Department of Health and Human Services
National Institutes of Health (NIH)
Office of the Director (OD)
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

Council of Councils Meeting
February 1, 2012

Meeting Minutes

I. WELCOME

James M. Anderson, M.D., Ph.D., Chair, welcomed participants, NIH staff members, and members of the public to the meeting of the Council of Councils (CoC). The meeting opened at 8:30 a.m. on Wednesday, February 1, 2012, in Building 31, 6th Floor, Room 6, on the NIH Campus, Bethesda, Maryland.

A. Attendance

1) Council Members Present

Chair: JAMES M. ANDERSON, M.D., PH.D., Director, DPCPSI, OD, NIH
Executive Secretary: ROBIN I. KAWAZOE, DPCPSI, OD, NIH
STEPHEN L. BARNES, PH.D., University of Alabama at Birmingham
LAVARNE A. BURTON, M.A., American Kidney Fund, Rockville, MD
F. XAVIER CASTELLANOS, M.D., New York University School of Medicine, New York, NY
DAVID W. CRABB, M.D., Indiana University School of Medicine, Indianapolis, IN
JACK A. ELIAS, M.D., Yale University School of Medicine, New Haven, CT
GARRET A. FITZGERALD, M.D., University of Pennsylvania, Philadelphia, PA
DANIEL H. GESCHWIND, M.D., PH.D., David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA
MAE O. GORDON, PH.D.,[1] Washington University School of Medicine, St. Louis, MO
*RICHARD M. GREENWALD, PH.D., Simbex, iWalk, Thayer School of Engineering, Lebanon, NH
PETER J. HOTEZ, M.D., PH.D., Baylor College of Medicine, Houston, TX
JEFFREY A. KAUFMAN, M.B.A., Adenoid Cystic Carcinoma Research Foundation, Needham, MA
GRACE LEMASTERS, PH.D., University of Cincinnati College of Medicine, Cincinnati, OH
MARK O. LIVELY, PH.D., Wake Forest University School of Medicine, Winston-Salem, NC
K.C. KENT LLOYD, D.V.M., PH.D., University of California, Davis, Davis, CA
HERBERT KIM LYERLY, M.D., Duke University Medical Center, Durham, NC

[1] Dr. Gordon was not present for the closed session.

JEAN MCSWEENEY, PH.D., R.N., F.A.H.A., F.A.A.N., University of Arkansas for Medical Sciences, Little Rock, AR
JOYCE A. MITCHELL, PH.D., University of Utah, Salt Lake City, UT
ROBERT F. MURPHY, PH.D., Carnegie Mellon University, Pittsburgh, PA
REGIS O'KEEFE, M.D., PH.D., University of Rochester School of Medicine and Dentistry, Rochester, NY
REGINA RABINOVICH, M.D., Bill & Melinda Gates Foundation, Seattle, WA
DAVID VALLE, M.D., Johns Hopkins University School of Medicine, Baltimore, MD
JOHN W. WALSH, Alpha-1 Foundation, Miami, FL
GARY L. WESTBROOK, M.D., Oregon Health and Science University, Portland, Oregon
TERRIE FOX WETLE, PH.D., Brown University Medical School, Providence, RI
LUTHER WILLIAMS, PH.D., Tuskegee University, Tuskegee, AL

*Appointment pending clearance

2) **Discussants**
VALERIE COPIÉ, PH.D., Montana State University, Bozeman, MT
DALLAS M. HYDE, PH.D., University of California, Davis, Davis, CA
M. CHRISTINE ZINK, PH.D., D.V.M., Johns Hopkins University School of Medicine, Baltimore, MD

3) **Liaisons**
JANINE A. CLAYTON, M.D., Acting Director, Office of Research on Women's Health, DPCPSI, OD
PAUL M. COATES, PH.D., Acting Director, Office of Disease Prevention, DPCPSI, OD
ROBERT M. KAPLAN, PH.D., Director, Office of Behavioral and Social Sciences Research, DPCPSI, OD
LOUISE E. RAMM, PH.D., Director, Office of Research Infrastructure Programs, DPCPSI, OD
ELIZABETH L. WILDER, PH.D., Director, Office of Strategic Coordination, DPCPSI, OD

4) **Presenters in Attendance**
Francis S. Collins, M.D., Ph.D., Director, NIH
Bruce A. Fuchs, Ph.D., Director, Office of Science Education, ORIP, DPCPSI
Franziska B. Grieder, D.V.M., Ph.D., Director, Division of Comparative Medicine, ORIP, DPCPSI
Louise E. Ramm, Ph.D., Director, ORIP, DPCPSI

5) **NIH Staff and Guests**
In addition to Council members, presenters, and Directors, others in attendance included NIH staff and interested members of the public.

B. Meeting Procedures

Ms. Robin Kawazoe reviewed the following:

- Council members are considered Special Government Employees during Council meetings and are therefore subject to the rules governing Federal employees.
- Each Council participant has completed and submitted a financial disclosure form and conflict of interest statement as a Federal requirement for membership on NIH advisory councils. Financial disclosures are used to assess real and perceived conflicts of interests, and Council members must recuse themselves from meeting during discussion of items for which conflicts have been identified.
- Discussants are subject to conflict of interest rules.
- Time has been allotted for discussion between the Council and presenters, but time for comments from other meeting attendees is limited. The public can submit comments in writing; instructions are available on the DPCPSI Web site and in the *Federal Register*.
- CoC members should not speak on the Council's behalf or on activities not yet cleared by Council.
- Approved meeting minutes will be posted on the DPCPSI Web site.

