

**Meeting Minutes**  
**Department of Health and Human Services**  
**National Institutes of Health**  
**National Institute of Diabetes and Digestive and Kidney Diseases**

**I. CALL TO ORDER**

*Dr. Rodgers*

Dr. Rodgers called to order the 193rd meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m., Thursday, September 26, 2013, in Building 31, C-Wing, 6th Floor Conference Center, Conference Room 10, NIH Campus, Bethesda, Maryland.

**A. ATTENDANCE – COUNCIL MEMBERS PRESENT**

Dr. Domenico Accili  
Dr. Sharon Anderson  
Dr. Gopal Badlani  
Dr. Judy Cho  
Dr. Gregory Gores  
Ms. Jane Holt  
Ms. Judy Hunt  
Dr. Francine Kaufman  
Dr. Kenneth Kaushansky  
Ms. Robin Nwankwo

Dr. Jerry Palmer  
Dr. Thomas Robinson  
Dr. Anil Rustgi  
Dr. Alan Shuldiner  
Dr. Irving Smokler  
Dr. Bruce Spiegelman  
Dr. William Steers  
Dr. Robert Vigersky  
Dr. Mark Zeidel

**Also present:**

Dr. Griffin P. Rodgers, Director, NIDDK and Chairperson, NIDDK Advisory Council  
Dr. Gregory Germino, Deputy Director, NIDDK  
Dr. Brent Stanfield, Executive Secretary, NIDDK Advisory Council

**B. NIDDK STAFF AND GUESTS**

Abankwah, Dora – NIDDK  
Akolkar, Beena – NIDDK  
Andersen, Dana – NIDDK  
Arreaza-Rubin, Guillermo – NIDDK  
Barnard, Michele – NIDDK  
Bavendam, Tamara – NIDDK  
Begum, Najma – NIDDK  
Bishop, Terry – NIDDK  
Bleasdale, John – CSR  
Blondel, Olivier – NIDDK  
Bourque, Sharon – NIDDK  
Buchanan, Sarah – The NephCure FDN  
Camp, Dianne – CSR  
Carrera, Krysten – NIDDK  
Carrington, Jill – NIDDK  
Castle, Arthur – NIDDK

Cerio, Rebecca – NIDDK  
Chandrasekera, Priya – Phys. Comm. for Resp. Med.  
Connaughton, John – NIDDK  
Cowie, Catherine – NIDDK  
Curtis, Leslie – NIDDK  
Densmore, Christine – NIDDK  
Desiderio, Ulyana – Amer. Soc. Hematology  
Dirks, Dale – Health and Med. Counsel of Wash.  
Donohue, Patrick – NIDDK  
Doo, Edward – NIDDK  
Drew, Devon – NIDDK  
Duggan, Emily – NIDDK  
Eggerman, Thomas – NIDDK  
Evans, Mary – NIDDK  
Farishian, Richard – NIDDK  
Feld, Carol – NIDDK

Flessner, Michael – NIDDK  
 Fonville, Olaf – NIDDK  
 Fradkin, Judith – NIDDK  
 Gansheroff, Lisa – NIDDK  
 Garofalo, Robert – CSR  
 Giambarresi, Leo – Amer. Urology Assoc.  
 Goter-Robinson, Carol – NIDDK  
 Graves, Reed – CSR  
 Grey, Michael – NIDDK  
 Guo, Xiaodu – NIDDK  
 Haft, Carol – NIDDK  
 Hamilton, Frank – NIDDK  
 Hoover, Camille – NIDDK  
 Horlick, Mary – NIDDK  
 Hoshizaki, Deborah – NIDDK  
 Hunter, Christine – NIDDK  
 Hyde, James – NIDDK  
 Jaakso, Joseph – The Endocrine Society  
 James, Stephen – NIDDK  
 Jones, Teresa – NIDDK  
 Karp, Robert – NIDDK  
 Karimbakas, Joanne – NIDDK  
 Ketchum, Christian – NIDDK  
 Kimmel, Paul – NIDDK  
 Kirkali, Ziya – NIDDK  
 Kranzfelder, Kathy – NIDDK  
 Krause, Michael – NIDDK  
 Krishnan, Krish – CSR  
 Kuczmarski, Robert – NIDDK  
 Kusek, John – NIDDK  
 Laimon, Ben – RTI International  
 Laughlin, Maren – NIDDK  
 Leschek, Ellen – NIDDK  
 Linder, Barbara – NIDDK  
 Malik, Karl – NIDDK  
 Malozowski, Saul – NIDDK  
 Maruvada, Padma – NIDDK  
 Margolis, Ronald – NIDDK  
 Martey, Louis – NIDDK  
 McGeehan, Edward – NIDDK  
 McKeon, Catherine – NIDDK  
 Morris, Ryan – CSR  
 Moxey-Mims, Marva – NIDDK  
 Mowery, Penny – NIDDK  
 Mullins, Christopher – NIDDK  
 Newman, Eileen – NIDDK  
 Nguyen, Van – NIDDK  
 Nurik, Jody – NIDDK  
 Patel, D.G. – NIDDK  
 Pawlyk, Aaron – NIDDK  
 Perrin, Peter – CSR  
 Pike, Robert – NIDDK  
 Podskalny, Judith – NIDDK  
 Polglase, William – NIDDK  
 Ramachandran, Vasam – Boston Univ. Sch. of Med.  
 Rankin, Tracy – NIDDK  
 Reiter, Amy – NIDDK  
 Roberts, Tibor – NIDDK  
 Rosenberg, Mary Kay – NIDDK  
 Rosendorf, Marilyn – NIDDK  
 Rushing, Paul – NIDDK  
 Rys-Sikora, Krystyna – NIDDK  
 Salaita, Christine – NIDDK  
 Savage, Peter – NIDDK  
 Scanlon, Elizabeth – NIDDK  
 Sechi, Salvatore – NIDDK  
 Serrano, Jose – NIDDK  
 Sheard, Nancy – CSR  
 Sheets, Dana – NIDDK  
 Sherker, Averell – NIDDK  
 Shepherd, Aliecia – NIDDK  
 Silva, Corrine – NIDDK  
 Smith, Philip – NIDDK  
 Spain, Lisa – NIDDK  
 Star, Robert – NIDDK  
 Tatham, Thomas – NIDDK  
 Torrance, Rebecca – NIDDK  
 Wallace, Julie – NIDDK  
 Wilkerson, Anita – NIDDK  
 Woynarowska, Barbara – NIDDK  
 Wright, Elizabeth – NIDDK  
 Vieweg, Johannes – Amer. Urological Assoc.

## C. ANNOUNCEMENTS

Dr. Rodgers made the following announcements.

### **Council Members Completing Their Terms**

Dr. Rodgers expressed appreciation to five Council members who were completing their terms with the September 2013 meeting.

