National Institutes of Health
Center for Scientific Review

Open House Workshop: Integrated Biology I

August 24, 2007
Natcher Conference Center, Bethesda, MD

Meeting Summary

Welcome and Introduction

Dr. Raymond Kington (Deputy Director, National Institutes of Health [NIH]) welcomed the participants and thanked them for taking the time to participate in this important meeting. He noted that the 140 scientific leaders in attendance included 20 study section chairs and 30 representatives from scientific and professional societies, in addition to program staff from several NIH Centers and Institutes, including several Institute directors. Dr. Kington asserted that peer review is the key to the continuing high quality of NIH-funded research. Although the peer review system is 60 years old, it is hardly static—beginning with the first study section in 1946 (topic: syphilis), the system has evolved in response to the evolution of biomedical science and the emergence of new public health challenges. The most recent restructuring began in 2000 with the report of the Panel on Boundaries of Scientific Review (PBSR), and the time has come to evaluate whether this is still the best alignment to match the mission and goals of peer review.

Dr. Toni Scarpa (Director, Center for Scientific Review [CSR], NIH) reiterated that peer review is the heart and soul of NIH. The reorganization of CSR that began in 2000 was a major 5-year effort, but science continues to evolve and peer review must evolve with it. He explained that this was the fourth of six workshops being held during 2007 to evaluate the current alignment of CSR's Integrated Review Groups (IRGs) and study sections. CSR has already added four new study sections, and will soon add a new IRG, in response to input from the first three open houses. He hoped that today's meeting would help CSR anticipate where the field of integrated biology is going by eliciting 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?

The breakout sessions are vital to this effort, and participants are asked to focus narrowly on the science of their disciplines—questions about process should be held for the afternoon, when time would be set aside to address them. Finally, Dr. Scarpa recognized the contributions of Dr. Mary Ann Guadagno (Scientific Review Administrator, CSR), who has labored long and hard to organize the workshops.

Overview of Changes in the Integrated Biology Study Sections

Dr. Donald Schneider (Director, Division of Molecular and Cellular Mechanisms, CSR) explained that the current alignment of study sections in integrated biology falls into four clusters:

1. Digestive Sciences (DIG), 5 study sections;
2. Endocrinology, Metabolism, Nutrition, and Reproductive Sciences (EMNR), 8 study sections;
3. Musculoskeletal, Oral, and Skin Sciences (MOSS), 6 study sections; and
4. Renal and Urological Studies (RUS), 3 study sections.

This alignment emerged in response to the PBSR report, which recommended (among other things) moving basic science into disease- or organ-based study sections when possible. Regular study sections are supplemented by fellowship study sections, small business/technology transfer study sections, and Special Emphasis Panels (SEPs). SEPs can meet a single time or on a recurring basis to address emerging scientific issues and often serve as the pilot for a new study section. In all, it takes about 9 months from the first meeting of a steering group to the creation of a new study section.

Explanation of and Charge to Breakout Groups

Dr. Cheryl Kitt (Deputy Director, CSR) explained that the breakout sessions are designed to facilitate a more detailed discussion of the two central questions posed by Dr. Scarpa. Participants have been preassigned to a specific group but are free to join another group as they feel appropriate. She cautioned them to focus on questions of science, since CSR does not talk about funding, and there will be time in the afternoon for process questions. The four breakout groups were:

1. Pathogenesis and Translational Research
2. Clinical
3. Molecular and Cellular Mechanisms
4. Basic and Integrative Physiology, Technology, and Bioengineering

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 consensus among the breakout groups that *integration* is one of the grand challenges of the next decade—the integration of molecular and cellular information into systems biology, interactions among multiple organs in disease and health, integration across disciplinary boundaries (particularly between developmental and integrative biology), integration of physical and behavioral approaches to health, integration of basic science and clinical practice.

There was also agreement about the most important enabling technologies for pursuing this challenge. For example, all of the groups identified one or more forms of *biomedical informatics,* including:

- Development, accessibility and integration of complex data sets
- Computational biology, such as the use of mathematical models to integrate data and supply predictive power
- New technologies for training, patient protection, and record-keeping
- Informatics tools that are usable for clinical trials, including objective and subjective endpoints

Three of the four groups identified *regulatory mechanisms* (the "omics") as an emerging technology that offers new tools and new opportunities:

- Integration of genomics, proteomics, metabolomics, and epigenetics to identify biomarkers of disease that can be used in the clinic
- Translation of "omics" data into a physiological context
- Development of proteomic technology
- Gene-environment interactions across the lifespan
- Individualized information at the protein, gene, and RNA level
- How genes coordinate the development of various organs and tissues

Similarly, three of the four groups identified *in vivo imaging* as an enabling technology of great potential value. In general, they conceive of this technology as a set of real-time, non-invasive tools for observing and measuring:

- Protein-protein interactions
- Biochemical events taking place within a living cell
- Cell-cell interactions
- How cells develop into tissues
- Dynamic structure and function of cells and tissues
- Larger organs, whole animals, and humans
- The diagnosis and treatment of disease

Several of the groups also suggested more unique questions that seemed particularly important to constituents, including:

