# LETTERS

*edited by Jennifer Sills*

## Keeping an Eye on the Prize

I WAS VERY DISAPPOINTED TO FIND OUT ("Fame inflation," Newsmakers, 1 February, p. 553) that I, like Steven Running, am not a Nobel laureate. According to the "Dear colleagues" letter I received from Ogunlade Davidson and Bert Metz on behalf of the IPCC, I am indeed a Nobel laureate, albeit perhaps along with many, many others. The letter says, "You no doubt have heard about the award of the Nobel Peace Prize to the IPCC, jointly with Al Gore of the USA. This makes all of you a Nobel laureate and we, as co-chairs, want to congratulate you wholeheartedly with this exceptional recognition." Additionally, a beautiful Nobel Peace Prize certificate with my name on it now adorns my wall. Although the financial remuneration has not yet arrived, I have enjoyed the celebrity status associated with the honor. **ROGER A. SEDJO**

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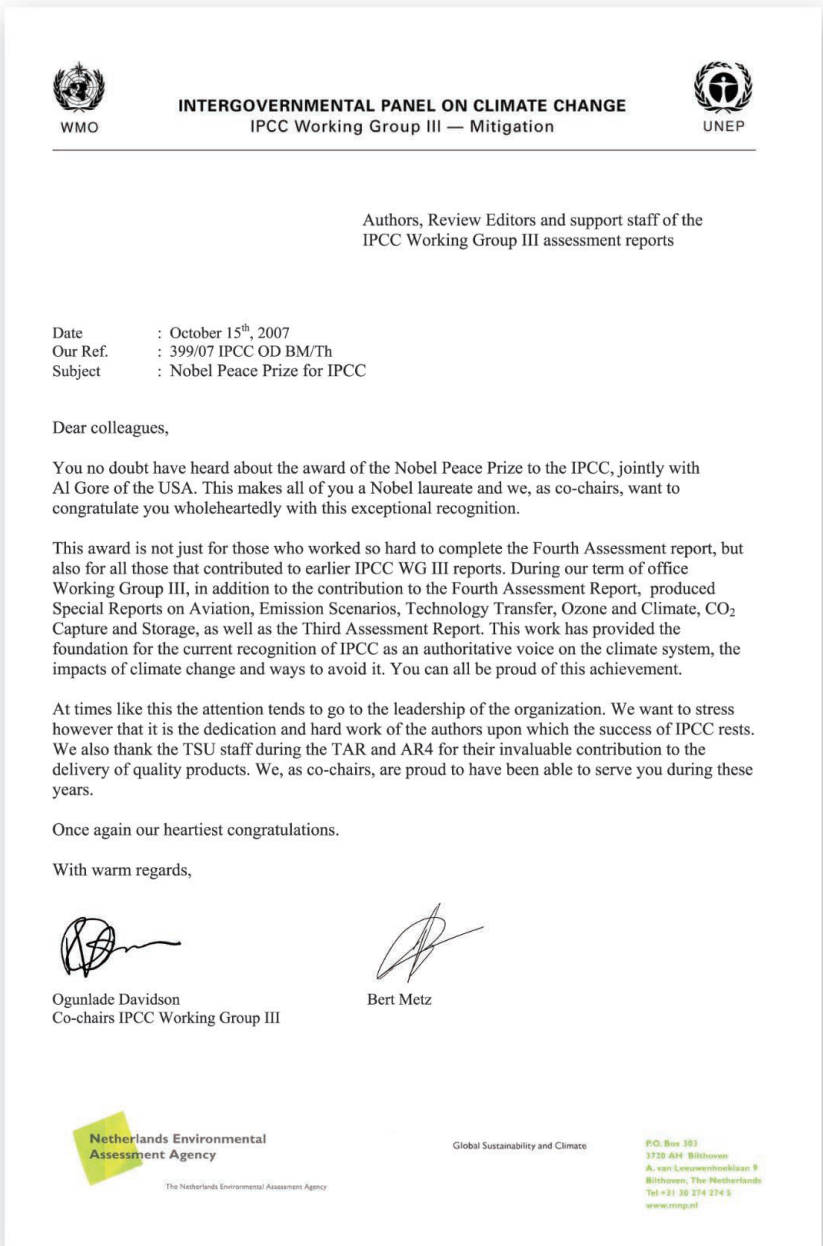