***Retiring from the Digestive Diseases and Nutrition (DDN) Subcouncil:***

- **Dr. Gregory Gores** has provided insightful scientific expertise coupled with the perspective of a career physician-scientist. He has contributed insights gained from working on the cutting edge of exploration into the fundamental mechanisms of cell injury and death, and on the translation of these findings into approaches to manage and ultimately treat patients with liver diseases. Dr. Gores' leadership in advancing scientific understanding of liver diseases and liver cancer is widely recognized--as reflected in his election as President of the American Association for the Study of Liver Diseases in 2007 and President of the International Liver Cancer Association in 2009. As the Ruben R. Eisenberg Endowed Professor and Chair in Gastroenterology and Hepatology at the Mayo Clinic, Dr. Gores has also demonstrated an extraordinary commitment to mentoring junior investigators and faculty. In early 2013, Dr. Gores was appointed the Mr. and Mrs. Ronald F. Kinney Executive Dean for Research at the Mayo Clinic. This position will undoubtedly bring further opportunities to guide the direction of basic-translational research and to mentor the next generation of physician-scientists.
  
- **Ms. Jane Holt**, a survivor of chronic pancreatitis, recognized an acute need for greater awareness and education with respect to diseases of the pancreas. To that end, she founded the National Pancreas Foundation in 1988. In recognition of the work she has done in the area of pancreatic research, she was named a member of the Executive Board of the Digestive Disease National Coalition in 2003 and the Chair in 2010. Ms. Holt was also appointed to the National Commission on Digestive Disease in 2006, and served as Chair of the Commission's Pancreas Working Group. She played an important role in the Commission's development of a Research Plan, which assessed the state-of-the-science in digestive diseases and the related NIH research portfolio, with a view toward identifying areas of research challenge and opportunity. During her tenure on the NIDDK National Advisory Council, Ms. Holt has distinguished herself as an informed, committed, and proactive member. She furthered NIDDK's review of its pancreas research portfolio, and played a major role in organizing two very successful workshops on the pancreas. Through the National Pancreas Foundation, Ms. Holt has continued to enhance pancreas research with mentoring efforts that match medical students and residents interested in pancreas research with senior clinicians and investigators in the field.
  
- **Dr. Anil Rustgi** has brought to the NIDDK Council many skills in basic research, medical education, patient care, and administration. Editor of the journal *Gastroenterology* from 2006 to 2011, Dr. Rustgi has a deep and broad knowledge of the fundamental biology of the digestive system, which he has shared with the Council. Dr. Rustgi is well known as an outstanding mentor to numerous trainees and faculty members, and his probing questions and suggestions often center on ensuring support for junior scientists. During the NIDDK's review of its Research Centers Program, the Center that Dr. Rustgi directs at the University of Pennsylvania was recognized as a model of excellence. Importantly, Dr. Rustgi played a key role in launching DDN's first consortium study devoted to a basic research subject, namely the NIDDK intestinal stem cell consortium. He was also instrumental in developing the Division's Exocrine Pancreas Program by organizing and publishing the proceedings of an important NIDDK workshop on acute and chronic pancreatitis in 2012. In May 2013, Dr. Rustgi became the President of the American Gastroenterological Association, which will clearly benefit from his knowledge and his leadership skills.

### ***Retiring from the Diabetes, Endocrinology and Metabolic Diseases (DEM) Subcouncil:***

- ***Ms. Judy Hunt*** is dedicated to combating type 1 diabetes through research, education, and advocacy. Since her daughter developed type 1 diabetes in early childhood, Ms. Hunt has devoted her remarkable talents to improving the lives and health of those with the disease, and to finding a cure. She has helped to shape the research agenda of the Juvenile Diabetes Research Foundation, which supports a wide range of research studies on type 1 diabetes. Ms. Hunt has brought keen insights and vision to the NIDDK Advisory Council. Over the past four years, she has helped the NIDDK advance its diabetes programs. Her contributions will extend well beyond her Council term as the Institute continues to benefit from initiatives that were begun during her term. She avidly pursues every opportunity to uncover new approaches to therapy and never hesitates to explore important questions and issues in diabetes research. She has greatly enriched the Council with her insights.
- ***Dr. Francine Kaufman*** has helped to shape a wide array of childhood diabetes research at the NIDDK. After devoting years to studying and treating type 1 diabetes, she recognized the emerging public health threat of type 2 diabetes in children. She led the development of two NIDDK studies: (1) the TODAY study, a major comparative effectiveness trial to determine how best to treat type 2 diabetes in children, and (2) the HEALTHY study, a school-based study to try to prevent the disease. Her passion for combating childhood diabetes also led her to work in industry in order to accelerate development of the artificial pancreas. The NIDDK Council has benefited from her broad and compassionate perspective, which includes caring for diabetes patients in the poorest communities of Los Angeles. Her expertise also derives from working on issues in public policy and public health, designing clinical trials, bioengineering an artificial pancreas, and developing approaches to provide insulin in communities that lack refrigeration.

### **Past and Current Council Members**

***Dr. Nancy Andrews*** will be presented with the Henry M. Stratton Medal for her accomplishments in the field of iron homeostasis by the American Society of Hematology (ASH) at their annual meeting in December. A former Council member, Dr. Andrews will receive the prize in recognition of her many contributions to the field of hematology.

***Dr. Kenneth Kaushansky*** is being honored by the American Society of Hematology with the presentation of the Ernest Beutler Lecture and Prize. A current Council member, Dr. Kaushansky is being recognized for his significant advances in the discovery of thrombopoietin, the platelet growth factor that regulates platelet production. The recognition will be shared with David J. Kuter, M.D., of the Massachusetts General Hospital Cancer Center.

### **In Memoriam**

***Dr. John Bieri***, an NIDDK intramural scientist, died this past July at the age of 93. He served at NIH from 1955 until his retirement in 1983 as head of the NIDDK Nutritional Biochemistry

Section. While at NIH, he authored 160 peer-reviewed research papers on the metabolism of vitamins A and E, and essential fatty acids.

### **Current NIDDK Staff**

*Dr. Daniel Wright*, Senior Scientific Advisor and Program Director for Hematology Research, is retiring from the NIDDK's Division of Kidney, Urologic and Hematologic Diseases. During his eight years with the NIDDK, Dr. Wright served as a Program Director for Hematology Basic Research, as well as for Hematology Small Business grants. Dr. Wright's expertise made him a key contributor to the success of NIDDK hematology research projects. He also led several NIDDK committees and groups; provided leadership to multiple workshops; and served as an Institute representative in several arenas within and external to the NIH. Prior to joining the NIDDK, Dr. Wright served as Director of the William Castle Hematology Research Laboratory, Chief of the Combined Section on Hematology and Oncology, and Director of the Hematopoietic Stem Cell Transplantation Program at Boston University School of Medicine and Boston Medical Center.

*Dr. Dana Anderson*, who served as Director of the Clinical Studies Program within the Division of Digestive Diseases and Nutrition, has left federal service to move to Portland, Oregon. Dr. Anderson will continue working with NIDDK as a contractor. In that capacity, the Division will continue to draw on his expertise, especially with respect to diseases of the pancreas and bariatric surgery.

*Dr. Karen Teff* is joining the Division of Diabetes, Endocrinology, and Metabolic Diseases as a Program Director for Bariatric Surgery, Gestational Diabetes and Hypoglycemia. Previously, she was a member of the Monell Chemical Senses Center, and held an adjunct position at the University of Pennsylvania, where she was Director of the Clinical and Translational Research Center and Director of the Translational Research Program within the Diabetes Research Center. Her primary area of expertise is the neural control of glucohomeostasis in the pathophysiology of human obesity and diabetes.

