SCIENCE

Published by the **American Association for the Advancement of Science (AAAS),** *Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, to advance education in science, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

Membership/Circulation
Director: Michael Spinella
Deputy Director: Marlene Zendell
Member Services: Rebecca Dickerson, *Manager*; Mary Curry, *Supervisor*; Pat Butler, Helen Williams, Laurie Baker, *Representatives*
Marketing: Dee Valencia, *Manager*; Jane Pennington, *Europe Manager*; Hilary Baar, *Associate*; Angela Mumeka, *Coordinator*
Research: Renuka Chander, *Manager*
Business and Finance: Jacquelyn Roberts, *Manager*; Robert Smariga, *Assistant Manager*
Administrative Assistant: Nina Araujo de Kobes
***Science* Member Services**
Marion, Ohio: 800-347-6969;
Washington, DC: 202-326-6417
Other AAAS Programs: 202-326-6400

Advertising and Finance
Associate Publisher: Beth Rosner
Advertising Sales Manager: Susan A. Meredith
Recruitment Advertising Manager: Janis Crowley
Business Manager: Deborah Rivera-Wienhold
Finance: Randy Yi, *Senior Analyst;* Shawn Williams, *Analyst*
Marketing: John Meyers, *Manager;* Allison Pritchard, *Associate*
Traffic Manager: Tina Turano
Recruitment: Terri Seiter, *Assistant Manager*; Pamela Sams, *Production Associate*; Debbie Cummings, Celeste Miller, Rachael Wilson, *Sales*; Charlotte Longhurst, *European Sales*
Reprints Manager: Corrine Harris
Permissions Manager: Lincoln Richman
Exhibits Coordinator: Arlene Ennis
Sales Associate: Carol Maddox

PRODUCT ADVERTISING SALES: East Coast/E. Canada: Richard Teeling, 201-904-9774, FAX 201-904-9701 • **Midwest/Southeast:** Elizabeth Mosko, 312-665-1150, FAX 312-665-2129 • **West Coast/W. Canada:** Neil Boylan, 415-673-9265, FAX 415-673-9267 • **UK, Scandinavia, France, Italy, Belgium, Netherlands:** Andrew Davies, (44) 1-457-838-519, FAX (44) 1-457-838-898 • **Germany/Switzerland/Austria:** Tracey Peers, (44) 1-270-760-108, FAX (44) 1-270-759-597 • **Japan:** Mashy Yoshikawa, (3) 3235-5961, FAX (3) 3235-5852
RECRUITMENT ADVERTISING SALES: US: 202-326-6555, FAX 202-682-0816 • **Europe:** Gordon Clark, (44) 1-81539-5211, FAX (44) 1223-302068 • **Australia/New Zealand:** Keith Sandell, (61) 02-922-2977, FAX (61) 02-922-1100
Send materials to *Science* Advertising, 1333 H Street, NW, Washington, DC 20005.

Information for Contributors appears on pages 112–114 of the 6 January 1995 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005.
Internet addresses: science_editors@aaas.org (for general editorial queries); science_letters@aaas.org (for letters to the editor); science_reviews@aaas.org (for returning manuscript reviews); membership@aaas.org (for member services); science_classifieds@aaas.org (for submitting classified advertisements)

LETTERS

AIDS Research Policy

Larry Kramer writes (Letters, 3 Mar., p. 1249) to criticize aspects of my recent policy forum ("Reexamining AIDS research priorities," 3 Feb., p. 633). Kramer has played an important role in the community response to human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS). All of us engaged in the struggle to conquer AIDS must salute his efforts. Nonetheless, his criticisms represent an inaccurate description of the role and the actions of the National Institutes of Health (NIH) Office of AIDS Research (OAR).

Kramer states that the OAR has abdicated or postponed its responsibility for the preparation of a comprehensive plan to guide NIH-sponsored AIDS research. Quite the opposite is the case. Within 6 weeks of my appointment as director of OAR (in February 1994), such a plan was completed and formed the basis for the development of the fiscal year (FY) 1996 budget request, now being considered by Congress. This plan was prepared with extensive input from close to 200 government, university, and industrial scientists and from representatives of a wide array of community organizations, including some that Kramer founded. The process produced a consensus on the goals, objectives, and strategies that lie before us. The plan states the scientific priorities and opportunities for which precious resources should be allocated. Implementation of this plan has already led to substantial redirections of the AIDS research effort in response to these new priorities, with the goal of finding new molecular targets and, most important, filling the "pipeline" of new therapeutic agents and potential vaccine candidates. The plan has been forwarded to the President, as required by law. The OAR is already completing the update of that plan to reflect priorities for the FY 1997 budget.