- High-resolution phenotyping, working toward the concept of a phenotypic "fingerprint" that captures cell diversity, cell response, and organ function
- Stem cell biology in health and disease, with an emphasis on development, aging, chronic disease, tissue engineering, and regeneration
- Clinical trials and clinical investigations for understudied clinical issues, including the development of guidelines and registries and an emphasis on evidence-based treatments
- Communication with the general population

Discussion

In the discussion that followed, participants were assured that their job was to point out what is needed, not how to make it happen. Nevertheless, several participants pointed out that they might have identified the same questions and enabling technologies 10 years ago. However, they also recognized that the questions are now being asked at a deeper level and that users are doing a better job of engaging the providers of bioinformatics and advanced imaging technology. There was agreement that it is in fact the job of NIH, in partnership with its grantees, to build the kinds of databases and communications networks that will be required. There was general agreement that the commonalities among the four breakout groups were *integration, real-time measurement,* and *applications at the clinical level.*

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 the current alignment of organ- or disease-specific study sections is appropriate for most disciplines, but that it must constantly evolve, and this will not happen spontaneously. There was a general feeling that the current alignment is not attuned to integrated approaches, crosscutting studies, or high-risk ideas. Overlapping study sections, in particular, can provide poor coverage; in other cases similar applications are distributed to many different study sections, losing the advantage of knowledgeable comparative review. Specific examples cited by the breakout groups include environmental science, therapeutics, multi-organ or multi-technique studies, effects of physical activity/inactivity, chronic kidney disease, toxicology, alcohol-related diseases, urology, urogynecology, pain syndromes, surgery, emergency medicine, and common ailments that affect large numbers of people.

In some the solution might be to create a new IRG (e.g., environmental sciences) or new study sections (e.g., urological sciences, urogynecology). In other cases, interdisciplinary applications will need many different expertises. One way to respond to this need is with a two-stage review: an initial "editorial" review by an independent expert to address a specific technical question or technique, followed by the usual study section review to address significance and impact. (Two groups specifically recommended that significance and impact be given more weight than methodology, and another group said that CSR should reevaluate how it reviews applications that involve large data sets.) Another solution would be a "modular study section" design that has a core of substantive reviewers (to maintain continuity) and a floating pool of technical reviewers who can support many different study sections as needed.

The breakout groups stressed the importance of face-to-face review meetings and rejected the use of mail, phone, videoconference, or asynchronous electronic discussion as a substitute for personal interactions. However, they agreed that the key to good peer review is good peer

reviewers. One group suggested putting a checkbox on NIH awards, asking grantees to serve as peer reviewers; another group said that such service should be mandatory and that *only* funded investigators should serve as reviewers. NIH might also suggest to the American Association of Medical Colleges that medical schools give recognition for service on study sections, or find new mechanisms to encourage clinicians to serve as reviewers. Inducements should be available, if they are needed, but so too should better orientation and training, especially for chairs and new members.

Discussion

In the discussion that followed, participants reiterated that all applications should be reviewed in the same way, and that face-to-face meeting enrich the discussion by providing context and identifying the key issues more clearly.

Questions of Process

Dr. Scarpa acknowledged that the discussion had already moved to the process of peer review, and he took the opportunity to review the steps that CSR has already taken to reform that process. Business as usual is no longer an option—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 applications reviewed.

In response, CSR has greatly increased the efficiency of the peer review process, notably by shifting to electronic submissions. Continuing evaluation and reorganization, of which this open house is a part, will further improve the alignment and performance of study sections. In the future, CSR will work to shorten the review cycle, moving from one to three cycles of applications per year, with the promise that all applications will be scored within 3 months. CSR is also testing a shorter application (perhaps half the current 25 pages) that might be in place for new investigators by November 2007. In the future, CSR will conduct pilot tests of continuous receipt of applications and “editorial board” reviews for complex interdisciplinary applications.

In the long term, however, there will be a growing need for reviewers, and CSR is constantly working to recruit and retain high-quality reviewers. CSR is already 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 conducted electronically in 2007. Response to these experiments have been 80 percent favorable. CSR is also 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. One goal of these inducements is to encourage broader participation by clinicians, physicists, computational biologists, and international public health experts. Changes in the future may include changes in the locus of review, a better firewall between program and review, changes in scoring to reflect the degree of difficulty and resubmissions, and a special review process for applications that are deeply innovative, translational, and/or interdisciplinary.

In response to questions, Dr. Scarpa said that during the pilot test, 87 percent of new investigators chose to use the experimental shorter application, and on average, they did better than other applicants in the scoring. Consequently, new investigators have a favorable view of this innovation. Applications are assigned to specific study sections by an artificial intelligence program that uses keywords and other characteristics to match the application with other applications, as well as the IRG and study section to which they will be assigned. Dr. Scarpa has made a special appeal to professional and scientific societies to nominate their members and potential reviewers, and CSR is currently working through a list of 500 or 600 such nominations. A possible inducement might be to extend the grants of funded investigators in recognition of their service as peer reviewers. In the end, however, the best approach will be to make peer review a learning experience, if not a pleasurable experience, for those who choose to serve.

The open house adjourned at 3:15 p.m.