## **II. CONSIDERATION OF SUMMARY MINUTES OF THE 192nd COUNCIL MEETING**

*Dr. Rodgers*

Following a motion that was made and seconded, the Council approved, by voice vote, the summary minutes of the 192nd Council meeting, which had been sent to members for review prior to the meeting.

## **III. FUTURE COUNCIL DATES**

*Dr. Rodgers*

The Council was reminded of future meeting dates.

### **2014**

February 5-6 (Wednesday and Thursday)

May 14-15 (Wednesday and Thursday)  
September 3-4 (Wednesday and Thursday)  
**Building 31, Conference Rooms 10, 6 and 7, respectively**

## **2015**

January 28-29 (Wednesday and Thursday)  
May 13-14 (Wednesday and Thursday)  
September 9-10 (Wednesday and Thursday)  
**Building 31, Conference Rooms 10, 6 and 7, respectively**

Dr. Rodgers said that most meetings are expected to be a single day; however, the Council is asked to reserve two days to ensure flexibility should a situation arise where a longer meeting is required.

## **IV. ANNOUNCEMENTS**

*Dr. Stanfield*

### **Confidentiality**

Dr. Stanfield reminded Council members that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council members regarding actions on an application must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

### **Conflict of Interest**

Dr. Stanfield reminded Council members that advisors and consultants serving as members of public advisory committees, such as the NIDDK Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur. Responsible NIDDK staff shall assist Council members to help ensure that each member does not participate in, and is not present during review of applications or projects in which, to the member's knowledge, any of the following has a financial interest: the member, or his or her spouse, minor child, partner (including close professional associates), or an organization with which the member is connected. To ensure that a member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. Dr. Stanfield said that a statement was provided for the signature of the each member, and this statement becomes a part of the meeting file. Dr. Stanfield asked each member to read the statement carefully regarding the conflict of interest in his or her review of applications, to sign it, and to return it to the NIDDK before leaving the meeting.

Dr. Stanfield said that, at Council meetings when applications are reviewed in groups without discussion, that is, "*en bloc*" action, all Council members may be present and may participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict.

With respect to multi-campus institutions of higher education, Dr. Stanfield said that an employee may participate in any particular matter affecting one campus of a multi-campus institution of higher education, if the employee's financial interest is solely employment in a position at a separate campus of the same multi-campus institution, and the employee has no multi-campus responsibilities.

### **NIH Initiative To Enhance Reproducibility and Transparency of Research Findings**

Dr. Stanfield reported that the NIH Director has formed an *ad hoc* group of NIH senior leadership to address underlying issues with respect to the reproducibility of research results. The group identified guiding principles, including: increasing community awareness; enhancing formal training of investigators; improving the review of grant applications while protecting the integrity of the science; and increasing funding stability for investigators, enabling them to use more appropriate and complex study designs. Based on these principles, the NIH is now exploring five recommendations: (1) to encourage the Institutes and Centers to discuss the issue with Advisory Councils to signal attention to stakeholder communities; (2) to integrate modules and/or courses on experimental design into existing required training courses, and award terms and conditions; (3) to consider options for an evaluation process of the "scientific premise" of a grant application; (4) to collaborate further with scientific journals and the scientific community on efforts to improve rigor; and (5) to adapt the NIH "bio-sketch" to allow investigators to place their work into a functional context. Dr. Stanfield noted that the NIDDK included in the Council members' pre-meeting materials the descriptions of several trans-NIH "Reproducibility Pilots" that are under way. He also provided examples of several NIDDK research efforts that have standardized research environments and test procedures, or use independent laboratories. These efforts help to ensure the use of appropriate animal models and reagents, and thus further the reproducibility of research findings. Dr. Stanfield asked the Council for input on the topic, both at and following the meeting.

During discussion, several Council members agreed with the importance of generating reproducible and transparent research findings. Various comments were made by Council members, including:

*Implications:* Recent estimates of the high percentage of non-reproducible research findings from both academic and industry studies can erode public confidence in the research establishment, and jeopardize congressional funding. This is a particularly critical issue if clinical research is undertaken based on faulty basic research findings. This issue can also have negative effects on junior colleagues who may become worried about their mentors and their careers.

*Possible Explanations:* The root of this problem may be sloppy science and a rush to publish, not fraud. Also, reproducibility problems may arise with mouse models that have slight differences. Unfortunately, reproducibility experiments by colleagues in the same field may have fallen off because low funding rates have driven scientists from research.

*Potential Corrective Actions:* Surveys of laboratory personnel and technicians would be useful in understanding the issue. Scientific journals could encourage or require that authors provide evidence or assurances of reproducibility prior to publication, rather than by dealing with the issue retroactively through published retractions and corrections. Investigators could share their mouse models with other researchers so that standardized tests of reproducibility could be conducted. The scientific community could think about what actions investigators should take when they can't reproduce a colleague's work. It was noted that the NIH should avoid placing additional, costly reporting burdens or regulations on scientists due to this issue. Science should continue to be self-correcting. A comment was made that the NIH should continue the helpful steps it is taking to standardize research methods, to sponsor symposia promoting standardized methods, and to create repositories for researchers to share data and reagents.

### **Percentage of NIDDK Funds Expended on Research Conducted Outside the United States**

In follow-up to a previous Council question, Dr. Stanfield reported that the NIDDK expends about 0.8 percent of its budget on research conducted in foreign countries. This is less than some other Institutes and about 0.1 percent less than the NIH as a whole. In many instances, a foreign application involves a domestic scientist's work that must be completed abroad for scientific reasons. Dr. Stanfield noted that there are special review considerations for such applications. In response to a Council member's question, Dr. Stanfield said that the funds expended on these applications would have a very marginal effect on paylines.

## **V. REPORT FROM THE NIDDK DIRECTOR**

*Dr. Rodgers*

### **Fiscal Year 2013 Budget**

Dr. Rodgers reviewed the status of the Fiscal Year 2013 budget. The funding levels for the NIH and most other government agencies and programs were adversely affected by the mandated percentage reductions of sequestration. The NIDDK lost about \$102 million from its regular appropriation, plus another \$7.65 million from the Special Statutory Funding Program for Type 1 Diabetes Research, which the Institute manages. The sequestration affected NIDDK's programs and funding approaches in many substantive ways. For example, in the category of research project grants (RPGs), the NIDDK funded thirty-two fewer new and competing grants, ninety-seven fewer non-competing grants, and six fewer grants in the Special Diabetes Program. Funding was reduced or constrained for institutional research training awards (T32s), the Special Emphasis Program, Collaborative Team Science programs, Core Mission Areas, and a number of emerging scientific opportunities.

### **Fiscal Year 2014 Budget**

Dr. Rodgers noted that the NIH and many other federal components are approaching the October 1 start of Fiscal Year 2014 in a state of budget uncertainty. The significant gulf between House and Senate budget plans has not been bridged to produce either a regular appropriations bill or a short-term Continuing Resolution (CR). Therefore, agencies whose regular appropriations bills

have not been enacted by October 1 will have to suspend operations as the new fiscal year begins due to a lapse in funding. If and when a Continuing Resolution is enacted, it is unclear whether it will include sequestration.