This planning function is not the same as the responsibilities of the evaluation working group Kramer refers to in his letter. The evaluation group consists of distinguished scientists, chaired by Arnold Levine of Princeton University. The working group has been asked to conduct an evaluation of all NIH-sponsored AIDS research. Such an evaluation must be an essential part of any serious effort to plan for AIDS research and will make possible the enunciation of guiding principles for such research over the next 5 years.

Kramer appears to be unaware of the high priority we at the OAR have placed on primate research, although this was clearly stated in our policy forum. NIH currently sponsors much primate research, and the National Institute of Allergy and Infectious Diseases has under review a series of research grant proposals aimed at further expanding such efforts. Kramer's view that drug development would be markedly accelerated by the use of the simian immunodeficiency virus/ macaque model is not supported by advice we have received from a number of senior scientists in the pharmaceutical industry who do not place such work on the critical path for drug development. By contrast, macaque research can make central contributions to the understanding of the pathogenesis of AIDS, to the development of novel interventions, and to the clarification of the nature of protective immunity. It is precisely this type of research that we intend to enhance. In fact, the OAR has provided emergency support to the National Center for Research Resources to purchase *nemestrina* macaques and import them into the United States.

Kramer scoffs at the use of conventional grant applications and at the process of peer review by knowledgeable scientists to determine priorities for funding innovative research. What does he propose as a substitute—the central direction of such research by a science "commissar?" Such "command science" is likely to be as ineffective as "command economics" proved to be. It is precisely the view that a small group of administrators, scientists, or activists can foresee where key breakthroughs are likely to occur that is of such concern. Peer review as a guide to science funding has proven over and over to be the most effective way to gain new knowledge. By contrast, efforts to exploit promising leads have been and will continue to be vigorously pursued by the more directed funding mechanisms available at NIH.

Finally, Kramer's contention that the U.S. taxpayers "are getting rotten value for their money" in their "$14 billion" investment in NIH-sponsored medical research is untrue, unsupportable, and extremely unfortunate. First, the total NIH budget is somewhat over $11 billion (not $14 billion, as stated in Kramer's letter). The nation's commitment to the support of medical science, through NIH-sponsored research, has contributed immeasurably to the health of the American people. New treatments for heart

disease, cancer, and infectious diseases, among others, have emerged from NIH-conducted and supported work. The mapping and identification of genes controlling susceptibility to various diseases is opening new vistas for diagnostic and therapeutic advances. NIH support has advanced research on gene therapy and formed the knowledge base for the biotechnology industry. Within the last few months a series of exciting and potentially important advances in AIDS research, sponsored by NIH funding, have been reported.

I applaud Kramer's personal commitment to furthering our efforts against AIDS and, indeed, all diseases. Nonetheless, I must differ fundamentally with him regarding the quality and the urgency of the government's efforts to deal with the HIV epidemic. In the past year we have consulted with a wide range of experts within the scientific community and, in collaboration with community representatives, have prepared the first truly comprehensive plan for NIH AIDS research. We have set in place refocused scientific priorities and have shifted resources to meet these priorities. We are preparing the first frank appraisal of the overall AIDS research program. We are confident that a new and effective course is being charted for the future of NIH AIDS research.

William E. Paul
Director,
Office of AIDS Research,
National Institutes of Health,
Bethesda, MD 20892–2340, USA

Congratulations to William Paul for so clearly and boldly laying out the key questions that must be addressed if we are to make progress in the coming 5 years of AIDS research.