C. Future Meeting Dates

The next CoC meeting will be held June 5, 2012. Because of the expanded role of the Council, the meeting scheduled for November 2012 has been moved to September 5.

CoC meeting dates in 2013 are January 22, May 14, and September 24.

II. DPCPSI UPDATE

Dr. Anderson noted that the role of DPCPSI continues to evolve, and he acknowledged that this continued evolution presents a challenge to the Council. He asked for Council members' understanding and encouraged their ideas and participation. He then reported on organizational changes within the Division, new responsibilities for CoC, Common Fund updates, a new Council working group, and early concurrence for grant applications.

The role of DPCPSI has continued to change since the Division was first created by the NIH Reform Act of 2006. On December 23, 2011, Congress passed legislation that appropriated an NIH budget for FY 2012 and established the National Center for Advancing Translational Sciences (NCATS). At the same time, this legislation dissolved the National Center for Research Resources (NCRR), and programs, grants and contracts, and staff from this Center were reassigned to NCATS, DPCPSI, the National Institute of General Medical Sciences (NIGMS), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), or the National Institute of Minority Health and Health Disparities. Additional realignments were made to align offices or programs with common interests.

The mission of NCATS is to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. The

Center will house the Cures Acceleration Network, which brings an appropriation of $10 million in FY 2012, and the Clinical and Translational Science Award program has moved from NCRR to NCATS. In addition, selected Common Fund programs, including the NIH-Food and Drug Administration (FDA) Regulatory Science Program which includes the Integrated Microphysiological Systems project jointly run by NIH/DPCPSI, the Defense Advanced Research Projects Agency (DARPA), with advice from FDA are now housed within NCATS.

Dr. Anderson presented diagrams to summarize the structure of DPCPSI before and after the December 23 legislation. The Office of Rare Diseases Research (ORDR) has moved to NCATS, and DPCPSI now has a new Office of Research Infrastructure Programs (ORIP), headed by Dr. Louise Ramm, formerly Deputy Director and Acting Director of NCRR. ORIP houses the Division of Comparative Medicine; the Division of Instruments, Infrastructure, Resources, and Construction; and Office of Science Education (OSE). OSE was moved from the OD Office of Science Policy. Dr. Anderson noted the Science Education Partnership Awards, a program that brings investigators together with institutions, museums, or schools to promote education in science, technology, engineering, and mathematics (STEM), and he reported that DPCPSI will conduct an internal review and inventory of NIH activities in science education between today's and the Council meeting on June 5. We will report in June about what we found, including suggestions about how to go forward, and how the Council may be involved in helping to advise on the role of OSE in NIH's contribution to national STEM education.

Additional reorganization action has moved activities and staff from the Office of Medical Applications of Research (OMAR) to the Immediate Office of the Director of the Office of Disease Prevention (ODP). ODP will continue OMAR's information dissemination activities, including a course to train journalists how to interpret scientific literature, as well as the consensus conferences formerly sponsored by OMAR. However, the state-of-the-science conferences will no longer be sponsored because this activity is done across NIH. NIH is completing a search for a new Office of Disease Prevention (ODP) Director, and following the retirement of founding ORWH Director Dr. Vivian Pinn, NIH has now started a search for a new ORWH Director. Dr. Anderson welcomed Dr. Ramm, OSE Director Bruce Fuchs, former NCRR staff, and three former NCRR Council members who are serving as discussants for second-level grant review.

Dr. Anderson reported that Common Fund activity is relatively quiet right now. However, he reminded the Council of the Early Independence Awards, a new grant mechanism to speed the time it takes for selected new investigators to acquire their first independent grants. Also known as the "Skip the Postdoc" program, the Early Independence Awards allow new investigators to develop their own research programs and manage their own budgets immediately after they have completed a Ph.D. or clinical training. Through the 2011 competition 10 awardees were selected out of 110 applications. This program is still in a proof-of-concept stage; if it proves successful, DPCPSI hopes to expand it and encourage the ICs to adopt this new mechanism for career promotion.

Dr. Anderson noted that since the Common Fund began, the role of CoC in concept clearance has differed from year to year. In the past, DPCPSI has presented concepts at late stages in their development, following portfolio analyses, workshop development, and input from the community. DPCPSI will now bring to Council a larger list of concepts that are at earlier stages in development and thus less defined. Dr. Anderson noted the broad expertise of CoC and expressed the Division's belief that the Council's input might contribute more at this stage. In addition, Dr. Anderson pointed out that because of the reorganization, DPCPSI now has a large and diverse grant portfolio focused on infrastructure, animal resources, facilities renovation, and science education, along with its Common Fund activities. CoC will also be responsible for future concept clearances for these areas.

Dr. Anderson went on to speak about the use of animals in research which has enabled scientists to identify new treatments, improve health, and extend life, noting that chimpanzees, which are closest to humans in terms of social networks and genetics, have been particularly useful. In 2010 the NIH Director asked the Institute of Medicine (IOM) to review the necessity of using chimpanzees in research and to establish criteria for circumstances where such research is needed. The IOM report, which was issued in December 2011, concluded that although chimpanzees have been valuable models in the past, the scientific necessity of chimpanzee research is now very limited. The IOM did acknowledge that some research areas, such as monoclonal antibody therapies, comparative genomics, or noninvasive studies of socials and behavioral factors affecting disease, might still require the use of chimpanzees. In addition, new, emerging, or re-emerging diseases might present challenges requiring research that uses chimpanzees. The IOM has established the following guiding principles for such research:

- The knowledge gained must be necessary to advance the public's health.
- There must be no other research model by which the knowledge could be obtained, and the research cannot be ethically performed on human subjects.
- The animals used in the proposed research must be maintained in either ethologically appropriate physical and social environments or in natural habitats.

