LETTERS

Outing the Conflicted: Et Tu, NIH?

WHAT SHOULD BE DONE WHEN THE BASTION of public-minded scientific research in the United States is revealed to have hundreds of potential, if not actual, conflicts of interest? According to a series of articles in the *Los Angeles Times*, some NIH officials have received hundreds of thousands of dollars over the past decade from hundreds of consulting arrangements with industry (*1*).

> **"For the sake of public trust and support, NIH must raise the bar. It should severely limit the amount of money employees can receive and the amount of time they can sell under consulting arrangements."**
>
> –JOHNSTON

The figures alleged are staggering, as are the connections made in the articles between the firms consulted to and the scientific work of NIH staff and their laboratories. But perhaps more surprising is that these consulting arrangements seemingly fall comfortably within NIH rules (*2*), were approved by NIH ethics officers, and were not generally disclosed. Apparently, 94% of NIH's highest-paid employees are not required to disclose their consulting income (*1*, *3*).

Former NIH Director Harold Varmus has said that he loosened consulting restrictions to "strengthen our ability to recruit" (*4*). Given the large earning potential of university scientists, it is not surprising to learn that NIH felt competitive pressure to loosen its rules (*5*).

If the consulting arrangements detailed by the *LA Times* fall within NIH rules and were approved by NIH officials, why has there been a public outcry? One concern is that if these scientists are contracted to industry, they may not be conducting impartial and objective research for the sole good of the American people. Can they realistically serve two, or three, or even four masters?

The suggestion that consulting can improperly influence the professional judgment of scientists is often angrily dismissed as an outlandish attack on character (*6*). However, even the most moral among us can be unconsciously influenced by outside interests, and in other fields such as law, accounting, and journalism, a reliance on virtue has rightly been superseded by requirements for full public disclosure and sometimes by limits or prohibitions on the type and amount of compensation or time spent on outside activities.

Another concern, less often voiced in these cases, relates to double-dipping. If a scientist's desirability as a consultant stems from her NIH post, can she be sure that the advice and time she sells to industry does not already belong to NIH? In response to this concern, one NIH employee told the *LA Times* that he undertook his consulting work on vacation time. Others said that the advice they provided was based on their general knowledge and expertise, rather than on their particular work at NIH (*7*). Nevertheless, given the sometimes six-figure sums involved, concerns should persist about whether salaried individuals can give their primary job the effort and attention it deserves while also undertaking considerable consulting work.

Given similar consulting arrangements in many of the nation's public and private universities, the real question of the moment is: Should we abandon the idea of impartial, disinterested science, or should NIH be the last stronghold of this ideal?

For the sake of public trust and support, NIH must raise the bar. It should severely limit the amount of money employees can receive and the amount of time they can sell under consulting arrangements. It should prohibit employees from consulting to companies with whom NIH has official dealings and make the details of all consulting arrangements available on its Web site. If NIH scientists are too embarrassed to have these details publicly known, then surely the propriety of the arrangements speaks for itself. As for recruitment, NIH will have to find ways of attracting employees that do not compromise research integrity.

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8. This research was funded by a grant from the Donaghue Foundation.

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or 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.

Dietary Restriction in *Drosophila*

DIETARY RESTRICTION IS ONE OF THE FEW environmental interventions that generally increases life-span (*1*). In their Report "Demography of dietary restriction and death in *Drosophila*" (19 Sept., p. 1731), W. Mair *et al.* found that short-term rather than long-term dietary restriction determined mortality rates in *Drosophila*. Dietary restriction was also found to affect only age-independent mortality, a result found before (*2*). Mair *et al.* did not, however, shed much light on the mechanistic basis of immediate changes in mortality rate arising from dietary change. We believe that we can.

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Dietary restriction tends to increase *Drosophila* life-span, reduce mortality rate, and reduce female fecundity drastically (*3*). As fecundity often has an antagonistic evolutionary relationship with longevity (*4*), diminished caloric intake may reduce costly physiological investment in reproduction, regardless of whether reproduction is occurring or not, and thereby reduce mortality.

We have some evidence for the existence of such a trade-off during abrupt nutritional change. Chippindale *et al.* (*3*) found that reproduction shifted upward when additional food was supplied in midlife and downward when food was reduced [see fig. 3 in (*3*)]. This transition took

about 3 days, in either direction, about the same magnitude of time as the 48-hour transition observed by Mair *et al*.

Chippindale *et al.* (*3*) also studied the short-term response of starvation resistance to a change in dietary regime. Starvation resistance is a major factor determining longevity in *D. melanogaster* (*5*–*7*) and is in turn determined by the total stored calories in the fly (*8*). When dietary regime is abruptly changed, Chippindale *et al.* (*3*) found a rapid shift in starvation resistance that was the inverse of the rapid shift in fecundity. This also matched the known evolutionary antagonism between starvation resistance and fecundity. Given the evidence linking starvation resistance to longevity, starvation resistance must influence mortality rates. In sum, our interpretation of the effects of abrupt dietary change is that when fewer calories and nutrients are ingested, fecundity falls, increasing the storage of calories, thereby reducing mortality rates, and conversely.

Furthermore, this interpretation can be extended to explain the findings of Mair *et al.* for both the increase and decrease in mortality rate in males and females with dietary change. That is, when caloric intake is increased, the storage of calories is reduced and reproductive activity increases, thereby increasing mortality rates. Conversely, when caloric intake is decreased, the storage of calories is increased and reproductive activity decreases, causing mortality rates to drop.