Dr. Rodgers noted that some major delays have occurred in the customary timeline for budget development. The President's Budget Request is usually submitted to the Congress a few days after the State-of-the-Union Address--usually the first week of February. However, largely because of delays in resolving the FY 2013 budget, the FY 2014 President's Budget was not submitted until April. The President's Budget included a request of \$31.3 billion for NIH. For the NIDDK, the Budget requested \$1.812 billion, plus \$150 million for the Special Statutory Funding Program for Type 1 Diabetes Research. The President's Budget was constructed to avoid sequestration, and was based on revenue increases, as well as spending cuts.

The NIH Director testified before the relevant House and Senate appropriations subcommittees in the Spring of 2013; however, the regular appropriations bill for the Department of Health and Human Services, which includes NIH funding, has not moved forward to completion. By summer, in the absence of appropriations bills for several agencies, it appeared that a Continuing Resolution would be needed to continue funding for the NIH and several other agencies into FY 2014. In the ensuing months, the terms of such a measure have been debated by the Congress without agreement. In addition to differences between the House and Senate about the funding level and the duration for a Continuing Resolution, a major point of contention has been whether the measure would contain language to make changes regarding the Affordable Care Act (ACA). The Administration said it would veto a bill having such changes.

Recognizing the uncertainty of the situation, the Office of Management and Budget has sent notice to NIH and other agencies in similar circumstances to begin planning for a possible government shutdown, and all NIH components have begun such planning. At best, on October 1, a Continuing Resolution will be in place--the funding level and length of which are not known at this time. At worst, many agencies of the federal government will be shut down for a period of time, until agreement on a Continuing Resolution can be reached. Recent events are not encouraging, especially when one considers that the FY 2013 budget was not resolved until May 2013.

Several Council members asked what they could do to prepare for a government shutdown, and Dr. Rodgers replied that, in the event of a shutdown, guidance will be forthcoming from the NIH Office of Extramural Activities. Council members underscored the continuing importance of communicating the public health and economic benefits of NIH research to the Congress.

## **VI. UPDATE: NIDDK WEBSITE PRESENCE**

### ***Dr. Germino***

Dr. Germino pointed out that the NIDDK website is an essential means of communicating with investigators, patients, and many others with an interest in the Institute's research mission, programs, advances, and funding opportunities. While the website has been generally well-received by patients and the public, the NIDDK found that it was not structured to be optimally useful to scientists. Therefore, a major effort was initiated with NIDDK communications,

computer technology and program staff to enhance the website’s appearance and functionality so that investigators can easily access and use information. The Council was given a “live” demonstration of parts of the updated website by NIDDK staff member Ms. Dana Sheets, who responded to a number of Council questions. Ms. Sheets said that one of the guiding principles in updating the website was to link, where appropriate, to relevant content on other websites maintained by the NIH—such as those developed by the Center for Scientific Review (CSR) and the NIH Office of Extramural Research (OER)—rather than to create content *de novo*. In response to a question about intramural information, Ms. Sheets said that during the redesign process the NIDDK has also reinvigorated its Intramural Research Program website pages (that include information for all intramural researchers and their research programs at NIDDK) and will link to an NIH website on which all intramural investigators and laboratories will be listed. This latter website will be searchable by organ, condition, and/or disease category.

In the future, Ms. Sheets said that the NIDDK hopes to take the concept underlying its current “research resources” table and expand it into a means of using the website to provide access to centralized datasets from its investments in clinical trials. In addition, the NIDDK is taking a first step toward creating “Research Area” search paths for different types of website visitors, including congressional staff. A “Research Area” would provide comprehensive information on a topic, including research advances, investigators working in the field, strategic plans, reports, meetings, funding levels, and other information. This idea is still evolving and will take time to implement.

## **VII. COUNCIL FORUM: M.D. Basic Researchers--A Threatened Species**

### **A. *Dr. Gregory Germino* *Deputy Director, NIDDK***

Dr. Germino’s presentation focused on NIDDK workforce data. From these data a pattern emerges regarding the diminishing participation of physician-scientists, and particularly M.D. basic scientists, in the research enterprise. He said that there have been warnings for years that the role of physician-scientists may be threatened, including admonitions in the book, *The Vanishing Physician-Scientist*, edited by Andrew I. Schafer, M.D. The reason for concern about this issue is that M.D. scientists play a distinct role in the biomedical research ecosystem because they have a unique bench-to-bedside perspective as clinicians. They are well-versed in the nature of diseases, and they understand the challenges of implementing therapies in the clinic. By speaking the language of both science and medicine, they can translate between these two arenas, and thus facilitate the integration of basic science into medical practice. While there are many contributors to research progress, the role of M.D. scientists is a critical one, and trends in their participation in research training and research investigation need to be analyzed carefully because they may signal the need for possible corrective actions.

Turning first to research training, Dr. Germino said that it is crucial to understand the meaning and implication of changes that have occurred over time in the NIH portfolio of research career development awards (K awards) for physician-scientists. (See description of NIH K awards: <http://grants.nih.gov/training/careerdevelopmentawards.htm>)

Dr. Germino said that NIDDK award numbers have dropped considerably in the K08 Clinical Investigator Award Program, which is aimed at clinical scientists doing bench research. Part of this decline appears to be offset to some degree by increases in the numbers of M.D.s receiving K23 Mentored Patient-Oriented Research Career Development Awards. However, the purpose of the K23 award program is to permit clinical investigators an opportunity to develop into independent clinical researchers involved in patient-oriented research; hence, that program cannot substitute for the loss of K08 awards, which have a focus on basic research. These observations raise questions about the state of M.D. researchers overall and have occasioned the NIDDK to conduct more detailed data analyses of M.D.s in the NIDDK workforce. The Institute has invited Council members to comment on the data, and to suggest how the various components of the biomedical ecosystem—including the NIDDK/NIH, academic medical institutions, professional societies and patient advocacy groups—can cooperate to address perceived needs.

### **NIDDK Historic Data on Applications and Awards**

Dr. Germino presented the results obtained from analyzing NIDDK data on M.D.s—either separately, or in juxtaposition to Ph.D.s and M.D./Ph.Ds—over a period of approximately 20 years. While the data show fluctuations over time, they also reveal trends that reinforce concerns about the participation of M.D.s in research. Regarding methodology, Dr. Germino noted that, in these analyses, Principal Investigators (PIs) were counted only once in a given fiscal year; hence, they are referred to as “unique”. All PIs on multi-PI applications/awards were included in the analyses.

*Number of Unique M.D. PIs Submitting R01 or Equivalent Applications from Fiscal Years (FYs) 1993 through 2013:* The number of R01 applications from M.D. PIs has fluctuated over the years, but overall, the number has risen by only about 18 percent, while the corresponding number for Ph.D.s has risen by more than 60 percent. The number for M.D./Ph.D. PIs has risen by about 215 percent.