IOM was unable to reach a consensus on the necessity of chimpanzees for the development of a prophylactic hepatitis C virus vaccine.

NIH Director Francis Collins has reviewed and accepted the IOM committee's recommendations. DPCPSI is planning to establish a working group of the CoC to explore how best to implement the principles of the report. Dr. Anderson reported that the working group would be charged with its task officially on February 2, 2012; that the public will be invited for a 60 day period to offer comments to assist the Working Group address their charge, and that the CoC will be provided with an update at its June meeting, and hopefully, initial recommendations may be available for discussion at the September meeting. The final report of the working group will most likely be ready for presentation to the CoC in early 2013. They will endorse recommendations and provide them to the NIH Director and these will be used to guide future NIH policy. There will be

a second period for pubic comment after the CoC makes it final recommendations to the NIH Director.

Dr. Anderson closed by noting that the advisory council for NCRR had begun its second-level review of applications with the expectation of a meeting on February 1, 2012. The review was completed for most applications, but a small number of applications had not yet been reviewed by the time NCRR was dissolved. Dr. Anderson noted that three members from the former NCRR advisory council were thus serving as discussants for this meeting and that they had completed the second-level review of the remaining applications. He added that the CoC would consider motions to accept early concurrence with the NCRR reviews for this round of applications.

Discussion Highlights

- The CoC will continue to vote to approve, approve with recommendations, defer, or disapprove concepts even though concepts will be presented at earlier stages in their development. Advisory councils for lead ICs will be tasked with later-stage concept clearance. Council members appreciate DPCPSI's desire for CoC input on a broader range of topics and the influence the CoC will have in the initial selection of concepts for further development. The CoC also understands that ICs, which will take over projects as they move out of the Common Fund, should be involved in concept clearance. However, some Council members feel that CoC should also be responsible for providing a later-stage review of developed concepts while they remain in the Common Fund. DPCPSI will continue to discuss the CoC's role in concept clearance and welcomes written comments.

- DPCPSI houses a wide range of activities in several areas, but it does not try to do everything in every area. In some areas, such as disease prevention or behavioral and social sciences research, the Division works with the ICs and its role is limited primarily to coordination and prioritization. In others, such as some areas of research infrastructure, DPCPSI manages the entire program for NIH.

- ODP works closely with the Centers for Disease Control and Prevention. Other potential partnerships will be decided by the new ODP Director.

- DPCPSI has projects, such as the Common Fund Health Care Systems Research Collaboratory, that focus on health outcomes and barriers to care, and Council input is invited on additional concepts for outcomes-focused projects.

- Some DPCPSI offices, such as OAR and ORWH, have their own advisory council/committee. DPCPSI welcomes ideas on how CoC can participate in an oversight or advisory capacity for the offices without their own advisory councils such as ODP, OBSSR and ORIP (which includes OSE). One of the Council members suggested that DPCPSI might consider having CoC members serve as liaisons to existing advisory committees for other DPCPSI offices. Dr. Anderson commented that these councils already had their own statutory governance structures.

- Because ORIP houses activities supporting research across all ICs, consistent with the mission of DPCPSI, the Division sees no immediate need for reconfiguring these activities.

- DPCPSI should consider developing an overall strategic plan as it works to become a seamless unit.

- DPCPSI does not have resources to support information technology infrastructure projects. However, NIGMS has mechanisms in place to support projects in computational research technology.

III. REMARKS BY THE NIH DIRECTOR

Dr. Collins noted that the promise of biomedical research has never been more exciting, and NIH faces the challenge of being a proper steward for the close to $31 billion for research entrusted to it by taxpayers, the Administration, and Congress. There are many opportunities to use the funds in exciting ways, and at the same time, the scientific research community must continue to make a case for the value of biomedical research not only in advancing human health, but also for benefiting the economy. NIH and the scientific community are engaged in a noble enterprise, that of understanding biology at a fundamental level and applying that understanding to improve human health.

Dr. Collins pointed out that 83% of the NIH goes to extramural research programs and that the distribution of funds to applied and basic research has not changed. He noted concerns that the recent push toward translational research means that NIH is no longer interested in basic science, but he assured the Council that that is not the case. The basic science supported by NIH is mostly in areas no one else would take on, and it serves as a foundation for new therapeutic discoveries. For example, the FDA has recently approved a cystic fibrosis drug that will provide substantial benefit to patients carrying a specific genetic mutation. This drug would not have been developed without NIH-supported work leading to discovery of the cystic fibrosis transmembrane conductance regulator gene. Dr. Collins emphasized that the future breakthroughs will require continued investment in basic science research.

In addition, Dr. Collins noted continued concerns about grant success rates, which have fallen substantially since the NIH budget doubling ended in 2003. The success rate for 2010-11 has fallen to 20% or even a bit less, which Dr. Collins acknowledged is very unhealthy. However, he also noted that as long as budget remains unchanged and the number of applications remain where they are, there is no easy solution. Dr. Collins expressed particular concern about early-stage investigators, who are trying to fund their laboratories, embark on stable careers, and propose innovative research in a climate where high risk research might be perceived as less acceptable than when there was a freer flow of funding.

