National Institutes of Health
Center for Scientific Review

Open House Workshop: Disease-Based Agenda

June 29, 2007
Natcher Conference Center, Bethesda, MD

Meeting Summary

Welcome and Introduction

Dr. Raymond Kington, Deputy Director, National Institutes of Health (NIH), welcomed participants and thanked them for taking time to participate in this important meeting. He noted that among the 180 scientists in attendance, there were 22 Chairs of Disease-based study sections, 20 professional society representatives, and NIH programmatic staff from 13 NIH Institutes and Centers. Dr. Kington asserted that peer review is the key to the continuing high quality of NIH-funded research. NIH is proud of how this system has performed over the decades, but science is constantly evolving, and the peer review system must evolve with it. From time to time it's appropriate to take a good hard look at what we do, and how we do it, and to ask if there are ways to do it better. The study sections are the backbone of peer review. The most recent realignment of the peer review study sections took place in 2000, in response to recommendations of the Panel on Scientific Boundaries of Review, and the time has now come to ask whether those changes achieved their goals.

Dr. Toni Scarpa, Director, Center for Scientific Review (CSR/NIH), explained that this was the third of six workshops being held during 2007 to evaluate the current alignment of CSR's initial review groups (IRGs) and study sections. These open houses are a vital mechanism for helping CSR anticipate where the field is going and how the IRGs and study sections might be realigned in the future. At the end of the process, CSR will have heard from all 300 Study Section Chairs, as well as 600 leaders of scientific communities including presidents of society disease-based groups. In each open house, the goal is to obtain the community's responses and input on two central questions:

1. What will be the most important questions and/or enabling technologies you see forthcoming within the science of your discipline in the next 10 years?
2. Is the science of your discipline, in its present state, appropriately evaluated within the current study section alignment? Suggestions?

For this reason, the breakout sessions were vital. Participants were asked to focus on the science. Questions about process were held for the afternoon, when time was set aside to address them. Finally, Dr. Scarpa recognized the continuing contributions of CSR's 31,000 peer reviewers and especially the Study Section Chairs.

Overview of the Current Organization of the Disease-based Study Sections

Dr. Donald Schneider, Director, Division of Molecular and Cellular Mechanisms, CSR, explained that, historically, there have been four disease-related IRGs:

1. AIDS and Related Research (AARR);
2. Infectious Diseases and Microbiology (IDM);
3. Oncological Sciences (ONC); and
4. Surgical Sciences, Biomedical Imaging and Bioengineering (SBIB).

AARR, which operates under a congressional mandate to process all grant applications in less than six months, began with five study sections in 1988 and now stands at nine study sections and one small business committee. IDM currently stands at eight study sections, three small business sections, and one fellowship section. ONC includes 15 study sections, three small business sections, and one fellowship section. SBIB stands at five study sections, five small business sections, and one fellowship section.

The current alignment of study sections under these four IRGs has emerged in response to the report of the Panel on Scientific Boundaries of Review (PSBR, January 2000), which recommended (among other things) moving basic science to disease or organ when possible. PSBR also recommended that CSR involve stakeholders in monitoring this alignment and evolving in response to changes in the science. This has already led to the creation of one additional study section in AARR, one in IDM, two in ONC, and new special emphasis panels in SBIB. Special emphasis panels often serve as the pilot for a new study section. Working groups are convened to analyze and recommend the restructuring of new study sections. In all, it takes about nine months from the first meeting of a working group to the creation of a new study section. For these IRGs, it has happened four times in the past four years, moving from 34 to the current total of 38 disease-based study sections.

Explanation of and Charge to Breakout Groups

Dr. Cheryl Kitt, Deputy Director, CSR, explained the goals and arrangements for the six breakout groups, which are designed to facilitate a more detailed discussion of the two central questions posed by Dr. Scarpa. Dr. Kitt reminded participants that CSR does not talk about funding issues, and she reminded them to concentrate their discussion on questions of science. Time would be made available in the afternoon for discussion of process questions. The six breakout groups were:

1. Basic Mechanisms;
2. Translational;
3. Molecular Mechanisms for Diagnosis and Therapy;
4. Pathogenesis;
5. Technology, Computational Biology and Bioengineering; and
6. Clinical.