*Number of Unique M.D. PIs Supported by One or More R01 or Equivalent Grant Awards from FYs 1993 through 2012:* Although the number of PIs with at least one R01 award has fluctuated over the past 20 years, some trends are apparent. Overall, as a percentage of awardees, M.D. R01 awardees in the NIDDK portfolio have been declining. In FY 2012 there was a 20 percent decline in the number of unique M.D.s supported by at least one R01 award compared to the number in FY 1994. The number of M.D./Ph.D.s and for Ph.Ds alone supported by at least one R01 have increased by 21 percent and 19 percent, respectively during the same time period (i.e., FY 2012 compared to FY 1994). While the number of M.D.s supported by at least one R01 in FY 2012 is marginally higher than in FY 1993, it is lower than at any other time since FY 1993.

Dr. Germino also presented data on the representation of M.D.s among Early Stage Investigators (ESIs). ESIs are New Investigators who are within 10 years of completing their terminal research degree or within 10 years of completing their medical residency at the time they apply for R01 grants. M.D. representation among ESIs has fallen since FY 2010 from approximately 32 percent of ESIs in FY 2010 to approximately 22 percent of ESIs in FY 2013. In contrast

representation of Ph.D.s and M.D./Ph.D.s have held fairly constant (Ph.D.s) or increased (M.D./Ph.D.s) during the same time period.

### **Next Generation of the NIDDK Workforce**

Dr. Germino presented data on research training and research career development programs that may provide insights regarding the future replacement rate of M.D.s in the NIDDK workforce.

*Research Career Development Programs (K Awards)--Numbers of Competing Awards for M.D.s--FY 2002 to 2012:* In the K08 classic research career development program for physician-scientists doing laboratory work, the absolute number awardees has undergone a relatively steady decline since 2002. The number of K08 awards during this time period has dropped by over 35 percent. This decline may have been enhanced by new award programs for individuals who are in the clinical investigator pathway (K23 Mentored Patient-Oriented Research Career Development Awards, K 24 Mid-Career Investigator Award in Patient-Oriented Research, and K99 Career Transition Award). More M.D./Ph.D.s are now supported by K08s than are M.D. holders, even though the pool of M.D. vs. M.D./Ph.D. among all K awardees has remained relatively constant over the past 11 years. Dr. Germino noted that the M.D. pool is also slightly more competitive than the M.D./Ph.D. pool for K08 awards. Thus, the decline in the number of M.D. K08 awards appears to be attributable to a decline in M.D. K08 application numbers.

*Pipeline Leakage from NIDDK Research Pathways to Private Practice:* Data analysis shows that 30 percent of M.D.s and M.D./Ph.D.s who were trained on NIDDK institutional research training grants (T32 grants) are in private practice within 10 years of their training. Follow-up data of M.D. recipients of K awards has also revealed a rapid increase in the proportion of those awardees in private practice within 5 years after their award (from below 10% in FY 2007 to above 20% in FY 2011). Academic clinical appointments have also declined--further suggesting that more M.D.s are going into private practice.

*Increasing Age of Awardees:* The median age of NIDDK awardees has increased for all categories of researchers (M.D.s, Ph.D.s, and M.D./Ph.D.s) but the median age for M.D. awardees has increased at a faster rate than for any other category of degree holders. In 1993, the median age of M.D.s vs. Ph.D.s approximately 45 and 44 years, respectively. In 2012, the median age for M.D.s vs. Ph.D.s was about 53 and 49 years, respectively. These data suggest that the M.D. awardee population is not being replenished as rapidly as the population having other educational degrees. This trend could portend significant changes in the composition of the future NIDDK scientific workforce.

### **Summary**

Dr. Germino synthesized the key points emerging from the various analyses of NIDDK data. The proportion of PIs that are M.D.s within the NIDDK workforce is declining. Fewer are entering the basic science research track than in the past, and, over the past eleven years, there has been a 35 percent decline in their numbers in the basic science training mechanism for M.D.s--the K08 Clinical Investigator Award Program. While the growth of the K23 Mentored Patient-Oriented

Research Career Development Award Program might be viewed as partially compensating for these changes, there are other trends regarding M.D.s in the NIDDK research portfolio, which collectively, may be worrisome. More M.D.s are dropping out of the research enterprise early, as evidenced by follow-up data on the professional choices of participants in NIDDK research career development programs and institutional research training programs (T32 awards). Proportionally fewer Early Stage Investigator Awards are being made to M.D.s. The median age of M.D. PIs is rising faster than that of Ph.D.s. Importantly, it is unclear whether the decline in M.D. participation in research disproportionately affects basic scientists as opposed to clinical scientists. It is possible that the increase of clinically focused M.D.s in some relatively new NIDDK research career development programs may be partially masking a true loss of M.D.s to basic research efforts.

Dr. Germino said that possible reasons for the decline of M.D. scientists in the NIDDK biomedical workforce include the high cost of medical education and perceptions regarding the high risk of failure for M.D.s who pursue research careers. Various types of changes may also play a role, including changes in the medical education system, and changes in the nature of medical centers, clinical practice, and medical reimbursement. An important factor may be changing expectations regarding issues of work-life balance. For example, an increasing number of M.D.s are caregivers, which may lead them away from committing to time-intensive research careers.

The NIDDK data analyses raise several questions that need to be addressed: Is the diminishing participation of physician-scientists in the NIDDK workforce an important problem? Can an increase in the number of M.D./Ph.D.s and K23-trained M.D.s make up for the loss of K08-trained M.D.s? Are M.D.s and M.D./Ph.D.s in the K 23 Award Program comparable to M.D.s in the K08 Award Program in terms of experiences, views, interests, and their potential contributions to science?

An overriding question is whether the NIDDK can and should take any actions to sustain and even grow M.D. participation in its research workforce. If so, it will be important to have a better understanding of the training process, how it can be made less risky or more attractive for M.D.s, and what means could be taken to address changing work-life balance issues. Clearly, these are questions that the NIDDK could only tackle with the cooperation and support of many research stakeholders.

Dr. Germino expressed his appreciation to the many NIDDK staff members who worked on the data analysis and slides he presented. He then he turned to Drs. Kaushansky and Zeidel for their comments.

***B. Dr. Kenneth Kaushansky, Senior Vice President Health Sciences Dean, School of Medicine, Stony Brook University***

Dr. Kaushansky agreed with concerns about the plight of physician-scientists, and he focused his comments on barriers to their participation in research and solutions to the problem. He echoed Dr. Germino's view that physician-scientists are critical members of the research community because their research is informed by a perspective gained from taking care of patients. Dr.

Kaushansky reviewed the pipeline for the development of physician-scientists. He noted that physician-scientists, who hold an M.D., but not a Ph.D., outnumber by fourfold their M.D./Ph.D. counterparts. The fact that about 80 percent of the physician scientists in the U.S. are exclusively M.D.s demonstrates the large pool of M.D.s that could be drawn into the research enterprise, and this context makes the NIDDK workforce data even more troublesome.

Dr. Kaushansky outlined some additional barriers facing M.D.s in science today. As early as the late 1970s, articles by leaders in the scientific community were questioning whether M.D.s were maintaining a sufficiently robust presence in the scientific workforce. A 1999 editorial in the *Journal of the American Medical Association* noted the influence of the new “primary-care oriented, cost-conscious health paradigm.”