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**INTERGOVERNMENTAL PANEL ON CLIMATE CHANGE**
IPCC Working Group III — Mitigation

UNEP

Authors, Review Editors and support staff of the
IPCC Working Group III assessment reports

Date : October 15th, 2007
Our Ref. : 399/07 IPCC OD BM/Th
Subject : Nobel Peace Prize for IPCC

Dear colleagues,

You no doubt have heard about the award of the Nobel Peace Prize to the IPCC, jointly with Al Gore of the USA. This makes all of you a Nobel laureate and we, as co-chairs, want to congratulate you wholeheartedly with this exceptional recognition.

This award is not just for those who worked so hard to complete the Fourth Assessment report, but also for all those that contributed to earlier IPCC WG III reports. During our term of office Working Group III, in addition to the contribution to the Fourth Assessment Report, produced Special Reports on Aviation, Emission Scenarios, Technology Transfer, Ozone and Climate, $CO_2$ Capture and Storage, as well as the Third Assessment Report. This work has provided the foundation for the current recognition of IPCC as an authoritative voice on the climate system, the impacts of climate change and ways to avoid it. You can all be proud of this achievement.

At times like this the attention tends to go to the leadership of the organization. We want to stress however that it is the dedication and hard work of the authors upon which the success of IPCC rests. We also thank the TSU staff during the TAR and AR4 for their invaluable contribution to the delivery of quality products. We, as co-chairs, are proud to have been able to serve you during these years.

Once again our heartiest congratulations.

With warm regards,

Ogunlade Davidson
Co-chairs IPCC Working Group III

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## Epigenomics: A Roadmap, But to Where?

RECENTLY, THE DIRECTOR OF THE NATIONAL Institutes of Health (NIH) allocated $190 million for an "Epigenomics" Roadmap initiative (*1*). As investigators in this area, we endorse the idea that chromatin biology is an appropriate, if not essential, area for the NIH to support, not only for its fundamental biological significance but also its relevance to human disease. Nonetheless, we believe that this initiative, at least in its current form, will not yield significant benefits. If the use of the term "epigenome" is intended to equate the value of this Roadmap initiative with the Human Genome Project, it fails on several grounds.

First, it does not consider our current understanding of the roles of sequence-specific DNA recognition events and transcriptional networks in controlling epigenetic changes. A multifaceted effort that elucidates transcriptional circuits that tell us where and when signal-responsive, sequence-specific regulators function would be more useful for understanding cell type programming. Second, merely cataloging modification patterns offers comparatively little new or useful information. We already know that most genes are associated with one of a few patterns of chromatin modifications and that the patterns themselves do not tell us how that gene is regulated or how its expression state is inher-





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ited. Most histone modifications are highly dynamic and change rapidly in response to changes in signals that turn genes on or off.

This initiative will divert substantial resources, enough to fund 200 multiyear individual grants. There is a notion favored by some that individual scientists need to be corralled to work together under a more rigid, directed framework to solve important problems. We disagree. Real innovation comes from the bottom up, and good science policy requires promoting the free market of ideas rather than central planning (*2*).

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**References and Notes**

1. NIH Roadmap for Medical Research (http://nihroadmap.nih.gov/epigenomics/).
2. Links to a full version of this letter and petition for readers to sign can be found at http://madhanilab.ucsf.edu/epigenomics/.

## Protecting Aggregate Genomic Data

A PAPER PUBLISHED RECENTLY IN *PLOS Genetics* (*1*) describes a statistical method for resolving individual genotypes within a mix of DNA samples or data sets containing aggregate single-nucleotide polymorphism data. This scientific advance may have important implications for forensics and for genome-wide association studies (GWAS). It has also changed our understanding of the risks of making aggregate genomic data publicly available. While we assess the broader scientific, ethical, and policy implications of this development, NIH has moved swiftly to remove aggregate genomic data from our publicly available Web sites. Further information about changes in NIH open-access policies for GWAS is available on the NIH's GWAS Web site (*2*).