Dr. Collins announced that Dr. Chris Kaiser will join NIH in April 2012 as the new director of NIGMS, one of the strongholds of basic research. He then turned his remarks to the extraordinary opportunities NIH has even in a severely constrained funding

environment. One such opportunity continues to be NIH's investments in basic research; 135 Nobel Prize-winning scientists have been supported by NIH. Extraordinary opportunities also abound in the acceleration of discovery through technology. DNA sequencing has become more efficient and accurate and dramatically less expensive, to the point where a single postdoctoral fellow has been able to define the epigenome of a human pancreatic islet cell. The discovery of human induced pluripotent stem (iPS) cells has yielded a tool not only to learn more about human development and the basic biology of disease, but also to model disease *in vitro* and screen potential therapeutic compounds without depending on animal models or exposing patients prematurely. Several iPS cell lines have been made for a wide variety of diseases. Recent work also has pointed to the potential use of iPS cells as cell therapy by removing iPS cells from a patient, repairing them and differentiating them into healthy cells, and introducing them back into the patient with a lower risk for rejection. A new Center for Regenerative Medicine has been established at the NIH to facilitate the application of iPS cells to new technologies.

The ability to advance translational sciences represents another extraordinary opportunity for NIH. Across diseases and potential therapeutics, the ability to develop a small molecule into an FDA-approved therapeutic remains challenging. Only one in 10,000 compounds makes it to FDA approval, and then only after an average of 14 years in development. Thus the cost of success is about $2 billion, when factoring in all the failures. Recently the Scientific Management Review Board reported that NIH has an opportunity, and even a responsibility, to organize efforts focused on the development pipeline to improve the rate of compounds moving forward. This suggestion led to the establishment of NCATS.

NCATS does not aim to replace therapeutic development in NIH ICs; rather, it aims to address bottlenecks within the pipeline, such as the ability to choose the right targets to develop. With the explosion of information in human genetics and molecular biology, NIH-supported scientists have an opportunity to identify potential therapeutic targets in new ways. Even now there are so many potential therapeutic targets that the pharmaceutical industry looks to NIH for help in filtering the list. Recently NIH leaders met with the leadership of pharmaceutical research and development to identify new ways to use genetics and genomics to identify appropriate drug targets. One promising example involves mutations in the PCSK9 gene, which might serve as a new target for cholesterol management.

Another potential bottleneck in drug development is toxicity, the most common reason for drug development failures. The methods for assessing toxicity, such as dose curves in animals and assessments of side effects, have not changed over the years and are not reliable methods. The NIH started very recently, as part of the Common Fund Regulatory Science Program, a collaboration with DARPA and the FDA to develop a chip with various human cell types to identify signals of toxicity. This project includes the differentiation of iPS cells into various cell types and the inclusion of genomics, epigenomics, proteomics, and metabolomics to provide readouts of toxicity. NCATS is also exploring the ability to identify abandoned compounds that might be repurposed for another use, thereby bypassing a lot of steps in the drug development pipeline. NIH is in talks with the pharmaceutical industry to develop a plan where NIH serves as an "honest

broker" to examine such compounds. Such an initiative could be particularly helpful in addressing rare diseases.

A mission statement, Web site, and organizational structure are in place for NCATS, and it is expected that this Center will not have the same wall between intramural and extramural research as do other NIH ICs. Dr. Collins emphasized that NCATS aims not to compete with the private sector or duplicate ongoing drug development in the ICs. Nor does this reduce NIH's commitment to basic research. Rather, NCATS will complement existing drug development efforts and can strengthen NIH's case for the value of research in promoting health. In addition, the establishment of NCATS could also be helpful to basic science investigators who might hesitate to advance their ideas.

Dr. Collins also discussed extraordinary opportunities in encouraging new investigators and new ideas. NIH has five programs, four of which reside in the Common Fund:

- The NIH-Lasker Clinical Research Scholars program to encourage new clinical researchers.
- The Transformative Research Award, NIH Director's Pioneer Award, and the New Innovator Award to encourage bold ideas.
- The Early Independence Award, to shorten the time for a new investigator to become independent.

Dr. Collins pointed out that the presentations given by the 10 new Early Independence Award winners were bold, innovative, and energetic. Moreover, five of *Forbes* magazine's Science and Innovators 30 under 30 are Early Independence awardees. Dr. Collins expressed his desire for the Early Independence Award program to expand.

NIH is also looking at the biomedical research workforce itself. Dr. Sally Rockey, Deputy Director for Extramural Research, and Dr. Shirley Tilghman, President of Princeton University, are co-chairing an Advisory Committee to the Director (ACD) Working Group on the Future Biomedical Research Workforce, which will develop a model incorporating all inputs and outputs for the workforce. Dr. Collins also noted that the scientific research community should consider not only the needs of academia, but also explore other career paths for doctoral students without stigmatizing them as "alternative careers."

Dr. Collins also expressed concern that despite a large amount of investment, NIH has not succeeded in making biomedical research careers appealing to members of underrepresented minority groups, and those who do go into research do not enjoy the same grant success as their non-minority counterparts. Dr. Collins and NIH Deputy Director Dr. Lawrence Tabak have published an editorial to express their concern and to outline efforts under way. Such efforts include an evaluation of current programs, an examination of the grant review process and develop interventions for bias, efforts to improve support and mentoring for grant applicants, an increase in the number of early-career peer reviewers, and an ACD working group on diversity.

Dr. Collins closed his remarks by noting that despite budgetary concerns, NIH has a lot to be excited about and that the country continues to believe that biomedical research should have continued support.

Discussion Highlights

- The Early Independence Award does not have an age cutoff. Applicants must be within a year of their final training at the doctoral level.

- It is difficult for universities to keep their balance sheets sustainable with the drop in grants success rates and administrative burdens such as regulatory requirements and the recently instituted salary cap. Unfortunately, many universities are considering tuition increases when a college education is already expensive. NIH is discussing ideas with the Association of American Medical Colleges (AAMC), the Association of American Universities, and the Association of Public and Land-grant Universities. Dr. Collins also encouraged CoC members to submit ideas.