Economic incentives and disincentives influence career choices. Training stipends are low and the debt burden of a medical education is very high. Moreover, the salary for medical leaders in academics is about 20 to 50 percent lower than that for their counterparts in private medical practice or industry. Another economic disincentive is that the perceived instability in NIH funding makes it difficult to commit to research as a long-term, sustainable career choice. Adding to those factors are the explosive growth of managed care, an increased emphasis on primary care, an increasing demand for physicians to see more patients, and declining revenues in departments of academic medicine that can be used to support research. Medical students may also be dissuaded from pursuing a research career because of poor mentoring. There may be a perception among medical students that their talents are being used to support the endeavors of senior scientists rather than being honed for their own independent careers.

Dr. Kaushansky focused the remainder of his remarks on mentoring, which he considers the key to duct-taping the leaky pipeline of physician-scientists. He thinks it is vital to nurture an individual’s interest in becoming a physician-scientist--the curiosity, the driving energy, the passion. To that end, established physician-scientists need to become more visible and meaningful in the lives of medical students, residents and fellows, and need to convey to them the excitement that attends the discovery and sharing of new knowledge.

It is important for physician-scientists to serve on medical school admissions committees and for academic institutions to teach an integrated curriculum. For example, learning about the physiology of insulin secretion could be coupled with clinical experiences with a patient suffering the ravages of diabetes. This integration can be accomplished, for example, through an M.D. program that includes a period of time for “scholarly concentration” in which a student develops rational and scholarly methods of investigation and shares the excitement of scientific discovery with a faculty mentor. Residency is another time in which medical trainees can be inspired by clinical investigation. A residency program that teaches the skills of patient-oriented research can include evidence-based reviews of clinically relevant research topics such as mechanisms of medicine. Residents in categorical areas can be given “protected time” for research-focused learning experiences. Dr. Kaushansky described a “research residency program” in which two years of protected research time was incorporated into a four-year residency in internal medicine approved by the Accreditation Council for Graduate Medical Education (ACGME). He also underscored the importance of recruiting a physician-scientist

into an environment with a “nascent critical mass” of scientifically focused mentors, colleagues and collaborators.

A major question is what type and extent of support academic institutions, other components of the research community, and society in general should provide to maintain a robust and replenishing cadre of physician-scientists. Regarding academic institutions, he believes that chairs of academic medical departments should speak with junior faculty annually to make sure that appropriate, dedicated scientific mentors, with back-ups, are in place. Academic institutions should also recognize, support and reward effective mentoring, and the professional societies and/or the NIH can also contribute in this regard.

Dr. Kaushansky described two programs supported by the American Society of Hematology. One program is the Clinical Research Training Institute, which provides a unique year-long education and mentoring experience for hematology fellows and junior faculty at academic medical centers. (<http://www.hematology.org/Awards/CRTI/2195.aspx>) This program offers a broad education about clinical research methods, research collaborations, statistical analysis, and managing the demands of family and career. The goal is to produce a group of researchers armed with ideas for clinical hematology research, and with the tools and access to resources to make their ideas a reality. Dr. Kaushansky also described the program on Translational Research Training in Hematology, which is co-sponsored by the American Society of Hematology and the European Hematology Association (EHA). The program is focused on helping early-career scientists build successful careers in hematologic translational research, including pathogenesis, diagnostics, and experimental treatment of hematological disorders. (<http://www.hematology.org/Awards/TRTH/2632.aspx>)

In closing, Dr. Kaushansky stressed several faculty interventions that can aid the development of physician-scientists: adequate start-up funding and protected time devoted to research; critical mentoring, including mentoring of the mentors; and a nurturing scientific environment with a nascent critical mass of scientific leaders and colleagues. He expressed his hope that programs that have proven successful in some venues can be replicated in others--with the support of academic institutions, the NIH, professional societies, and industry.

***C. Dr. Mark Zeidel, The Herman Ludwig Blumgart Professor of Medicine at Harvard Medical School, and Physician-in-Chief and Chairman of the Department of Medicine at the Beth Israel Deaconess Medical Center***

Dr. Zeidel agreed with the concerns expressed by Drs. Germino and Kaushansky about the participation of M.D.s in the research enterprise--noting that chairs of medicine tend to discuss this issue at every meeting. He agreed that there is a need for more scientists on medical school selection committees. He also said that it can be difficult to ascertain whether students have a real interest in science. A summer research project may be merely a rite-of-passage, not a meaningful indicator of a person’s attraction to science. Moreover, many such projects are poorly planned by academic institutions and mentors; hence, they do not stimulate a student’s intellectual curiosity or result in any feeling of accomplishment. It would probably be better to engage students more meaningfully at an earlier point in their medical education.

Some institutions have developed two tracks for residents and fellows--one for research and one for medical practice. However, if attending physicians on the in-patient side are non-scientific hospitalists, the students are unlikely to learn about intriguing research areas, such as physiology, and therefore unlikely to envision a career dedicated to scientific investigation. It is therefore important to have stellar, charismatic research investigators accompany hospitalists in these settings, or students may develop the unfortunate viewpoint that basic science is irrelevant to clinical care. Institutions need to make certain that students understand the central role science plays in medicine. Inculcating this principle in students during their medical education requires a cultural change that must be fostered among hospitalists and others in academic institutions throughout the country. Dr. Zeidel noted that his institution is making an effort to include hospitalists in a one-week program in which residents and general surgeons study comparative biology at a marine biology station. This program has proven very effective in conveying the importance and excitement of science.

Dr. Zeidel said that institutions may need to make a determination early on about which medical students, residents, or fellows show promise as scientists, and then, based on this assessment, concentrate on promoting and supporting their participation in research tracks that are exciting and nurturing. Dr. Zeidel said that the view at his institution is that all fellows should do research, and there is an extremely high rate of research-track fellows who compete successfully for NIH regular research grants (R01 grants).

Dr. Zeidel emphasized the importance of skills development among faculty members so that they can identify students with the necessary attributes for committing to a research career, and then provide adequate support for their development into physician-scientists. Substantial resources are required for this process, and institutions, philanthropists, professional societies, and government can help provide needed financial packages and training programs for research-oriented candidates. A complementary approach is for institutions to foster the cross-fertilization of Ph.D.s and M.D.s. When Ph.D.s are brought into the clinic, they can expand their research approaches. Similar benefits occur when Ph.D.s train M.D.s in research methods. Such cross-fertilization is necessary today given technologic advances in science that drive a team approach to answering complex research questions.

In closing, Dr. Zeidel expressed his view that the numbers of physician-scientists in research are likely to go down for a period of time until NIH funding opportunities increase. A generation of physician-scientists may be lost to research if institutions and other components of the research community don't assign greater value and resources to their development. However, when the funding landscape improves, it may be possible to devise more effective ways to fund pre-medical education and medical education so that medical students and M.D.s are nurtured to become physician-scientists, and do not face the disincentive of an enormous debt load. For now, the best approach is probably to be proactive in identifying and investing in scientifically-oriented medical students, residents and fellows, rather than to rely on the traditional process of natural selection in the physician-scientist career path.

## **Council Questions and Discussion**

*Decline in Physician-Scientists More Dire When Viewed Against Expanded Faculty Pool:* The diminishing participation of M.D.s in science may be even more problematic than suggested by the analyses of NIDDK workforce data. The numbers of physician-scientists should be increasing, not decreasing, given the burgeoning pool of M.D. faculty members over the past 20 years.