The paper by Homer *et al*. showed that a new statistical technique applied to aggregate data can determine whether a specific individual's genomic data are part of a given data set, including whether they are in the control group or the case (affected) group. It may also be possible to statistically infer whether a relative of the individual is a member of the case or control groups. The method requires having an individual's high-density genotype data in hand from another source. Though the specific identity of the individual who was the source of the data could only be determined if that source were known through other means or reference data, this discovery nonetheless has implications for how these summary data should be protected. As a result, NIH has removed from open-access databases the aggregate results (including *P* values and genotype counts) for all the GWAS that had been available on NIH sites (such as dbGaP and CGEMS). NIH intends to move the aggregate genotype data to the controlled-access database, where there is a firewall as well as protections and policies in place for appropriate data access, including review and approval of data access requests. The new finding does not have the same implications for data available through controlled access, and NIH access policies for individual-level genotype and phenotype data have not changed.

Sharing genomic data and, particularly, allele frequencies has become common practice, if not an imperative, in science. Yet, the protection of participant privacy and the confidentiality of their data are of paramount importance. These new statistical approaches have implications far beyond NIH data-sharing policies, as aggregate GWAS data have been provided in publicly available form in many other ways, including other research databases and Web sites, journal articles and other publications, and scientific presentations. NIH urges the scientific community to consider carefully how these data are shared and take appropriate precautions to secure aggregate GWAS data in order to protect participant privacy and data confidentiality.

In short order and over the coming months, NIH will work with our advisory groups and the wide range of stakeholders related to GWAS to further explore and address the policy implications of this finding. We call on our colleagues in the scientific community to join us in these important deliberations.

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1. N. Homer *et al*., *PLoS Genet.* **4**, e1000167 (2008).
2. NIH Genome-wide Association Studies Web site: http://grants.nih.gov/grants/gwas/.

## Closing a Loophole in the FDA Amendments Act

IN THEIR POLICY FORUM "MOVING TOWARD transparency of clinical trials" (7 March, p. 1340), D. A. Zarin and T. Tse caution that "FDAAA 801 still leaves areas of 'opacity.'" We would like to point out another loophole: FDAAA 801 will only cover future drugs. The thousands of drugs on the market today, including the controversial examples cited by Zarin and Tse, will be grandfathered in and not covered.

Whether this matters to public health depends on whether today's uncovered drugs will soon become obsolete. To address this

### Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

### CORRECTIONS AND CLARIFICATIONS

**Reports:** "Cell identity mediates the response of *Arabidopsis* roots to abiotic stress" by J. R. Dinneny *et al*. (16 May, p. 942). On page 945, the URL for the supporting online material was incorrect. The correct URL is www.sciencemag.org/cgi/content/full/1153795/DC1.

**Books *et al*.:** "The social origin of mind" by A. Jolly (7 September 2007, page 1326). The caption to the photograph should have read "Chacma baboons (*Papio hamadryas ursinus*) in the Okavango Delta, Botswana."

**Reports:** "The FERONIA receptor-like kinase mediates male-female interactions during pollen tube reception" by J.-M. Escobar-Restrepo *et al.* (3 August 2007, p. 656). On page 657, second column, second paragraph, the sentence "The *FER* open reading frame contains a single 175-bp intron in the 5′ untranslated region and produces a transcript of 2682 bp, which encodes a putative receptor-like serine-threonine kinase (RLK) (Fig. 1F)" contains two errors. It should read, "The FER primary transcript contains a single 175-bp intron in the 5′ untranslated region and produces an open reading frame of 2682 bp, which encodes a putative receptor-like serine-threonine kinase (RLK) (Fig. 1F)."

**Reports:** "Virus-enabled synthesis and assembly of nanowires for lithium ion battery electrodes" by K. T. Nam *et al*. (12 May 2006, p. 885). Reference 28 should be D. Guy, B. Lestriez, D. Guyomard, *Adv. Mater*. **16**, 553 (2004).





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question, we examined prescribing trends over the past 8 years for three drug classes cited by Zarin and Tse. From listings of the top 200 drugs (*1*) for the years 2000 through 2007, we extracted the numbers of prescriptions dispensed in U.S. retail pharmacies. Within these three drug classes, we totaled the annual number of prescriptions of brand and generic drugs that had been first marketed in the United States within the past 20 years.

We found that oral drugs for diabetes, including Avandia (*2*, *3*), are (as of 2007) being prescribed 265,000 times each day; their prescribing rate has been increasing 8% annually. Cholesterol-lowering drugs, including Zetia (*4*) and Baycol (*5*), are now being prescribed 528,000 times each day; this rate has been increasing 10% annually. Finally, antidepressants (*6*) are being prescribed 673,000 times each day; this rate has been increasing 22% annually.

