# Editorial & Letters

## EDITORIAL

## Science and the Control of AIDS

This has been a year worth celebrating for AIDS research. For the first time in the history of the HIV epidemic, after nearly two decades of increasing mortality, the U.S. death rate attributable to AIDS has dramatically declined. Satisfyingly, the explanation is almost entirely based on science: A logical sequence of discoveries and tests has led to highly effective antiviral therapies.

It is commonplace, when citing this triumph, to qualify it by pointing to the many drug failures, the expense of the regimens, the continued high rate of virus transmission in the United States (especially among minority groups), the growing magnitude of the epidemic in the poorer parts of the world (where the successful drugs are simply unaffordable), and the difficulties of developing an effective HIV vaccine. But before addressing these serious problems, it is valuable to contemplate the success itself, because it illustrates principles that extend well beyond HIV.

The progress made against HIV exemplifies the potency of molecular medicine—based, in this case, on full disclosure of viral genes, analysis of viral dynamics and pathogenesis, and development of protein-targeted drugs. This is strong evidence that the prospects are bright for rational treatments of many other complex disorders once we understand their genetic origins and pathophysiological mechanisms. Ongoing efforts to decipher the genomes of humans and microbes and to understand how cells cycle, signal, and die are bringing us to a new level of understanding of human biology and disease. If the recent success with AIDS is any guide, this new knowledge will soon transform the practice of medicine.

The challenge of developing treatments for AIDS has also provided a test of our biomedical research establishment, in which federal agencies and private foundations largely fund investigator-driven basic science, the pharmaceutical industry and biotechnology companies undertake most drug discovery and development, and these two components interact to transfer knowledge and foster its application. The recent success has affirmed the vigor of this system. Basic research, some dating back well before the advent of AIDS, recognized retroviral enzymes that are essential for replication and pathogenesis; medicinal chemistry, informed by structural biology, generated many enzyme inhibitors, a few of which survived rigorous screening to become the drugs now prolonging the lives of AIDS patients. This experience can serve as a paradigm for controlling other chronic progressive diseases.

We must also acknowledge the limits of the therapeutic success and speak to the challenges that remain. First, there is a need for improved versions of current drugs—for drugs that are longer acting or better tolerated in order to promote adherence to complex regimens, and drugs that are less expensive and more practical for use in developing countries. A better understanding of viral variation might also help us cope with drug resistance. Active research programs are needed to seek classes of compounds targeted against other viral functions, with the prospect of complementing existing drugs. In addition, behavioral research has the potential to improve compliance with current regimens, as well as to enhance current strategies to reduce transmission.

A safe and effective vaccine is probably the single most important long-term goal of current research efforts. A vaccine that fully prevents the establishment of HIV infection, however, is a daunting and perhaps an impossible goal; even one that offers significant reduction of disease and mortality appears to be a difficult task, judging from the limited progress thus far. The National Institutes of Health (NIH) has committed increasing resources to the challenge of developing an AIDS vaccine, while working in concert with other federal and private agencies and with industry, in the United States and abroad. We have expanded a program that enhances current understanding of the immune response to viral antigens; seeks candidate immunogens; tests them in primate (and perhaps other animal) models; and then evaluates safety, delivery, and efficacy in clinical trials of the most promising candidates. We recognize the magnitude of this challenge and the fact that it may well be necessary to deploy vaccines that have modest efficacy while simultaneously developing future generations of more effective immunogens. But we also believe that the still-expanding global dimensions of AIDS are likely to be checked only if science can succeed as admirably with vaccines as it has done with therapies.

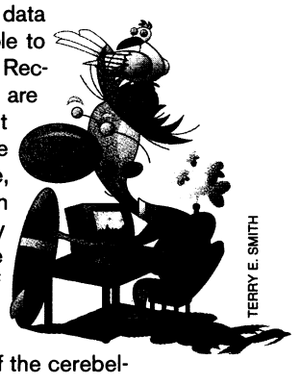
**Harold Varmus and Neal Nathanson**

H. Varmus is the director of NIH. N. Nathanson is the director-designate of the Office of AIDS Research at NIH.

## LETTERS

### The endless search

Are scientific data easily accessible to Web surfers? Recommendations are put forth about what should be posted, where, and how it can be permanently archived. The practicality of tokamak fusion is questioned. The function of the cerebellum is explored. And observations about progression from HIV infection to AIDS are clarified.




