

Letter from Bruce Alberts to William F. Raub

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SCHOOL OF MEDICINE
DEPARTMENT OF BIOCHEMISTRY AND BIOPHYSICS

SAN FRANCISCO, CALIFORNIA 94143
(415) 666-4324

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Dr. William F. Raub
Department Director for Extramural
Research and Training
National Institutes of Health
Building 1, Room 107
Bethesda, Maryland 20205

Dear Dr. Raub:

I apologize for the long delay in responding to your letter in reply to my initial suggestions for improving the peer review system. In the interim, I have had a number of conversations with others who have helped me to refine my views, and I have had more experience with the review system as Chairman of the Molecular Cytology Study Section. Hopefully, this time around I can do a much better job of presenting my suggestions clearly.

Again, I want to emphasize that I strongly believe in the NIH peer review system. Indeed, I feel that the best and only way of protecting this system is to be certain that it functions optimally, and it is for this reason that I have been writing to you to suggest reforms. Six major points that I feel are worthy of serious discussion follow.

1. In many cases, the NIH permits too narrow a peer review and, as a result, it generously funds research in some specialized areas long after they have lost their importance.

As one arbitrarily-selected example of this type of problem, I suggest that you study the grants in radiation biology that have been funded by the Radiation Study Section in the past five years. This study section consists almost entirely of members of Radiation Biology and Radiation Oncology Departments. At one time, the scientific community badly needed any information on the effect of radiation on living cells and tissues. Forty years have passed, and I contend that descriptive studies of the effect of radiation on living systems are no longer of high priority. I may be wrong, but I strongly suspect that the Radiation Study Section does not share this view. As I mentioned to you in my previous letter, our study section accidentally became aware of this problem when we disapproved a terrible cell biology grant from an investigator who had just been funded for a similar project by the above Study Section.

I want to emphasize that the example of the Radiation Study Section is offered merely as one symptom of a much wider problem. For example, a worse situation probably exists in endocrinology, a field in which a great deal of mediocre descriptive work is still being funded by the NIH. I suspect that, in this field as well, there are study sections composed primarily of narrowly-focused members that are largely responsible for maintaining an over-funded research area. I am certain that similar situations exist in other disciplines that are even further from my area of expertise.

The major point is that the success of peer review demands a constant change in the nature and composition of the study sections. These should be continuously adjusted to emphasize new research areas of great importance and quality (e.g., oncogenes, the molecular biology of *Drosophila* development, studies with transgenic mice, etc.), while deemphasizing older areas that once were exciting but are no longer productive. Such changes might in part be made by adding a related research area to an older study section, using the occasion to expand the membership of the section significantly and increase its scientific breadth and quality (e.g., creating a "Radiation and Mutagenesis" Study Section to replace "Radiation", or creating a "Cell Signalling and Hormone Action" Study Section to replace one of the endocrinology sections).

II. Large Program Project grants tend to allow mediocre scientists to obtain undeserved funding; this situation could be improved by replacing site visits with a more anonymous, remote review process.

Like some other very large grants, Program Projects tend to have a life of their own, continuing to be refunded at a stage when most of the individual projects in them would not receive a fundable priority as a R01 grant. The reasons are clear. Like many military projects, the sudden cancellation of a large program project would be very disruptive at a personal level. There is therefore a strong presumption among reviewers to try to find enough merit to allow some continued funding. Moreover, in any large effort, some of the components are likely to have been productive in the past grant period. These will tend to carry some of the weaker projects.

The already bad situation is exaggerated by the fact that Program Projects are typically reviewed by site visits, rather than anonymously by a study section. In any such review, the evaluation process suffers in two ways. First of all, the reviewers are known to the scientists being reviewed, often being colleagues in the same field. This fact greatly increases the tendency to be lenient in a review, especially since the reviewers are bound to meet during their visit a number of individuals who will lose their jobs if the grant is not funded. Secondly, it is exceedingly difficult to get outstanding scientists who are not themselves doing the type of work being reviewed to spend the large amount of time necessary to participate in a site visit. Such scientists will have no particular interest in hearing about the ongoing work, nor will they have the motivation of making the trip to renew old acquaintances. Yet these are precisely the type of impartial reviewers who would be

needed to judge the work in a broad perspective, as required to evaluate it fairly against competing requests for funds. Thus, the customary reliance on the site-visit type of review has the additional disadvantage that it tends to promote reviews by narrowly-focused insiders, who take it for granted that the type of research being reviewed is very important (this is the same problem described in (I) above for certain study sections).