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Response

RAUSER *ET AL.* SUGGEST THAT THE REDUCTION in mortality rate in *Drosophila* in response to dietary restriction (DR) is caused by reduced fecundity and/or increased stress resistance.

Increased life-span in response to DR in diverse organisms is accompanied by a reduction in daily and lifetime fecundity (*1*–*3*). The suggestion that this reduction in fecundity is causal in the extension of life-span under DR has been made several times previously (*4*–*7*), including in the Perspective accompanying our paper (*8*). The idea may be correct, but at present, there is no direct experimental evidence for or against it. Experiments in which costly aspects of reproduction are blocked directly, and the effect on the response of life-span to DR examined, could throw some light on the issue.

Increased stress resistance has also frequently been shown to accompany extension of life-span in response to DR and has again previously been suggested to be causal (*9*–*14*). As for the effects of fecundity, there is no experimental evidence, and direct manipulation of the stress responses in DR and control animals could prove informative.

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Support for a Colleague

AS COLLABORATORS OF ANDERS PAPE MØLLER, we were shocked and surprised to read that he was accused of data fabrication ("Ecologists roiled by misconduct case," G. Vogel, F. Proffitt, R. Stone, News of the Week, 30 Jan., p. 606). We have never had cause to be concerned about any aspect of our collaborations with Møller. He is an amazing scientist, and his great organizational skills are a model for how to be productive in the face of competing time demands. Most of us are capable of much more than we actually accomplish, but we lack the dedication and self-discipline to follow through like Anders Møller. This is the secret of his phenomenal effectiveness that has been so puzzling to the scientific community. His achievements may have caused negative responses from some of his competitors. We would like to see a full, objective, and independent inquiry into the allegations. Our experience tells us that Anders Møller has an exceptionally complete focus on any task at hand, be it fieldwork, data analysis, or paper writing; this, combined with more than a little natural talent, is sufficient to explain his exceptional productivity. We have worked with him on a variety of projects, including collecting data, sometimes under arduous conditions, and in all our dealings with him, his behavior has been beyond reproach. We would ask colleagues to restrain from further public condemnation until such time as any allegations have been proven beyond doubt.

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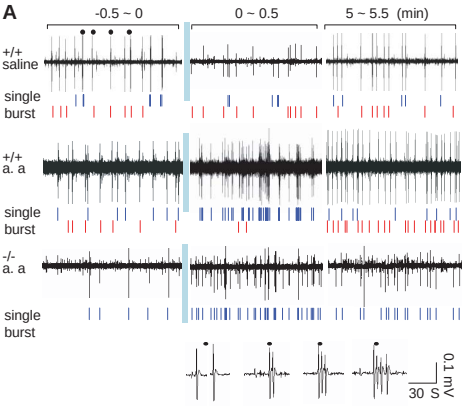
CORRECTIONS AND CLARIFICATIONS

Reports: "Larsen Ice Shelf has progressively thinned" by A. Shepherd *et al.* (31 Oct., p. 856). There were two errors in the printed form of Equation 1: an incorrect expression of the density-related factor of the mass fluctuation terms and an incorrect expression of the mass flux divergence. The correct equation, which the authors used in their analysis, appears below.

$$\frac{\partial h}{\partial t} = \frac{\partial \Delta_s}{\partial t} - M\frac{\partial}{\partial t}\left(\frac{1}{\rho_w}\right) + \int_0^M dm \frac{\partial}{\partial t}\left(\frac{1}{\rho_f(m)}\right) + \left(\frac{1}{\rho_{ice}} - \frac{1}{\rho_w}\right)\left(\dot{M}_s + \dot{M}_b + \nabla.(Mv)\right)$$

The authors thank David Holland for bringing these errors to their attention.

Report: "Thalamic control of visceral nociception mediated by T-type Ca^{2+} channels" by D. Kim *et al.* (3 Oct., p. 117). In Fig. 3A, four panels were reversed to white on black. The correct image is shown here.



Reports: "A microRNA as a translational repressor of *APETALA2* in *Arabidopsis* flower development" by X. Chen (*Science* Express, published online 31 July; 10.1126/science.1088060). A second revision to this Report was posted on *Science* Express on 25 February 2004. This revision included changes both to the second version of the Report itself and to the Supporting Online Material accompanying the Report. This revision corrects a previous error in the paper. In engineering silent mutations into the miRNA172 binding site in the AP2 cDNA, an amino acid change was inadvertently introduced. New experiments indicate that the mistake does not alter the conclusions of the paper. The corrected PDF of the *Science* Express article (including a list of the corrections made) can be found at www.sciencemag.org/cgi/rapidpdf/1088060v3.pdf; the corrected Supporting Online Material, including an explanation of the corrections made, can be found at www.sciencemag.org/cgi/content/full/1088060/DC1. This latest version is the most recent version and supersedes all other versions. The Report will appear in print in the 26 March issue.

Research Articles: "A comparison of whole-genome shotgun-derived mouse chromosome 16 and the human genome" by R. J. Mural *et al.* (31 May 2002, p. 1661). On p. 1662, third column, second paragraph, the second sentence, "Seven BACs from the Cat eye syndrome region on chromosome 16 (*15*) have been sequenced..." should have read "Several BACs from the Cat eye syndrome region on chromosome 6 (*15*) have been sequenced..." The alignment of these BACs to the corresponding Celera scaffold (GA_x5J8B7W4YGF) in Fig. 1 was meant to illustrate the correspondence of whole-genome shotgun assembled scaffolds to "finished" BACs. This mislabeling in no way affects the validity of that result.