These data indicate, in our opinion, that these drugs—none of which will be covered by FDAAA 801—are widely prescribed and unlikely to disappear soon from the U.S. market. It is unfortunate that FDAAA 801 grandfathers in currently marketed drugs. While this act provides for a registry and results database that is prospective, we need one that is also retrospective. Such a database has in fact existed for decades at the FDA (*7*). If we can make better use of it, a solution to this area of "opacity" lies readily within our grasp.

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2. S. E. Nissen, K. Wolski, *N. Engl. J. Med*. **356**, 2457 (2007).
3. B. M. Psaty, C. D. Furberg, *N. Engl. J. Med*. **357**, 67 (2007).
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6. E. H. Turner, A. M. Matthews, E. Linardatos, R. A. Tell, R. Rosenthal, *N. Engl. J. Med*. **358**, 252 (2008).
7. E. H. Turner, *PLoS Med*. **1**, e60 (2004); http://dx.doi.org/10.1371/journal.pmed.0010060.

## Response

TURNER AND COLLEAGUES ARE CORRECT THAT the "basic results" provisions of Section 801 of the FDA Amendments Act (FDAAA 801) will not apply to trials that were completed prior to 27 September 2007. Thus, the body of data that was used to support approval for products currently on the market will not necessarily be made public under this provision. As all of the top 20 brand drugs by total U.S. prescriptions in 2007 (*1*) were approved prior to 2005, based on Initial Year of Original FDA Approval data listed in Drugs@FDA (*2*), it is readily apparent that much of the data underlying current medical decisions are unlikely to be submitted to ClinicalTrials.gov. The scope of the law is determined by the timing of the trial, however, not the date of approval of the drug; therefore, non–phase I trials of these approved products initiated after or ongoing as of late 2007 would meet the time criterion for applicability under FDAAA 801 and be required to report results.

Turner calls for public access to FDA reviews contained in all approved NDAs (*3*). In addition to this possibility, FDAAA 801

includes a provision whereby the Secretary of Health and Human Services may require registration and results reporting for certain clinical trials of FDA-approved drugs, biologics, and devices retrospectively to protect public health (trials completed up to 10 years prior to enactment of the act, i.e., September 27, 1997). Finally, FDAAA 801 explicitly provides for consideration, during the 3-year rule-making process, of mandatory results reporting from certain clinical trials of drugs, biologics, and devices not approved by the FDA. Such a policy would substantially broaden the evidence base available to the public.

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2. Food and Drug Administration. Drugs@FDA (www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/).
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## Big Payoffs Possible for Small-Molecule Screening

IN THE NEWS FOCUS "INDUSTRIAL-STYLE screening meets academic biology" (8 August, p. 764), J. Kaiser presents the discovery of several potential small-molecule therapeutics and probes for cellular function along with skeptical views from industrial scientists questioning "whether this massive effort is worth the time and money." The goals of the pharmaceutical industry and academia are very different. Industry scientists are focused on discovering a highly specific and potent compound that can benefit human health. Academic scientists focus on finding compounds that can reveal novel cellular mechanisms, a basic tenet in chemical biology (*1*). It is this pursuit that allows the academician to foster student learning and interdisciplinary collaborations with faculty that could lead to a novel biological probe or a potential therapeutic. The current $100 million-per-year funding from the NIH Molecular Libraries Initiative (MLI) is a wise investment in the training of future scientists and teachers. Students working with faculty mentors on these screening efforts learn how to solve problems across all areas of science and mathematics; indeed, the "challenge of merging two cultures—biologists and chemists" is an opportunity for a better education (*2*). Such an interdisciplinary approach to science education is timely, given the recently passed Public Law 110-69, "America Competes Act," which includes appropriation of $896 million for "education and human resources" (*3*) that will promote the training of future science and mathematics teachers. Regardless of the skepticism, I believe that the NIH MLI could "pay it forward" to our society in many ways.

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2. R. L. Stein, *J. Biomol. Screen*. **8**, 615 (2003).
3. Public Law 110-69 (H.R. 2272), sec. 7002, fiscal year 2008.