell count was 5500 per cubic millimeter with a normal differential count, the hemoglobin concentration was