### Access to Information on the Web

Y. Poumay's letter of 22 May, (p. 1173) raises an important and often discussed question about the persistence of scientific and technical information on the World Wide Web. What is often forgotten is that one of the early motivations for developing the Web was to provide easy access to scientific data for more scientists. This trend is continuing in many areas where recent results are published and posted for all to read and use (for example, the Los Alamos National Laboratory e-Print Archive, http://xxx.lanl.gov/). It could even be argued that information on the Web is far more accessible than that in libraries for most scientists.

We believe that references to possibly short-lived material should be avoided when possible, but such references are better than omitting relevant work. References to the Web in addition to traditional references can also make material more readily obtainable by scientists. More important is the issue of ensuring that scientific material is long-lived and easily accessible, regardless of whether it exists online or in traditional media; for example, see the Persistent Uniform Resource Locator service (http://purl. oclc.org/) or the Handle System (http:// www.handle.net/). Also, the archival intermemory project (*1*) at the NEC Research Institute hopes to provide an Internet-distributed memory resource that would enable robust archival information storage on the Web.

*Lee Giles*
*Steve Lawrence*

*Bob Krovetz*
*NEC Research Institute,*
*Princeton, NJ 08540, USA*

**References**

1. A. G. Goldberg and P.N. Yianilos, "Towards an Archival Intermemory" (IEEE Conference on Advances in Digital Libraries, IEEE Press, Piscataway, NJ, 1998).

Poumay raises an important issue related to Web publishing and archivability. His solution to the perceived impermanence of Web material, however, would hamper the evolution of Web science publishing. As a publisher of a Web scientific journal, *Optics Express* (www.osa.org), I think there is room for several approaches to the archiving of Web information. For example, material can be stored indefinitely on servers or duplicated on "mirror" sites elsewhere, or copies can be made and stored in other media.

What is important is that the publishing organization be fully committed, financially and organizationally, to this enterprise—a major change in direction for most publishers and for-profit organizations. That leaves scientific societies and associations, which are beginning to take steps to ensure that such a change takes place.

To suggest, as Poumay does, that only articles that have equivalents in print should be cited is not practical and slights fully reviewed and archived electronic journals.

**G. N. *Rassam***
*Optical Society of America,*
*Washington, DC 20036, USA*
*E-mail: grassam@osa.org*

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## Investment in Tokamak Fusion

The debate over the future of the International Thermonuclear Experimental Reactor (ITER) (J. Glanz, "Requiem for a heavyweight at meeting on fusion reactors," News & Comment, 8 May, p. 818), unfortunately, does not go far enough. The real issue is not how much money should be invested in the next large tokamak, but whether any further investment in tokamak confinement is warranted at this time.

The tokamak has been the main approach to magnetic confinement fusion since its inception almost 50 years ago. During the intervening half century, great progress has been made in understanding the physics of toroidal confinement and in translating that understanding into improvements and innovations in tokamak design. Although tokamak design is still based on empirical scaling laws, confidence in these laws has been strengthened by a wealth of experimental data. Numerous reviews of the ITER design have concluded that if the machine is built to the ITER design specifications, there is little doubt that it can achieve its scientific goal of a sustained thermonuclear burn.

This statement reflects both the triumph and the tragedy of fusion research, because it also implies that if a tokamak is significantly smaller than the ITER design, it will not achieve a sustained thermonuclear burn and thus will not provide the basis for a power-producing reactor. The scientific community needs to reexamine the premise on which the public was originally asked to support fusion research, namely, that it would lead to the development of a practical, power-producing technology. In light of today's knowledge, it is highly unlikely that further development of the tokamak will lead to that outcome.

***Alexander J. Glass***
*Bay Area Regional Technology Alliance,*
*Fremont, CA 94538–2209, USA*
*E-mail: http://www.barta.org*

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## Cerebellum and Learning: A Complex Problem

There is increasing experimental support for