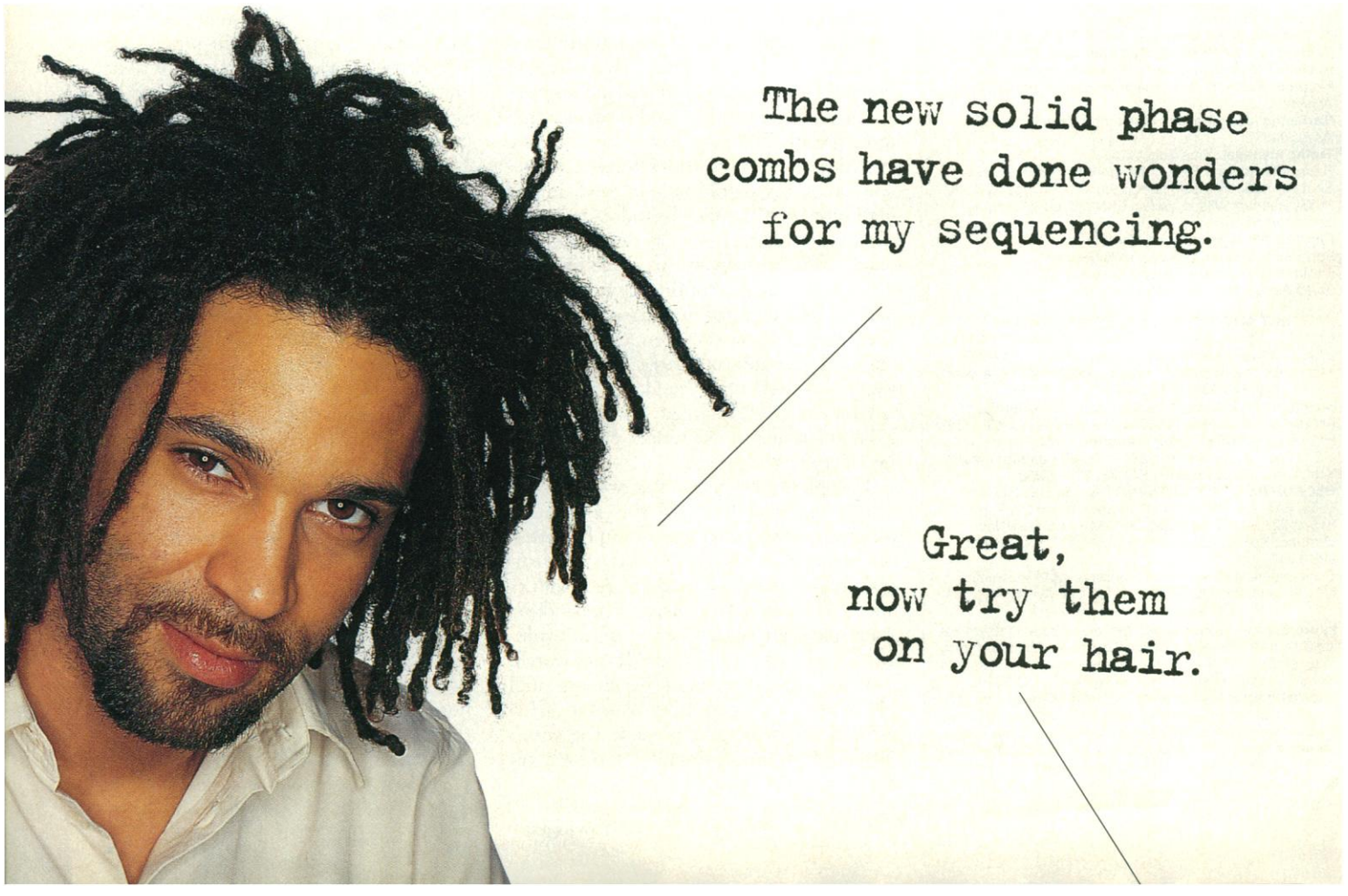
To many AIDS patients, myself included, the systematic process of the scientific method has often seemed brutally insensitive to the pressing realities of living with AIDS. For the first 15 years of the epidemic, scientists and activists alike sought fast answers, shortcuts, and ways to jimmy-rig the system, in hopes of avoiding the difficult step-by-step effort to answer basic questions. That we have made little progress in preventing the spread of HIV or treating AIDS suggests a need to abandon these failed policies and to methodically create a solid evidential basis for future behavioral and therapeutic research, as well as for vaccine research programs.