- A major challenge will be the deluge of data coming from advances in sequencing, increased availability of electronic medical records, and other developments. Dr. Tabak is leading an ACD working group and an internal group to assess NIH resources and ensure they are appropriate to deal with the explosion of new information. One challenge is the ability to keep resources such as the National Center for Biotechnology Information viable at a time when overall funding is not growing.

- Many CTSAs have been formed with several capabilities, but they have not been allowed to build on their special talents, and NIH has not capitalized on the diversity of talent across these sites. In addition, the intent for the CTSA program to build a linked enterprise for joint projects has been only partially realized. Existing CTSAs are encouraged to reorganize their goals, and a new request for applications will be released in June 2012.

- Graduate medical training is under threat from a loss of $10 billion per year. Such severe financial constraints might push individuals who were interested in clinical research to focus solely on clinical care. Although NIH cannot directly influence the medical pipeline, leadership recognize that the future of clinical research depends on the provision of training opportunities. NIH is in talks with AAMC.

- In its discussions with the pharmaceutical industry, NIH is working to identify and develop partnerships to support projects NIH cannot conduct alone. NIH is also working more closely with other Federal agencies, including the Centers for Medicare and Medicaid Services, the Centers for Disease Control and Prevention, FDA, and DARPA, and it is talking with private foundations.

IV. WORKING GROUP ON THE USE OF CHIMPANZEES IN NIH-SUPPORTED RESEARCH

A motion was forwarded to establish a CoC Working Group on the Use of Chimpanzees in NIH-Supported Research. This working group will be charged with identifying ways to implement the recommendations and principles of the IOM report. In response to questions from the Council, Dr. Anderson emphasized that the working group's charge would be limited strictly to NIH-owned chimpanzees and NIH-supported chimpanzee research projects. He reminded the Council that although the IOM feels that the continued use of chimpanzees should be very limited, it recognizes that there are or will be areas where such research is needed. The Working Group will not revisit the question of whether to use chimpanzees, but it will focus solely on how to implement the report.

The motion passed unanimously. Co-chairs and members have accepted their appointments. Updates will be given to the CoC at the June and September meetings.

V. INTRODUCTION TO THE OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS (ORIP)-SCIENCE EDUCATION

Dr. Anderson told the Council that he wants them to be very familiar with the programs and function of the ORIP, noting that the presentations would start with an overview of the Office of Science Education (OSE). He indicated that NIH has a terrific opportunity to bring together activities of OSE with the Science Education Partnership Award grant program which moved to DPCPSI from NCRR.

A. Office of Science Education

Dr. Bruce Fuchs, OSE Director, pointed out that the United States is in "the middle of the pack" or worse in international assessment exams for science and math education and that contrary to popular opinion, the best science and math students in the United States are not the best worldwide. Between 1850 and 1970, the United States led the world in several measures of educational attainment, and in the years after World War II, as gross domestic product (GDP) doubled, so did median household income. Now the United States is not even among the top 20 nations with respect to a high school diploma, nor is it in the top 10 nations with respect to a college degree. A study for the World Bank has found a strong correlation between the performance of a nation's students on these international assessment exams and the rate of growth for that nation's economy. The data also indicate that society needs both highly educated innovators, and a well-educated workforce to sustain industries created by innovations. These data appear to be supported by trends in the United States. Median earnings for men peaked in 1973, and even though the GDP has doubled since then, median household incomes have only risen slightly. Thus, in the United States, the negative consequences of declines in education, especially on the economic well-being of our middle class, have already begun.

OSE was founded in 1991 as the Office of Science Education Policy. Since then the Office has represented NIH interests in on many Federal initiatives and committees. With a budget of $4 million per year and a staff of eight Federal employees and seven

contractors, OSE plans, develops, and coordinates a comprehensive science education program to strengthen and enhance NIH's efforts to improve overall science literacy and to attract individuals to biomedical and behavioral science careers. It has become a popular rotation destination for American Association for the Advancement of Science Fellows, Einstein Fellows, Presidential Management Interns, and others. OSE emphasizes the creation of tools and resources to aid science teachers across the nature.

Premier among these tools is the NIH Curriculum Supplements Series. In collaboration with ICs and curriculum development experts, OSE has developed 19 curriculum supplements that pair cutting-edge NIH research with innovative curricular content. The curriculum supplements contain 1 to 2 weeks of lesson plans and are aligned with state education standards. More than 400,000 supplements have been requested by more than 90,000 educators in more than 16,000 ZIP codes. Other tools include a Web portal to help teachers identify resources by topic, grade level, and format, and the LifeWorks® Web site, which helps middle- and high-school students explore careers in science. LifeWorks® provides a searchable database and profiles over 200 different careers in the health and biomedical sciences. An example of another science education activity was Dr. Collins demonstrating a strawberry DNA precipitation at McKinley High School, which led to U.S. Secretary of Education, Arne Duncan, challenging NIH to develop 100 similar activities for teachers to try with their students. NIH has solicited ideas for such activities through challenge.gov and will be publishing the winning entries later this year. OSE has also sponsored a series of National Academy of Sciences Workshops on 21st Century Workplace Skills to demonstrate that certain skills valued in the workplace were similar to skills that could be taught and practiced in STEM courses. These skills, e.g., problem solving and data analysis) are valued outside traditional STEM careers. The workshop series has spurred a consensus conference which is being funded by several private foundations, and will lead, in about a year and a half, to a consensus paper on necessary skills in the workforce.