Report Out on Question 1

> *What will be the most important questions and/or enabling technologies you see forthcoming within the science of your discipline in the next 10 years?*

There was a remarkable convergence among the breakout groups with regard to enabling technologies, with all of them identifying one or more forms of biomedical informatics, including:

- Record keeping and data management;
- Computational sciences, data processing, data analysis;
- Systematics and mathematical modeling of biological systems;
- Data integrity;
- Data sharing and communications, particularly between disciplines.

The breakout groups also agreed on the need for broad-based, multidisciplinary approaches that bring fresh perspectives and expertise to bear. One group went so far as to assert that "integration *is* a technology," while another called for "greater precision in small things, greater integration in large things." A third group called for better communication and collaboration among disciplines (including physics, mathematics, chemistry, and engineering), and a fourth called for "multidisciplinary studies of complex systems and whole organisms."

Several breakout groups also pointed to two additional issues and supporting technologies that will be important in the next ten years:

1. Personalized medicine, including a better understanding of individual risks and responses and the development of patient-specific diagnosis and therapy; and
2. Better models of human disease, including both animal and mathematical models that are relevant to diagnosis and treatment.

In addition, individual breakout groups pointed to the importance of questions and technologies that were specific to their particular focus. For example, the Basic group pointed to the importance of proteomics, biomarkers, small-molecule screening, and the need to study cell-environment interactions. The Translational group called for greater integration of the results from clinical trials. The Molecular group called for novel technologies for drug development, as well as new assays for in vivo drug distribution. And the Clinical group called for virtual diagnostic and therapeutic technologies for use in rural and emergency medicine, as well as better follow-up on implementation in the developing world.

Discussion

In the discussion that followed, participants recognized that this new emphasis on integration is very different from the vision of PSBR in 2000, which focused on individual organs and diseases. Even within oncology, however, there is a need for greater integration among

pathogenesis, diagnosis and therapy, as well as better communications with other disciplines about the impact of larger systems on cancer and vice versa. This situation may be amenable to "big science" approaches, like those that have been so successful in physics and astronomy, but this would have undesirable impacts on CSR and the NIH grant system. There will always be a need for "small science" and individual discovery, even in the context of big science; what's really needed is better communication – for example, between researcher and clinician, so the information gets out in a form that will get it used, and so application will inform discovery. Participants also suggested that cancer should be added to AIDS and opportunistic infections as threats to public health in the developing world.

Report Out on Question 2

> *Is the science of your discipline, in its present state, appropriately evaluated within the current study section alignment? Suggestions?*

The breakout groups reported that, in general, participants were satisfied with the evaluation of their disciplines under the current alignment of CSR study sections. One group estimated that 90 to 95 percent of all applications are appropriately reviewed, but this means that 5 to 10 percent are not, usually because certain disciplines or diseases are underrepresented in the existing study sections or because there is a need for new study sections:

- The Basic Mechanisms group maintained that biochemistry, toxicology and gene therapy might be underrepresented, along with melanoma and other "neglected" diseases.
- The Translational group maintained that areas such as pain, environmental toxicology, sleep, and mitochondrial injuries were not receiving appropriate review.
- The Molecular Mechanisms group identified toxicology and ecology as areas that are underrepresented in existing study sections.
- The Pathogenesis group reported that matrix biology is not appropriated reviewed and that a new IDM study section is needed for pathogenic microbes and opportunistic pathogens currently reviewed by AARR.
- The Clinical group suggested that surgery applications are scattered among organ-based study sections, and that endocrine and other metabolic disorders aren't adequately represented under the current disease/organ alignment. There might be benefits from a new clustering of clinical and human studies study sections, and there is an emerging need for better reviews in the area of emergency and disaster medicine.
- In addition, both Translational and Molecular groups suggested that there needs to be a greater appreciation of non-hypothesis-driven applications.

All of the breakout groups recognized the difficulty of recruiting a sufficient number of peer reviewers with the appropriate expertise, particularly when (in some areas) the different study sections are competing with one another for the same talent. Consequently, most of the groups offered suggestions for how CSR can meet this challenge:

- The Basic group suggested that CSR recruit more ad hoc reviewers for particular applications, including more clinician-scientists on all study sections. They also suggested that CSR's scientific review administrators attend more scientific conferences to keep up with emerging science and identify expert reviewers.
- The Molecular group suggested that CSR recruit academic, industry and government reviewers with broad or specialized expertise needed to increase flexibility.
- The Pathogenesis group suggested that, given the limited number of experts in a rapidly emerging area, it might be more efficient to create a floating pool of experts who can be shared across study sections.
- The Translational group also suggested recruiting more ad hoc reviewers, but they added that new reviewers would be more effective, sooner, if they receive better education and training before their first meeting.