Paul has brought together our nation's leaders in the fields of immunology and virology in an effort to develop a comprehensive program to investigate the AIDS pandemic. Now we must ensure that policy-makers continue to provide the monetary and political support that will be needed to answer these questions. Without the kind of concerted effort proposed by Paul, it is unlikely that our clinical research effort will offer credible hope to those currently living with or at risk for acquiring HIV and AIDS.

Spencer Cox
Treatment Action Group,
200 East 10 Street, #601,
New York, NY 10003, USA

Paul clearly sets forth the mandate of the OAR to create a comprehensive blueprint for the study of HIV disease. A key prerequisite for this plan is that everyone needs to be speaking the same language.

With the focus of AIDS research shifting away from CD4 T cells and toward CD8 T cells, antigen-presenting cells, cytokines, and viral load, an obvious problem with both basic science and clinical trials is that important immunological data may not be examined or reported in these studies. Consequently, a fundamental task for the OAR should be to set standards for all NIH-funded research in terms of the immunological parameters to be monitored. As a guideline for these



parameters, one could draw from the factors mentioned by Paul: Th1/Th2 cytokines; natural killer cells; markers that define cytotoxic, suppressor, activated, naïve/memory, or primed T cell subsets; and quantitative HIV polymerase chain reaction.

The language of AIDS immunology has changed over the years. It is imperative for the OAR to provide a much needed immunological thesaurus in order to give meaning to future AIDS trials.

Billi Goldberg
Dinitrochlorobenzene Study Group,
San Francisco, CA 94114, USA
Raphael B. Stricker
HemaCare Corporation,
450 Sutter Street, Suite 1504,
San Francisco, CA 94108, USA

■

Biosphere 2

Gary Taubes' article about Biosphere 2 (News & Comment, 13 Jan., p. 169) does not acknowledge that "the previous management" were, in fact, the creative team that beginning in 1984 partially owned, designed, built, and then experimentally tested Biosphere 2 until April 1994 (*1*). Taubes writes as if Biosphere 2 materialized by itself. I conceived and invented Biosphere 2 and directed its research and development division; Margret Augustine co-designed and built Biosphere 2; William Dempster devised and supervised engineering systems, making essential patented inventions; Abigail Alling created and brought to sustained life the extraordinary ocean and marsh systems; Mark Nelson worked with me on biospheric theory and in convening international scientific conferences on closed ecological life systems (biospheres)—at the Royal Society (1987), at Krasnoyarsk, Russian Republic (1989), and at Biosphere 2 (1992).

Taubes states that "Mission One" experienced "technical glitches and [was] criticized for producing little of scientific value." We lifted off a complexly engineered $150-million project and ran it for a 2-year experimental test, as scheduled. Our "glitches" should be compared with those of any new experimental project.

John Allen
Founder, Biosphere 2,
Director, Biospheric Design, Inc.,
Director, Planetary Coral Reef Foundation,
Director, Institute of Ecotechnics,
Director, EcoFrontiers, Inc.,
32038 Caminito Quieto,
Bonsall, CA 92003, USA

References

1. J. Allen, *Biosphere 2: The Human Experiment* (Penguin, New York, 1991); *Space Biospheres* (Orbit/Synergetic, Malabar, FL/Tucson, AZ, 1987); *Biological Life Support Technologies* (National Aeronautics and Space Administration, Washington, DC, 1990); H. Odum, *Ecological Mesocosms* (Springer-Verlag, New York, 1994); M. Nelson *et al.*, *Bioscience* **43**, 225 (April 1993).

■

Oncogenes and Cancer

Most cellular oncogenes were discovered because they share their coding sequences with retroviral oncogenes. On that basis, it was postulated that cellular oncogenes could function like viral oncogenes, provided they have "somehow gone awry" (Jean Marx, Research News, 23 Dec., p. 1942). However, in the excitement about homology, nonhomology was overlooked, and cellular and viral oncogenes received the same names. But retroviral oncogenes have promoters that are 100 to 1000 times stronger than the promoters of the corresponding oncogenes from both normal and cancer cells (*1*). Therefore cloned viral oncogenes and artificial genes, in which the coding regions of unmutated cellular oncogenes (*ras*, *src*, and *myc*) are linked to retroviral