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ASIP Public Affairs

1999 ASIP Response to CSR

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Bruce M Alberts, PhD, President
National Academy of Sciences
Washington, DC 20418

c/o Linda W. Engel, M.S.
Associate Director for Planning and Outreach
Center for Scientific Review
National Institutes of Health
Bethesda, MD 20892

Dear Dr. Alberts,

The American Society for Investigative Pathology (ASIP) is an organization of approximately 2,000 physicians and scientists who share an interest in the investigation of disease pathogenesis and mechanisms of disease; the work of individual members ranges from the most basic projects to translational and clinical research. This letter was prepared by the [ASIP Task Force on Research and Training Opportunities in Pathology](#) and was approved by the members of the [ASIP Council](#), many of whom have served on NIH study sections. We believe that the views expressed here are broadly representative of those of our membership.

First, we wish to congratulate the Panel on Scientific Boundaries for Review. The draft document is broad in scope, comprehensive, thoughtful and remarkably detailed. There can be little argument with either the "goals of the research grant review process" or the "guiding principles" of the proposed structure of the integrated review groups that the panel articulated at the beginning of the document. Moreover, we feel that many of the specific recommendations of the draft are perceptive, appropriate, and, in some ways, long overdue.

We were particularly pleased to read the recommendation that reviewers be instructed to abandon a single-minded aversion to proposals, no matter how meritorious, that could be stained with the charge of not being "hypothesis driven". There can be no doubt about the benefits of hypothesis-driven research. Just as clearly, "discovery research" also can be both exciting and enormously rewarding, with results that will greatly advance the goals of the NIH. Perhaps the most widely recognized example of this is the Human Genome Project itself. Another example is the recognition (by an investigative pathologist) of the role of *Helicobacter pylori* in the pathogenesis of gastric ulcers.

We also solidly endorse the sentiment that the peer review process should not be distorted by objectives other than the "honest and informed" attempt to identify and advance the research that is most likely to



serve the goals of the NIH and the public. We certainly agree that the NIH peer review process is not an appropriate mechanism to use to sustain a particular discipline or to "preserve an entitlement" for individual "interest groups".

However, in the conclusion (section V) of the document, the panel requested the comments of members of the "wider community" of the NIH, in the hope that panel's fine product could be even further improved by the input of others. We therefore offer the following thoughts in the spirit in which they were requested, to advance the goals of the NIH through appropriate changes in certain aspects of the peer review process.

Our specific suggestions are as follows:

1. Include investigators with specific training and proven expertise in the cell- and tissue-specific analysis of human disease, and animal models of these disorders, on any advisory panels and study sections that will consider the assignment and review of proposals focused on individual diseases or general mechanisms of disease.

Cell- and tissue-specific analysis of diseases is particularly critical when the disease process affects tissues and organs that have a heterogeneous cellular composition. For example, in many neoplasms, the malignant cells represent a small fraction of the total mass of the tumor. Without cell-specific analysis of such disorders, parallel types of genomic or proteomic analyses will be unable to distinguish definitively between genes and proteins that are expressed by the malignant cells versus the other, resident or recruited (e.g., inflammatory) cells that comprise the lesion. Cell-specific analysis requires expertise in the identification, classification and staging of disease, as well as in the identification of the individual cells that participate in the process.

Investigative pathologists and others who have acquired similar training can provide essential expertise in the formulation of IRGs, study sections or RFAs, or in the evaluation of individual proposals, that have a disease orientation. Accordingly, we feel that investigators drawn from this group should be involved extensively in Phase 2 of the process articulated in the draft report, in which "expert groups of extramural scientists and NIH staff will create the scientifically related study sections that will populate each IRG on the basis of the principles outlined in this report".

2. Consider the specific designation of certain study sections within several of the proposed new IRGs as review groups for proposals that employ cell- and tissue-specific methods of analysis for innovative projects designed to advance understanding of disease pathogenesis and mechanisms.

The laser capture dissection microscope--which was developed in conjunction with investigative pathologists at the NCI--represents one example of a powerful new method for conducting cell-specific analysis of heterogeneous normal and diseased tissues. Because of the very nature of many types of cell- and tissue-specific analyses, expertise in pathology (i.e., expertise in the identification, classification and staging of disease, as well as in the identification of the individual cells that participate in the process) will be required to formulate and to successfully pursue such projects.



Accordingly, it would seem reasonable to include Pathology or Pathogenesis in the names of such study sections. This would not be to "sustain a discipline", but to indicate the type of expertise that will be concentrated in such study sections and to identify these study sections as a venue for the review of proposals whose evaluation will require such expertise. This use of the name Pathology or Pathogenesis would thus be analogous to the use of the terms Hematology or Immunology in the proposed names of other study sections.

We agree with the Panel that a critical mass of reviewers with the relevant expertise is needed if an IRG or study section is to provide an "informed" assessment of the proposals that are assigned to that group for review. Therefore, we suggest that IRGs or study sections whose portfolios include proposals focused on the cell- and tissue-specific analysis of disease pathogenesis or mechanisms should appoint a significant fraction of investigative pathologists and other members with expertise in this area.