OSE continues to work with the ICs to connect educational programs to national education priorities and break down research silos. A final draft of a 5-year strategic plan for Federal STEM education investments is also under development by the OSTP/NSTC Committee on STEM Education, and NIH will align its educational programs with that. OSE is also working to align all NIH educational resources to Common-Core State Science Standards. The District of Columbia and 46 states have already signed on to core standards in English, language arts, and mathematics.

Dr. Fuchs pointed out that textbook development will be driven by the common core standards in science. He closed his presentation by noting President Obama's call for all scientists who work for the Federal government to do their part in promoting science education.

Discussion Highlights

- Education in the United States is currently driven by No Child Left Behind Act, which aims to have all students proficient in reading and math by 2014. However, the Obama Administration agrees that No Child Left Behind should be reauthorized to

change the target to ensuring that all children graduate high school "college or career ready." If good assessments are developed to support the common core standards, these standards and assessments will be used to drive the quality of instruction.

- In line with Dr. Collins' call to support all science careers, efforts should be made to encourage interested doctoral and medical students to careers in science education. Lessons can be learned from Finland, which has limited the number of slots in schools of education, thereby increasing the social capital associated with becoming a teacher. As a result, teachers are drawn from students in the top 15% of the college population.

- OSE should consider employing a fraction of its budget to identify and recruit talented undergraduates into science education. Lessons can be learned from a program at Tuskegee University, which recruits students with honors-level grade point averages.

- Many doctoral students are looking at other science careers but do not know how to make that transition. NIH should consider an innovative postdoctoral fellowship, for example to help such students move into science education while maintaining a presence in university laboratories.

- OSE should consider using its web site to provide a portal to alternative state certification pathways for scientists who wish to become science teachers.

B. Science Education Programs from NCRR

Dr. Ramm described the Science Education Partnership Awards (SEPA) program, which helps scientists and clinicians collaborate with educators, community organizations, and science centers to increase participation of diverse population of elementary, middle, and high-school students in basic and clinical research. The SEPA program includes science museums to educate the public about NIH-funded research and links to health. A SEPA funding opportunity announcement is released every 3 years and uses the R25 mechanism to provide approximately $1.3 million for 5 years. Any nonprofit organization can apply in any NIH-supported research area, and collaborations are strongly encouraged. Applicants must show innovative pedagogy, align with state and national education standards, and include a rigorous evaluation plan.

The program currently funds 48 university projects and 11 science museum projects. In FY 2010, SEPA projects reached more than 82,000 students and 5,700 teachers at more than 2,000 schools. SEPAs are widely distributed across the United States and have multiple areas of focus. In addition, SEPA projects have collaborated with other NCRR award sites, such as CTSAs and Institutional Development Awards (IDeAs), which are available to states that typically receive only 5% to 7% of NIH funds. These collaborations have supported a pipeline of students from elementary and high school into universities with IDeAs or CTSAs. Successful SEPAs include:

- The University of Alabama at Birmingham GENEius program, a collaborative effort among the Center for Community Outreach Development, the Birmingham City Schools, and the McWane Science Center. This program includes a strong professional development piece for teachers and several summer and weekend programs where high-school students work with graduate students and staff.
- The University of Utah's Genetic Science Learning Center, which houses an award-winning Web site and holds Genetics 101 for the Masses, a course that teaches about genetics, epigenetics, stem cells, evolution, and the genetics of addiction. The Center has a web-based professional development program for teachers and strong community outreach.
- Wake Forest University's Center of Excellence for Research, Teaching, and Learning, which promotes problem-based learning, reinforces existing knowledge, and has 171 high-school mini-fellowships. Many students who have participated in the Center have gone on to matriculate at a 4-year college in a STEM major. Almost half of the students are underrepresented minorities, and more than half are first-generation college students.
- The Yale University Peabody SEPA, which is focused on climate change patterns and vector-borne disease. Like other SEPAs, this program has a strong component devoted to professional development for teachers.
- Project Advancing Rhode Island Science Education (ARISE), which has several activities for high school biology teachers. Project ARISE is no longer a funded SEPA, as it has become self-sustaining through other sources of funding.

Dr. Ramm also noted that CTSAs at Boston University and in Pittsburgh have developed mobile laboratories that travel around their respective States and attract high school students to science careers by having them conduct sophisticated experiments. In 2010, approximately 5,000 students participated in the Boston mobile laboratory, and more than 3,500 students participated in the Pittsburgh mobile laboratory.

Discussion Highlights

- Despite difficulties in establishing a control group, approximate baselines should be established to better assess the progress associated with SEPA programs.
- Ten percent of the SEPA budget is devoted to evaluation, and awardees are required to have both external and internal evaluators. The SEPA program itself has undergone a feasibility study, and a process evaluation of the program is underway.
- None of NCRR's education programs has been eliminated; they have been transferred to other areas. DPCPSI will inventory science education activities in order to identify areas of synergy and determine the best way forward.

VI. OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS

Following discussions of educational programs, Dr. Ramm introduced other ORIP components. Among these is the Division of Comparative Medicine (DCM), which houses the National Primate Research Center (NPRC) Program, the Chimpanzee Management Program and Sanctuary, Biorepositories and Other Resources, research project grants, and career development and training programs.