*Surgeon-Scientists:* Aren't surgeon scientist at great risk of disappearing from the research enterprise? In addition to other suggestions, there is a special need for incentives and for research team-building efforts that include surgeon-scientists. Programs aimed specifically at attracting M.D.s and surgeons to research careers can be appealing if they are competitive with other opportunities presented to these talented individuals. NIH research solicitations that involve surgery can give surgeons an opportunity to maintain their skills while working in a research mode.

*Model Programs:* Council members offered examples of successful programs that could be replicated. For example, the American Neurological Association largely follows the models of the American Society for Hematology described in the presentations. The National Pancreas Foundation offers a weekend symposium in which fellows are matched with committed mentors to seed long-term productive relationships. The success of the program derives from a careful application process to select fellows most interested in research; the quality and commitment of the mentors; and the inclusion of time for student-mentor social interactions. It was noted that inspirational, engaged mentors are vital because medical students and M.D.s may be deterred by the amount of time, work, and financial sacrifices they associate with a research career.

*Bridge Funding:* A key step is to provide mechanisms that "bridge" certain points in the research career continuum so that talented individuals don't drop out of the system due to lack of funds. One approach for addressing this issue would be to have center grants offer funding opportunities to junior scientists who need bridge support.

*Team-Science Model:* Advances in basic and clinical research have made it virtually impossible for any individual (M.D. or Ph.D.) to have the breadth and depth of knowledge and skills to perform research independently today. Team science addresses that issue by bringing the intellectual acumen and skills of several talented individual to bear on complex scientific issues for the advancement of translational research. To that end, K23 awards often include a basic science aim. Having co-Principal Investigators on multidisciplinary grants enables clinical and basic scientists to work together to advance the research agenda.

*Testing and Evaluating Models:* A systematic approach is needed to test different models aimed at increasing the number of M.D.s who stay in research careers. Studies in educational achievement suggest that fairly minimal interventions can change trajectories of educational success and career paths, especially among minority youth. The NIDDK and NIH could fund research on the development of career paths.

## **VIII. BREAK**

## **IX. UPDATE FROM THE DIRECTOR, EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**

*Dr. Alan Guttmacher*

Dr. Guttmacher began his presentation by underscoring the strong and productive relationship that exists between the NIDDK and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). Both Institutes are dedicated to advancing science discovery, and their cooperation and collaboration spring from that mutual goal. Dr. Guttmacher touched briefly on NICHD's origin and mission, examples of collaboration with the NIDDK, the shared NIDDK/NICHD vision for the next decade, and future research directions.

### **NICHD Overview**

The NICHD was established in 1962 to support and conduct research and training on human development across the lifespan, intellectual and developmental disabilities, and key processes during pregnancy. The formal mission of the NICHD is to ensure that every person is born healthy and wanted; to ensure that women suffer no harmful effects from reproductive processes; to ensure that all children have the chance to achieve their full potential for healthy and productive lives--free from disease or disability; and to ensure the health, productivity, independence, and well-being of all people through optimal rehabilitation.

Dr. Guttmacher noted that the Institute's title includes the name of Eunice Kennedy Shriver because she was instrumental in its establishment due to her interest in research on intellectual developmental disabilities. Dr. Guttmacher pointed out that, although the term "child health" is in the Institute's name, the NICHD supports the plurality of NIH research in that area, which is shared among many other Institutes and Centers, including the NIDDK. In leadership, however, the NICHD contributes exceptional expertise and perspective to the overall NIH portfolio of child health research, and considers itself a particular voice for the interest of child health and of children. Dr. Guttmacher noted that, unlike most of the Institutes, the NICHD is not focused on disease processes, organs or tissues. Rather, it is more about life stages and developmental processes.

Dr. Guttmacher stressed that the NICHD's mission is actually much broader than that of child health or even human development. Today, the NICHD supports multiple areas of scientific inquiry, including: developmental biology, child development, pregnancy and perinatology, reproductive health, gynecology, rehabilitation, targeted pharmacology, population dynamics, and global health. Dr. Guttmacher noted that the NICHD has been the home for 23 years of the National Center for Medical Rehabilitation Research.

For Fiscal Year 2012, the NICHD enacted budget was \$1.32 billion, which does not include \$193 million in funding for the National Children's Study, which the NICHD manages for the

Office of the NIH Director. Approximately 81 percent of the NICHD budget is spent extramurally; the remainder is spent on the intramural program and on research management and support functions.

### **NICHD-NIDDK Collaborations**

Dr. Guttmacher described several examples of NICHD-NIDDK collaborations:

*Hypoglycemia and Adverse Pregnancy Outcome (HAPO) Study*--This ambitious, multi-year, international study has found that, as maternal glucose levels increase (even within the accepted normal range), so do risks of certain complications, e.g., cesarean delivery, macrosomia, and neonatal hypoglycemia. This study has led to efforts to redefine gestational diabetes. The NICHD is now providing co-funding to NIDDK for a follow-up study.

*Gestational Diabetes Mellitus (GDM) Consensus Conference*--Planned jointly by the NICHD and the NIDDK, this conference was held in March 2013 to review scientific evidence and reach a better understanding of the benefits and risks of various GDM screening and diagnostic approaches. The panel recommended continuation of the current diagnostic approach until further studies provide more evidence of the potential benefits and risks of adopting a new approach.

*Lifestyle Interventions for Expectant Moms*--NIDDK's LIFE-Moms Consortium is testing interventions among overweight/obese pregnant women to control gestational weight gain, among other outcomes. This consortium may lead to evidence-based guidelines for weight reduction in obese pregnant women. The NICHD supports a clinical trial at the University of Puerto Rico as part of this initiative.

*Biomarkers of Nutrition for Development (BOND)*--This NICHD program supports discovery, development, and use of biomarkers for all essential nutrients. It harmonizes decision-making about which are the best biomarkers for research, program development, evaluation, and generation of evidence-based policy. The program is supported in part by trans-NIH Division of Nutrition Research Coordination, which is located within the NIDDK.

*Intramural Collaborations*--The NICHD and the NIDDK collaborate in several intramural areas including the Inter-Institute Endocrine Training Program, an accredited subspecialty training program for adult endocrinologists, and the Pediatric Endocrinology Inter-Institute Training Program. The NICHD also developed and currently manages a Clinical Trials Database, which supports the NIDDK and the other Institutes and Centers. In addition, there are dozens of collaborations among individual intramural Principal Investigators from different Institutes.

Other areas of NICHD-NIDDK collaboration include research on breastfeeding and human lactation, childhood obesity, congenital obstructive uropathy, neonatal acute kidney injury, nuclear receptor signaling, and prebiotics/probiotics.

## **NICHD's Scientific Vision: The Next Decade**

Dr. Guttmacher described the ideas that have emerged from an NICHD-initiated process to identify the most promising scientific opportunities for the next ten years across the Institute's mission. Individuals from a wide range of disciplines and professional backgrounds provided input to framing an ambitious NICHD research agenda that inspires the Institute, its partners, and the research community to achieve critical scientific goals and improve health. Approximately 700 individuals participated in the NICHD's "Vision" meetings. Participants represented a total of 229 institutions and organizations from 39 states and 6 foreign countries. The scientific areas addressed included reproduction and pregnancy; developmental biology and early origins of health/disease/growth/development; behavior/cognition; plasticity/rehabilitation; and population dynamics. Dr. Guttmacher gave a few examples of the ideas/goals that were identified for certain topics.