In our view, two of the current study sections, PathA and PathB, are representative of the type of review panels that emphasize analysis of disease pathogenesis and mechanisms. To date, investigative pathologists have represented a significant fraction of the members of PathA and PathB. Since the members of our Task Force and our Council have served on these study sections, we can report that there is an excellent synergy among the themes of inflammation, vascular diseases, and renal inflammatory diseases (in PathA) and inflammation, immunopathology and neoplastic diseases (in PathB). Indeed, in our view it seems reasonable to consider capitalizing further on the expertise of these study sections, in order to provide appropriate scientific review for proposals in certain topics that are now widely distributed to multiple study sections. For example, at least two dozen study sections have reviewed applications in the area of angiogenesis, a major area of interest in PathA. Consideration should be given to referring proposals in this field to PathA and a few other study sections with depth of expertise in angiogenesis, rather than to the large number of study sections that currently are utilized.

To retain this concentration of relevant expertise, one approach would be to designate an IRG with the theme: DISEASE PATHOGENESIS AND MECHANISMS, which would consider applications focused on pathogenetic mechanisms in disease, and in particular would deal with those proposals that employ cell- and tissue-specific analytical methods. One advantage of a specific IRG on Disease Pathogenesis and Mechanisms is that this approach would readily permit reviewers to provide their expertise in the evaluation of proposals that are being considered at joint meetings of related study sections in that IRG.

However, given the importance of pathogenesis research to the missions of several of the proposed new IRGs, we do not favor the creation of another IRG on Disease Pathogenesis and Mechanisms. Instead, we suggest retaining the current emphases of PathA and PathB by placing these study sections appropriately in the proposed new IRG structure. For example, in the current draft, Pathology is mentioned specifically as a theme in the ONCOLOGICAL SCIENCES IRG (11), and this IRG might have a study section, much like the current PathB, to consider applications on cancer pathogenesis and disease mechanisms. Similarly, the CARDIOVASCULAR SCIENCES IRG (13) might represent the best location, in the proposed new group of IRGs, for a study section much like the present PathA. In addition, new study sections with a major focus on pathogenesis (as opposed to physiology or pathophysiology) should be considered for inclusion in multiple new IRGs that have a disease focus.



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3. Introduce the term "pathology" in certain parts of the document, to acknowledge that this discipline, and more importantly the expertise in cell- and tissue-specific disease analysis that it embodies, has as much relevance to the scientific investigation of disease as do other specifically named areas of work such as biochemistry, genetics, and statistics. Similarly, the term "pathogenesis" should be introduced wherever appropriate, to distinguish investigation into the series of pathological events that result in disease (i.e., "pathogenesis") from investigation into the disordered function of diseased organs or organ systems (i.e., "pathophysiology").

Since the mission of NIH is to advance health, in part through the better understanding of disease pathogenesis and mechanisms, it seems inappropriate not to mention specifically in several parts of the document the "discipline" that focuses virtually entirely on this area of work. Examples include, in section 4 under III Cultural Changes, "There are true disciplines (e.g., biochemistry, genetics, physiology, statistics, ...) that have come to underlie and be deeply entwined in all kinds of research." In our view, pathology certainly belongs on this list. The same can be said, a few lines below in the same section, for the sentence: "...the Panel recognizes the need for well-informed biochemists, geneticists, physiologists, and statisticians on many diverse peer review groups."

We hope that the Panel will find these suggestions to be helpful. We would be delighted to discuss these points further, and in more detail, should that be desired. We shall also be pleased to offer suggestions about individual investigators in our society who would be willing to participate in the important work that will take place during Phase 2 of this process.

We also extend our thanks to the Panel for all of the hard work and thought they clearly have devoted to this critically important topic.

Sincerely,
Mark E. Sobel, M.D., Ph.D.
President

American Society for Investigative Pathology

ASIP Task Force on Research and Training Opportunities in Pathology

(Current and Former ASIP Council Members)

- Stephen J Galli MD, Task Force Chair
Chair, Dept of Pathology
Stanford U Med Ctr
- Tucker Collins MD PhD
Dept of Pathology
Brigham & Women's Hosp



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- Nelson Fausto MD
Dept of Pathology
U Washington
 - Stanley R Hamilton MD
Dept of Pathol & Lab Med
U T MD Anderson Cancer Ctr
 - Sue C Heffelfinger MD PhD
Dept Pathol & Lab Med
U Cincinnati Med Ctr
 - Agnes B Kane MD PhD
Chair, Div of Pathology
Brown U
 - David G Kaufman MD PhD
Dept Pathol & Lab Med
U North Carolina Med Sch
 - Vinay Kumar MD
Dept of Pathology
U Texas SW Med Sch
 - Mary F Lipscomb MD
Chair, Dept of Pathology
U New Mexico
 - Richard G Lynch MD
Chair, Dept of Pathology
U Iowa Col of Med
 - Bruce M McManus MD PhD FRCPC
Chair, Dept Pathol & Lab Med
U British Columbia
 - William A Muller MD PhD
Dept of Pathology
Cornell Med Col
 - Jordan S Pober MD PhD
Dept of Pathology
Yale Univ
 - Fred P Sanfilippo MD PhD
Dept of Pathology
Johns Hopkins Medical Institutions
 - Mark E Sobel MD PhD
Bethesda, MD
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Potomac, MD

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- Scott R VandenBerg MD PhD
Dept of Pathology
U Virginia Hlth Sci Ctr



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Program Committee Chair-Elect

- William A Muller MD PhD
Dept of Pathology
Cornell Med Col