- The NPRC Program was established in the 1960s and currently supports eight centers that work together in a consortium. These centers provide researchers with access to more than 27,000 non-human primates representing 20 species, and they provide infrastructure support to approximately 2,000 scientists funded by more than 1,000 NIH grants. NPRCs facilitate research in aging, dementia and other neurodegenerative diseases, HIV/AIDS, reproductive biology, and re-emerging infections such as tuberculosis.
- The Chimpanzee Management Program includes several cooperative agreements and contracts that support the long-term housing and maintenance of facilities nationwide. Dr. Ramm noted that the terms of the Chimpanzee Management Plan will be guided by the recommendations of the Council's Working Group on the Use of Chimpanzees in NIH-Supported Research. The Chimpanzee Sanctuary is supported under an NIH contract and houses about 130 animals. A new request for proposals in support of the sanctuary was issued, proposals have been reviewed, and an award will be made in 2012 for the sanctuary.
- DCM supports several biorepositories, including the National Resource for Zebrafish, the Caenorhabditis Genetics Center, the National Stem Cell Resource, and several biorepositories housing rodent and other mammalian models. In addition, ORIP is one of three NIH components that assist in supporting the Bloomington Drosophila Stock Center, which is supported primarily by the National Science Foundation.
- ORIP supports a number of career development and training programs and is the only Office across all of NIH that supports training for veterinarians interested in research.
- ORIP also supports several R01 and R21 research project grants across a wide range of disease areas and across the interests of several components of NIH. Examples include development of a zebrafish model for studying Fanconi anemia, stem cell therapies for tissue repair, and symbiosis between squid and bacterial toxin as a model for organ development.

DCM also supports a resource and Web site, Linking Animal Models to Human Disease Initiative (LAMHDI), which assists investigators in identifying the best animal model for their areas of interest.

Another ORIP component is the Division of Instruments, Infrastructure Resources, and Construction. This Division houses the Shared Instrumentation and High-End Instrumentation Grant programs, which support the purchase of large equipment that would otherwise consume a significant percentage of an individual investigator's grant.

These programs were augmented by funds from the American Recovery and Reinvestment Act of 2009 (ARRA). The Division also includes the Construction/Renovation Award program, which supports major alterations and renovations. Initiated in 1994, this program reached a budget of $115 million in FY 2004, but the budget was cut dramatically in 2005 and received no additional funding until ARRA, which infused $1 billion. Another program supports minor alterations and renovations, defined as those costing $500,000 or less. According to the terms and conditions of awards, ORIP must monitor NIH-supported facilities for 20 years after construction is completed to ensure they are used for biomedical research.

Dr. Ramm concluded by noting that construction awards in 2009 and 2010 were disbursed across the entire nation, because the wealth of meritorious applications allowed NCRR to employ a geographic distribution. Dr. Ramm also acknowledged NCRR program staff and the NIH Center for Scientific Review, who worked hard to review applications and make awards in the short time allowed by ARRA. She further noted that from the time an award is disbursed to the time construction is complete, projects are monitored by high-level NIH staff who review every phased of construction.

Discussion Highlights

- Most stock centers provide resources on a cost-recovery basis.

- NPRCs must undergo a thorough site visit and review every 5 years. Their renewed funding depends on the results of these reviews.

- Even though DCM and the CTSA program have moved to different NIH entities, program staff still works in the same building and maintain their interactions.

- A more effective system is needed to evaluate the success of the Shared Instrumentation and High-End Instrumentation grant programs. These grants are provided only for 1 year, and progress reports do not show how effective these programs are. NCRR, and now ORIP, asks for help from the scientific community in ensuring that instrumentation grants are cited in publications. ORIP can also measure effectiveness by noting applications for the next generation of instruments already purchased with NIH funds.

- Particularly at a time when funds are limited, measures are needed to identify, evaluate, and eliminate redundant and duplicative core facilities. Research is needed to explore the impact of core facilities, their management, and their challenges. At some institutions, efforts are under way to consolidate or unify core facilities.

- NIH can assist in core consolidation by increasing investigators' access to all cores, making institutional track record a review criterion, and increasing competition among companies that manufacture equipment. For ideas on increasing access, NIH can look to the Virginia Genetics Network of core facilities. This network has a searchable database to help investigators identify cores that have the capabilities they need.

- The transition from NCRR to DPCPSI and other entities was planned carefully to assure continued coordination and to keep successful functions from getting lost. DPCPSI is reviewing existing interactions between its new programs and other former components of NCRR.

- DPCPSI is continuing to examine how to strategically plan for the activities to be undertaken and supported by OSE and ODP, and the Council will be asked for input in the future.

- Because of the diversity of functions that have shifted from NCRR to DPCPSI, the responsibilities of CoC have grown.

VII. CONCEPT CLEARANCES

Dr. Franziska Grieder, DCM Director, presented two concepts to the Council. Any initiatives resulting from these concepts would be funded by DCM, not the Common Fund, and DCM hopes to secure co-funding from other ICs.

Ms. Kawazoe reminded the Council that DPCPSI will ask for a motion, discussion, and vote and that concepts are cleared by a single majority. If a concept is deemed unlikely to achieve its goals, CoC will be asked for specific recommendations. Once the recommendations have been incorporated into the proposed concept, it is not necessary to bring the revised concept back to CoC for discussion.

A. Gene Discovery for Common Diseases via the Collaborative Cross Mouse Project

Genome-wide association studies (GWAS) have identified many common genetic variants that are associated with specific traits or influence disease. However, finding the association of genetic variants with specific traits can more definitely be performed in laboratory settings and in individuals with known genetic backgrounds. The Collaborative Cross (CC) is a panel of up to 1,000 mouse strains generated from eight founding laboratory and wild-type mouse strains through a series of pair-wise screening and inbreeding. Each strain in the CC is isogenic and homozygous at every locus. This concept clearance would use mouse strains housed in a Mutant Mouse Regional Resource Center, another DCM-supported resource.