My personal opinion is that most very large Program Project grants should be eliminated and replaced either by several RO1 grants or by smaller Program Project (PO1) grants. I believe that the criteria for PO1 grants should be more narrowly defined, so that they serve mostly to provide shared facilities and resources, rather than funding research components that could be perfectly well evaluated as RO1 grants. In any case, the way in which Program Project grants are evaluated should be changed, with much less emphasis on site visits and much more emphasis on anonymous outside reviews by outstanding scientists.

Finally, and perhaps most importantly, a substantial number of large Program Project grants have enabled the principal investigator to set up a very large, "German-style" laboratory. In such laboratories, assistant and even associate professors become dependent on the professor for continued financial support, and they often publish with the professor as coauthor. The strength of American science has traditionally come from our emphasis on exactly the opposite approach: creating opportunities for young people to "sink or swim" on their own in a non-authoritarian setting. Limiting the annual budgets of Program Projects to below \$400,000 per year would not only force mediocre projects out into the open, but also help eliminate the damaging effects of very large laboratories on American biological science.

III. The NIH could do more to make sure that everyone is treated equally in the review process.

Since becoming Chairman of the Molecular Cytology Study Section, I have become aware that the NIH generally allows investigators the right to select the study section that will review their RO1 grants. However, at present this policy is not widely known. I suggest that the appropriate information be provided to everyone as part of the application package, along with a list of study sections and their members.

It is important to recognize that the right to choose study sections can be misused. During the last review cycle, a grant dealing with the molecular biology of gene expression in the chick oviduct was initially assigned to the Molecular Cytology Study Section. Prior to our review, the grant was reassigned at the principal investigator's request to the Reproductive Biology Study Section, even though this study section is not well-qualified to evaluate the type of research involved. In order to avoid inappropriate reviews of the above type, I suggest that the principal investigator's right to choose a study

section be limited to providing a list of three suitable study sections, from which the NIH will select one (unless none are appropriate, in which case the principal investigator's request will be ignored).

On a number of occasions, special study sections composed entirely of ad hoc reviewers have been set up for a one-time review of a relatively small number of grants. This policy seems to me to be unwise and unnecessary. It sets up a situation in which the reviewing body as a whole has had too little experience to be able to distinguish a priority score of 1.4 from one of 1.8, a crucial difference considering the present situation. I also do not see how the NIH can defend this policy when it has recently removed the voting rights of those ad hoc reviewers who serve as visiting members of regular study sections. If more study sections are needed, new regular sections should be established by the fission of existing study sections. If the grant being reviewed is a very specialized one, then extensive use should be made of expert outside reviews, and/or ad hoc reviewers, both of which are assigned to a regular study section.

Last month, I became aware of one case in which the principal investigator has been allowed to have a site visit replace a regular study section review for the past ten years. I view all such cases of special treatment, including any unusual consideration given to grants from study section members, as threats to the integrity of the peer review system.

IV. The NIH and the scientific community need to work together to make every outstanding biological scientist feel an obligation to serve on a study section for a total of two-five year terms, during his or her career.

The same type of judgements that need to be skillfully applied to carry out a focused, productive research program are essential for evaluating the research of others. For this reason, as a general rule, the best scientists make the best grant reviewers. We need to continue to improve the quality of study sections. This can be done by a cooperative effort, in which the NIH provides to study section secretaries a computerized list of scientists who have been running their own laboratories for at least six years, and who have consistently obtained very high priority scores on their own applications. This list should contain, next to each name, information on the individual's past NIH and NSF service, if any, and the titles of his or her current grants. The study section secretary should then enlist the help of scientists in his section in recruiting an appropriate person from the list, initially to serve as an ad hoc reviewer. Most scientists are much less likely to refuse a fellow scientist whom they know than an unknown NIH official, especially if a sense of obligation is implied during a phone call.