Finally, the breakout groups suggested a number of additional issues for CSR to deal with. In the area of emerging technologies, for example, it will be important to distinguish between transient trends and persistent changes. CSR might also want to reevaluate its scoring system, for example by scoring technical merit and impact separately, or by scoring applications by category (basic, translational, observational, clinical). It might also be useful to incorporate some measure of past performance, at least for senior investigators – what is their track record and productivity, their impact or citations? In addition, CSR may want to formalize a more transparent process to evaluate complaints.

Discussion

In the discussion that followed, participants suggested that there is a need for better training for study section chairs, as well as peer reviewers, in order to get everybody up to the same level. This will increase confidence on the part of applicants. There was general agreement about the desirability of evaluating senior investigators, but less agreement about how to do it. CSR will have trouble developing a single standard of measurement, and the grants are made for the work proposed – merit awards exist to recognize past work. On the other hand, not every application is for truly new or innovative work.

There was greater agreement on the need for a new way of dealing with resubmissions. The current "triage" mechanisms do not work – they all submit again. Study sections need to be responsive to second and third submissions, but they don't need to treat them as new applications. In fact, by the third time they see the same application, the study section has essentially rewritten it for the applicant, and responsiveness to comments isn't the same as merit. The study section needs some mechanism to cut them off, some kind of coherent discouragement like "unscored with extreme prejudice."

Questions of Process

Dr. Scarpa returned to give a summary of the progress CSR has made in reforming the process of peer review, as well as the remaining challenges and opportunities for the peer review process. The principal drivers for change are the number of applications, the workload for individual reviewers, and a limited budget. The number of applications received by CSR nearly doubled between 2001 and 2006, reaching 80,000 last year, and a further increase is expected in 2007. This has led to complaints that the process is too slow, that it places too great a burden on the applicants and reviewers alike, that there are too few senior reviewers, and that this situation favors predictable science instead of innovation. At the same time, the peer review budget is limited – $60 million for CSR itself and another $40 million for the Scientific Review and Evaluation Awards that cover the honoraria and expenses of peer reviewers. This total amount represents less than 0.2 percent of the amounts requested in the proposals reviewed.

In response, CSR has greatly increased the efficiency of the peer review process, notably by shifting to electronic submissions. Continuing reorganization and evaluation, of which this open house is a part, will further improved the alignment and performance of study sections. In the future, CSR will work to shorten the review cycle, moving from one to three cycles per year to three and ensure that all applications are scored within three months. It is also conducting a pilot test with shorter applications, perhaps half the current 25 pages for an R01 grant, and rolling reviews with no submission deadlines; these changes might be in place for new investigators by November 2007.

CSR is constantly working to recruit and retain high quality reviewers. To make better use of these volunteers, it is experimenting with new electronic review techniques, such as telephone- and video-enhanced meetings and asynchronous electronic discussions, with the goal of having 10 percent of all reviews be electronic in 2007. Finally, CSR is considering a system of rewards for reviewers that will increase the intellectual value of the experience and provide grant support to cover the time they volunteer as a reviewer. Deeper changes in the future may include changes in the locus of review, a better firewall between program and review, changes in scoring to reflect degree of difficulty and resubmissions, and greater recognition of applications that are deeply innovative, translational and/or multidisciplinary.

In response to questions, Dr. Scarpa said that R01 funding should remain relatively stable in the near future, but that R21 funding is poised for considerable growth. At present, 45 percent of grants go to new investigators, 18 percent to established investigators, and 33 percent to renewals. Women typically succeed 10 percent better than men. There was some debate about video vs. asynchronous study sections – response to video reviews was generally positive, but several audience members said that asynchronous review loses much of the richness and complexity of synchronous and face-to-face meetings, particularly when there are disagreements.

Dr. Scarpa said that this experience is not reflected in review comments. The results of a user survey are posted at the CSR website.

The open house adjourned at 4:15 p.m.

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