DCM proposes an initiative to fund R01 projects using CC strains in challenge studies to identify genes that cause human diseases with complex genetics. The National Cancer Institute, the National Institute on Aging, and the National Institute of Environmental Health Sciences have expressed an interest in co-funding this initiative. Studies could explore nutritional, physiological, infectious, or immunologic challenges, and proposals to identify potential drugs and biomarkers would be given high priority. Dr. Grieder envisioned a DCM database that would require R01 grantees supported under this initiative using CC strains to deposit their data, positive or negative, so that it would be available to other CC investigators.

Discussion Highlights

- The proposed database will need clear ontologies for the description of phenotypes and transcriptomics. Although harmonization of bioinformatics has not yet been addressed, Dr. Grieder expected that it would be integral to the initiative.
- DCM could consider using the cooperative agreement mechanism, encouraging a cooperative group that agrees on a common ontology.
- The need for the CC mouse model system might have already been bypassed by advances in sequencing technology to be used in humans. DCM should consider convening a panel of experts to assess whether we are more likely to discover disease associated genes by the next generation of GWAS, the full sequence GWAS, or via CC-based model systems.
- As illustrated by findings in a recent *Nature Genetics* paper, the genome is not static across generations. How this drift will affect studies using CC mice should be considered.
- Although CC strains have been successfully used in two studies, it is not clear whether CC studies will have enough power to assess epistasis at the effect sizes that have already been identified in human diseases.
- DCM should consider requiring that common measures be collected in CC-supported studies to strengthen the CC database as a resource.
- DCM should consider conducting an evaluation, after the first set of grants has been awarded, to gauge the success of the initiative.
- CC is aligned with similar initiatives around the world..
- DCM/ORIP/DPCPSI is expected to oversee the CC initiative.

A motion to defer a recommendation on this concept was forwarded and seconded. Deferral would allow DCM to provide the Council with more information and clarify areas of ambiguity. During the discussion, some Council members expressed support for the initiative, with the view that CC could be a powerful resource and that the proposed initiative could be done in parallel with advanced sequencing efforts in human subjects.

The motion for deferral passed, with 12 votes for, 9 votes against, and 2 abstentions.

B. Development of Translational Animal Models for Rare Diseases

The Institute of Medicine has identified 8,000 serious diseases as rare, and almost 70% of these diseases have been shown to arise from defects in single genes. Because these diseases affect relatively few patients, and because there is less interest in studying them, little is known about rare diseases. Yet NIH continues to have a significant interest in them. Existing gaps between genetic association studies and translational models could be bridged by new technologies, including the Human Genome Project, faster and cheaper DNA sequencing, exome sequencing, and advances in the manipulation of model organism genomes.

DCM proposes an initiative to support studies that will produce and characterize genetically modified animals carrying mutations analogous to those in patients with rare diseases. Such an initiative would not be restricted to mouse models. Rather, it would support the development of a wide range of models, from single-cell organisms to flies, zebrafish, and mammalian models. Investigators supported by the initiative would be clinical scientists who work with rare disease patients collaborating with researchers who are experts in genetic modification of models and model characterization. The funded researchers would share their characterized animals, associated biomaterials, and expertise.

Discussion Highlights

- The best models might also focus on disease-modifying genes, as opposed to just the major genetic defect.
- DCM does not envision the creation of humanized mice. Instead, it aims to support the development and sharing of models that validate mutations.
- DCM should also consider including low-passage human tumor xenografts from common cancers and other diseases.
- The initiative will emphasize not only the targeting of specific mutations, but also the phenotypic characterization of them.
- The proposed initiative will align with the National Human Genome Research Institute-National Heart, Lung, and Blood Institute initiative to create Centers for Mendelian Disease Genomics. These Centers aim to sequence genomes from rare-disease patients around the world. The DCM initiative will complement this effort by supporting additional biological research.

A motion to accept this concept as proposed was forwarded and seconded. The motion passed unanimously.

VIII. REVIEW OF GRANT APPLICATIONS

This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c)(4), 552b(c)(6), Title 5 U.S. code, and 10 (d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2). Members were instructed to exit the room if they deemed that their participation in the deliberation of any matter before the Council would be a real conflict or that it would represent the appearance of a conflict. Members were asked to sign a conflict-of-interest/confidentiality certification to this effect. The *en bloc* vote for concurrence with the initial review recommendations was affirmed by all Council members present. During the closed session of the meeting the Council reviewed 251 applications with total direct costs of $112,807,362.

IX. CLOSING REMARKS

Dr. Anderson thanked Council members and especially the discussants for their work at this meeting and for helping DPCPSI through the transition. He reviewed several themes and action items from the meeting:

- DPCPSI is in evolution; it has different parts, and we are still learning how the parts can best work together.
- DPCPSI will review SEPA and OSE and prepare a more in-depth presentation on how to move forward.
- CoC will hear an update from the Working Group on Chimpanzees in NIH-Supported Research.
- The CoC will conduct the second level review of grant applications using early concurrence at its next meeting.
- It is expected that a new Director of the Office of Disease Prevention will be selected by the next meeting, and a plan will be presented for strategic review of that office at a later CoC meeting.

X. ADJOURNMENT

Dr. Anderson adjourned the meeting at 4:43 p.m. on February 1, 2012.

XI. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing summary minutes are accurate and complete.

James M. Anderson, M.D., Ph.D.
Chair, NIH Council of Councils
Director, Division of Program Coordination,
Planning, and Strategic Initiatives (DPCPSI)
Office of the Director (OD)
National Institutes of Health

3-8-2012
Date

Robin I. Kawazoe
Executive Secretary, NIH Council of Councils
Deputy Director, DPCPSI
OD, NIH

3/8/2012
Date