Letters

Reproducing Results

Marjorie Sun's article "NIH developing policy on misconduct" (News and Comment, 14 May, p. 711) juxtaposes "misconduct" and "dispute" in its headline and subheadline and thereby seems to imply that I have been dishonest. I have not. The article also contains both incorrect and incomplete descriptions of fact. I should like to address some of them.

First, contrary to an assertion in the article, both the findings of abnormalities of pyruvate metabolism (*1*) and of low activity of the pyruvate dehydrogenase complex (PDHC) in some families with Friedreich's ataxia have been reproduced by others (*2*). Technique is critical (*2–4*) and, to the best of my knowledge, no one who has reexamined lipoamide dehydrogenase (LAD), an enzyme component of PDHC, has used our technique for preparing specimens and assaying the enzyme.

Second, a research group at the National Institutes of Health (NIH) made critical changes in the method for preparing platelets in trying to repeat our studies (*3, 4*). They used an assay for PDHC that differed from the conventional one in equipment, procedure, and timing (*3, 5*) and that was inhibited to such a degree by small changes in the ratio of cofactors to cell protein (*5*) that, as they showed us in 1978, protein had to be estimated first and a particular weight added to each assay tube. The conventional assay is linear with respect to added cell protein. Thus, contrary to the assertion in *Science* that the NIH group had used the same methodology as ours, we concluded that they had used a significantly different methodology.

Third, contrary to what is stated in the article, Padma Arunachalam and Howard Sachs did not participate in the 1979 experiments in question—they were not yet in Los Angeles. There were two sets of experiments, each with a few coded samples from one of two patients (brothers) and from two controls, myself and co-workers, assayed simultaneously. The code was unknown to all of us in the laboratory. The first brother's study was done satisfactorily. The second study dealt with PDHC and the Michaelis-Menten constant (K_m) for LAD with respect to one substrate, dihydrolipoamide. A change was made in the methodology for the second study to improve it, but the change led to scatter of data and caused the specimens to lose activity too rapidly for the assays to be repeated. By then, the patient had returned to the eastern United States. Before decoding, I used only the Michaelis-Menten and Lineweaver-Burk plots with regression analyses to judge which points in the kinetic assays were valid and to calculate the K_m values from those points. Because of the code, any mistaken assumptions in applying the analytic methods seemed to me as likely to work against the hypothesis as for it. When the K_m values were decoded, those for the patient appeared to be consistently and statistically different from those for the simultaneous controls. The PDHC values also appeared to be statistically different. The findings were submitted in a letter to an editor (*6*). It later turned out that a technician had, in fact, failed to divide the PDHC activity per assay tube by protein; still later, there was criticism of aspects of the methodology, including that which I had used to exclude scatter and to compare results.

The fourth inaccuracy concerns the retraction of the errors. When Arunachalam discovered the error in the PDHC calculations, it was too late to withdraw the letter or the PDHC data in it. However, the PDHC data were not presented at any subsequent scientific conference. We prepared to retract the errors, were interrupted by an investigation of allegations of cheating, and then resumed work on the retraction before discussing the matter with the associate dean. Therefore, I was in complete agreement with the associate dean that the entire work be recalculated, mistakes be corrected, and conclusions not supported by the correct data be retracted.

Kinetic data for LAD were then recalculated by the more precise and unambiguous Eadie-Hofstee method. The values for the first patient and his controls were essentially unchanged (*7*). In hindsight, the scatter with the second patient was too great to merit publication; in addition, the differences were not statistically significant, although they were still in the appropriate direction (*8*). Because of this, because of our unhappiness at having published inadvertent errors in calculation, results based on ambiguous analyses and experiments with scatter, and because we had previously studied these patients carefully and in considerable detail, we retracted the entire letter, correct and incorrect data (*8*).

I deeply regret the errors in the study and their publication. I strongly believe that part of responsibility in scientific work is to retract results that are later found to be erroneous.

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References and Notes

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4. D. M. Becker, W. G. Knipprath, S. L. Perlman, C. Nissenson, R. A. P. Kark, *Clin. Chim. Acta* **121**, 1 (1982).
5. G. Constantopoulos, C. S. C. Chang, J. A. Barranger, *Ann. Neurol.* **8**, 636 (1980).
6. R. A. P. Kark, D. M. Becker, S. L. Perlman, *ibid.*, p. 342.
7. The values for the first patient were those for the K_m for LAD with respect to the cofactor reduced nicotinamide adenine dinucleotide, the rate of inactivation of LAD by heat, and the theoretical maximal activity for LAD (as a ratio to a marker enzyme) in both the physiological direction and in reverse (*6*).
8. R. A. P. Kark, D. M. Becker, S. L. Perlman, *Ann. Neurol.* **9**, 514 (1981).

USDA Security Checks

With reference to the article by Eliot Marshall (News and Comment, 7 May, p. 600) concerning security checks of political compatibility of scientists who serve on peer review panels for the U.S. Department of Agriculture Competitive Grants Program, the Staff Association of the Connecticut Agricultural Experiment Station unanimously passed the following resolution:

The Connecticut Agricultural Experiment Station Staff Association strongly opposes the use of criteria other than scientific expertise in the choosing of scientists for the peer review panels of the USDA Competitive Grants Program, and urges all scientists not to agree to serve on such panels until scientific expertise is the only criterion which is used in the selection of reviewers.

We are pleased to hear this policy is no longer in effect (News and Comment, 4 June, p. 1085).

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