Asking a prospective study section member to serve initially in an ad hoc capacity serves two functions. It allows the prospective member to become acquainted with the section, so that he or she can later be encouraged to join by its members. It also serves as a trial run, in which the study section

chairman and secretary can evaluate the reviewing capabilities of the individual. Some scientists who do very well in their own work are exceedingly narrow in their knowledge of other fields, while others are unwilling to spend the time and effort required to produce a fair review. In both of these cases, the individual would clearly make a poor permanent addition to the section.

V. The NIH should examine ways of saving money that would minimally disrupt scientific quality.

I feel least comfortable in making recommendations in this area. However, to begin a discussion, I toss out the following three ideas for your consideration.

a) As I have written in the attached editorial for Cell, very large laboratories should be discouraged for many reasons. In general, the best science produces surprises and is done when outstanding individuals have the time to focus intensively on their projects. There is therefore a big difference between funding a grant that will enlarge a laboratory from five to ten members, and funding one that will enlarge the same laboratory from fifteen to twenty members. Most principal investigator's are unable to manage a laboratory of twenty people efficiently. Therefore, I strongly believe that the NIH should state that very special merit will be required to fund any grant proposal that will bring a principle investigator's total grant support from all sources above some maximum value: for example, \$300,000 per year.

b) In reviewing grants, I have come to resent the mode of operation of certain institutions, which have essentially set themselves up as fully NIH grant-supported entities, and yet have been free to set their own very high salary scales. I see no reason why individuals should have their salaries paid in full by the NIH at exorbitant rates. Researchers should either have a major part of their salary paid by their institution, or be willing to work for some base salary set by the NIH. For example, I hold an ACS Lifetime Research Professorship which currently contributes a maximum of \$35,000 per year to my salary. I suggest that the NIH make a similar stipulation, so that in no case will the total NIH contribution to an individual's salary (from all grants) exceed a certain maximum value. Implicit in my proposal is the idea that doing full-time research with no teaching obligations is a luxury, and principal investigators at certain "soft-money" institutions should be willing to accept a lower salary for the privilege.


c) I believe that the NIH, outsmarted by clever accountants, is overpaying overhead rates at many institutions. I suggest that a reasonable maximum percentage of indirect costs be set, which will not be exceeded at any institution (e.g., 50 percent?). Those institutions that are so inefficient that they cannot operate at this rate should be forced to become more efficient, or go out of business. It is obvious that the current "pay as you go" plan, apparently modeled after the disastrous systems used by the military to procure weapons, encourages both inefficiency and chicanery.

VI. The NIH currently lacks efficient institutional mechanisms for continuously generating, evaluating and instituting proposals for improving its operations.

In my experience with the NIH over the past few years, I have been dismayed to discover the extent to which it appears to be run by a slow-moving and autocratic beaurocracy. It should be obvious that time is bringing rapid changes in the biological sciences and that the NIH needs to be able to adapt its policies continuously to meet new challenges. In my opinion, a failure to address the types of concerns raised above seriously weakens the entire peer review process, and makes it much more vulnerable to those critics who wish to destroy it.

I note that a recent study sponsored by the National Academy of Sciences has come to similar conclusions concerning the need for reforms in the NIH Administration. I am not qualified to give advice in this area, but it is clear that the Institute Directors need to be able to put aside parochial interests in order to work closely together as a group on general policy matters. It is also obvious to me that some input is needed from a group of outside scientific advisors, especially if needed changes are to be made in the study sections to reflect the dramatic changes occurring in modern biological research.

Respectfully submitted,



Bruce M. Alberts
Professor of Biochemistry
American Cancer Society Research Professor

cc: Dr. Ruth Kirschstein, National Institute of General Medical Sciences
Dr. Halvor Aaslestad, Division of Research Grants

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