Regarding the early origins of health/disease/growth/development, some of the key ideas that emerged include: to identify mechanisms in the pre- and peri-conception, fetal and childhood periods that lead to the most pressing child and adult health concerns; to engage specific populations representing unique biologic opportunities and exposures; to exploit the placenta as a record of intrauterine gene-environment interactions; and to define the mechanisms of multi-generational effects on health, growth, and development.

With respect to the culture of science, the identified goals include: to improve rewards for and de-risk trans-disciplinary research at all career stages; to standardize ontology, nomenclature, and data standards across disciplines; to change the predominant model for data use to one of open access; and to incorporate qualitative and quantitative assessment of quality of life in a wider range of scientific studies.

In the area of clinical trials and public involvement, one major goal is to consolidate currently available information from clinical trials and other studies and make it easily accessible to researchers, clinicians, and the public. Another important goal is to redesign privacy and confidentiality rules and regulations to address the real needs of both participants and researchers, so that research maximally advances the public good.

Regarding research training and the scientific workforce, goals include: to increase graduate students' exposure to physiology, pathophysiology, and behavioral sciences; to increase interdisciplinary fluency, specifically in biocomputation; and to build a global infrastructure of mentored partnerships to increase research capacity.

## **Spotlights on Selected Future Research**

Dr. Guttmacher gave examples of some of the major areas of the NICHD's continuing research and future directions.

*National Children's Study:* This ongoing, longitudinal study will continue to collect data with the goal of improving the health and well-being of children by identifying the antecedents of healthy adulthood. Researchers will examine the multiple effects of environmental influences

and biological factors on the health and development of approximately 100,000 children across the U.S.--following them until 21 years of age. Dr. Guttmacher noted that this is not a conventional study, but a data resource with linked environmental and biological samples.

*Newborn Screening and Genomics:* This new effort will assess the potential value of genomic sequencing in the newborn period. Pilot projects will consider technical, clinical, and ethical aspects. The NICHD is undertaking this initiative in collaboration with NHGRI and at an initial funding level of \$25 million over five years.

*Human Placenta Project:* This proposed initiative would be a coordinated international project to understand and monitor, in real time, the structure and function of the human placenta. Dr. Guttmacher described current gaps in knowledge about the placenta and gave some examples of how a ten-year research project could fill them. For instance, the proposed initiative could support the application of functional genomics and other high-throughput “omics” tools to improve molecular definition of placental biology and disease phenotypes, and the development of non-invasive tools to understand the human placenta in real time throughout pregnancy--ultimately defining normal and abnormal trajectories. It could also further the determination of the impact on the placenta of such factors as obesity, multiple gestation, maternal diet, and exposure to toxins, and also enable the illumination of placenta-mediated mechanisms of immune tolerance and protection. An increased understanding of host-pathogen interactions and host responses for transplacental infections and other insights could likewise be achieved. The proposed project is envisioned to run from 2015-2025, with the guidance of an international coordinating council. An emphasis would be placed on applying and developing scientific approaches and technologies. Rapid and open data-sharing, with appropriate intellectual property rights, would be built into the project, which would encourage the intellectual involvement and potential financial involvement of multiple NIH Institutes and Centers. A Workshop is planned in early 2014 to develop an initial research plan.

### **Council Questions and Discussion**

*Does the NICHD address the prevention of incontinence and prolapse, an area of NIDDK research?* Dr. Guttmacher responded that gynecology is a particular and growing interest of the NICHD. In general, however, the NICHD has a life-span perspective, not an organ-specific or tissue-specific interest. The NICHD cooperates not only with the NIDDK, but also with several other Institutes and Centers on areas of shared research interest.

*Could there be a trans-Institute initiative to consider how microbial colonization of the gut in the immediate post-natal period may influence the development of the immune system in ways that may have life-long implications in terms of disease acquisition?* Dr. Guttmacher said that the NICHD is interested in the colonization that occurs in children born via C-section vs. the traditional method.

*Can animal models be expected to provide significant insights into placental biology, or must this research be pursued in humans?* Dr. Guttmacher replied that animal models in this area have been helpful, but limited. There is a need to improve such models to make them more

useful. At the same time, to answer some questions, it may be necessary to find ways to study placental biology in humans.

*Can experiences with the National Children's Study be used to inform the design and conduct of other large, longitudinal studies? Also, can that study be used to emphasize the importance of NIH research to the public?* Dr. Guttmacher responded that the National Children's Study has been informed by previous studies, and can definitely serve as a model for similar longitudinal studies in the U.S. and abroad--provided that adjustments are made for different environmental exposures, different patient populations, and other factors. In general, he hopes that studies can be designed so that any researcher can access and use data from various sources. Ideally, data should be made available through interoperable platforms so that a researcher can combine similar data from several studies in order to gain keener insights regarding disease processes and therapeutic interventions. Similar types of efficiencies may also be achieved in the ways that Institutional Review Boards operate. Clearly, it is important for research organizations to keep each other informed of ongoing and planned studies, and to share information that will enable studies to be designed, conducted, and presented in the most efficient ways for maximizing their utility and benefit for the broader research community. Regarding public outreach via the National Children's Study, Dr. Guttmacher said that NICHD has engaged in such efforts. Because the Study is being conducted in multiple communities, the awareness of NIH research achieved through this Study is quite broad. Importantly, these outreach efforts optimize patient retention in the Study, and serve to acknowledge and extend appreciation for the significant contributions that study participants are making to a landmark research endeavor.

*Is the NICHD making any efforts to coordinate or consolidate data from registries established by different organizations?* Dr. Guttmacher responded affirmatively--noting that, ideally, such registries should at least be interoperable, if not built on the same platforms. As stewards of public funds, the NIH Institutes and Centers are definitely moving in that direction. Other organizations are also likely to see the benefits of enhanced data coordination, access, and analysis for the goal of advancing science.

**X. SCIENTIFIC PRESENTATION: Role of Urothelium in Urological Diseases**  
*Dr. Mark Zeidel, The Herman Ludwig Blumgart Professor of Medicine at Harvard Medical School, and Physician-in-Chief and Chairman of the Department of Medicine at the Beth Israel Deaconess Medical Center*

## **XI. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS**

A total of 215 grant applications, requesting support of \$ 57,046,266 were reviewed for consideration at the September 26, 2013 meeting. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1191 applications requesting \$ 353,239,852 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the September 26, 2013 meeting.

## **XII. ADJOURNMENT**

*Dr. Rodgers*

Dr. Rodgers expressed appreciation to all the presenters and discussants. He thanked the Council members for their attendance and valuable input. There being no other business, the 193rd meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m., September 26, 2013.

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



Griffin P. Rodgers, M.D., M.A.C.P.  
Director, National Institute of Diabetes and Digestive and Kidney Diseases, and  
Chairman, National Diabetes and Digestive and Kidney Diseases Advisory Council