

**National Diabetes and Digestive and Kidney Diseases Advisory Council**  
National Institute of Diabetes and Digestive and Kidney Diseases  
National Institutes of Health  
Department of Health and Human Services

**I. CALL TO ORDER**

*Dr. Rodgers*

Dr. Griffin Rodgers, Director, NIDDK, called to order the 201<sup>st</sup> meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on May 18, 2016, in Building 31, Conference Room 10, the NIH Campus, Bethesda, Maryland.

**A. ATTENDANCE – COUNCIL MEMBERS PRESENT**

Dr. Sharon Anderson	Dr. David Klurfeld
Dr. Gopal Badlani	Dr. Ellen Leake
Dr. Joseph Bonventre	Dr. Craig Peters
Dr. David Brenner	Dr. Alan Saltiel
Dr. Eugene Chang	Dr. Jean Schaffer
Dr. Mark Donowitz	Dr. Irving Smokler
Dr. Joel Elmquist	Dr. Bruce Spiegelman
Ms. Cindy Luxhoj	Ms. Pamela Taylor
Dr. Caren Heller	Dr. Beverly Torok-Storb
Dr. Lee Kaplan	

**Also Present:**

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

**B. NIDDK STAFF AND GUESTS**

Abbott, Kevin – NIDDK	Boyce, Vanessa - CSR
Abraham, Kristin – NIDDK	Burgess-Beusse, Bonnie – NIDDK
Adurota, Yetunde – NIDDK	Byrd-Holt, Danita – NIDDK
Akolkar, Beena – NIDDK	Calvo, Francisco – NIDDK
Andersen, Dana – NIDDK	Camp, Dianne – NIDDK
Arreaza-Rubin, Guillermo – NIDDK	Carrera, Krysten – NIDDK
Barnard, Michele – NIDDK	Castle Arthur – NIDDK
Begum, Najma – NIDDK	Cerio, Rebecca – NIDDK
Bishop, Terry – NIDDK	Chen, Hui – CSR
Blondel, Olivier – NIDDK	Cheng, Clara – CSR
Bremer, Andrew – NIDDK	Christiansen, Dane – HMCW
Brooks, Robin – NIDDK	Chowdhury, Bratati – NIDDK
Brookes, Catherine – NIDDK	Connaughton, John – NIDDK

Cox, Lisa – Am. Diabet. Assoc.  
Curtis, Leslie – NIDDK  
Davila-Bloom, Maria – NIDDK  
Dayal, Sandeep – NIDDK  
Densmore, Christine – NIDDK  
Dirks, Dale – Hlth. & Med. Council Was.  
Doherty, Dee – NIDDK  
Donohue, Patrick – NIDDK  
Doo, Ed – NIDDK  
Drew, Devon – NIDDK  
Duggan, Emily – NIDDK  
Eggerman, Thomas – NIDDK  
Evans, Mary – NIDDK  
Fisher, Rachel – NIDDK  
Fleischhacker, Sheila – NIDDK  
Flessner, Michael – NIDDK  
Fonville, Olaf – NIDDK  
Fradkin, Judith – NIDDK  
Froyd, Erica – Louis Burke Assoc.  
Fox, Edward – Perdue Univ.  
Gallivan, Joanne – NIDDK  
Gansheroff, Lisa – NIDDK  
Gletsu-Miller, Nana – Perdue Univ.  
Gossett, Daniel – NIDDK  
Haft, Carol – NIDDK  
Hall, Sherry – NIDDK  
Hanlon-Tilghman, Mary – NIDDK  
Hoover, Camille – NIDDK  
Hoshizaki Deborah – NIDDK  
Hunter, Christine – NIDDK  
Ivins, Jonathan – CSR  
James, Stephen – NIDDK  
Jenkins, Connie – NIDDK  
Jerkins, Ann – NIDDK  
Jones, Teresa – NIDDK  
Karp, Robert – NIDDK  
Ketchum, Christian – NIDDK  
Kilmarx, Peter – FIC  
Kimmel, Paul – NIDDK  
Kirkali, Ziya – NIDDK  
Kirkham, Perry – Perdue Univ.  
Kranzfelder, Kathy – NIDDK  
Kuaban, Alice – Am. Soc. of Hematology  
Kusek, John – NIDDK  
Lee, Christine – NIDDK  
Laakso, Joseph – Endo. Soc.  
Leschek, Ellen – NIDDK  
Li, Yan – NIDDK  
Linder, Barbara – NIDDK  
Lynch, Christopher – NIDDK  
Malik, Karl – NIDDK  
Maruvada, Padma – NIDDK  
Martey, Louis – NIDDK  
Martinez Winnie – NIDDK  
Michels, Kathleen – FIC

Miller, David – NIDDK  
Moxey-Mims Marva – NIDDK  
Mullins, Christopher – NIDDK  
Narva, Andrew – NIDDK  
Newman, Eileen – NIDDK  
Nguyen, Van – NIDDK  
Niebylski, Charles – NIDDK  
Norton, Jenna – NIDDK  
Olumi, Aria – Am. Urol. Ass.  
Pawlyk, Aaron – NIDDK  
Payne, January – NIDDK  
Perrin, Peter – NIDDK  
Perry Jones, Aretina – NIDDK  
Pike, Robert – NIDDK  
Pileggi, Antonello – CSR  
Ramani, Rathna – NIDDK  
Rankin, Tracy – NIDDK  
Rasooly, Rebekah – NIDDK  
Roberts, Tibor – NIDDK  
Rojas, Raul – CSR  
Rosenberg, Mary Kay – NIDDK  
Rosendorf, Marilyn – NIDDK  
Roy, Cindy – NIDDK  
Rys-Sikora, Krystyna – NIDDK  
Sanovich, Elena – NIDDK  
Saslowsky, David – NIDDK  
Sato, Sheryl – NIDDK  
Savage, Peter – NIDDK  
Sechi, Salvatore – NIDDK  
Serrano, Jose – NIDDK  
Sheets, Dana – NIDDK  
Sherker, Averell – NIDDK  
Shepherd, Aliecia – NIDDK  
Sierra-Rivera, Elaine – CSR  
Silva, Corinne – NIDDK  
Singh, Megan – NIDDK  
Smith, Philip – NIDDK  
Spain, Lisa – NIDDK  
Star, Robert – NIDDK  
Stoeckel, Luke – NIDDK  
Tatham, Thomas – NIDDK  
Teff, Karen – NIDDK  
Tilghman, Robert – NIDDK  
Torrance, Rebecca – NIDDK  
Tuncer, Diane – NIDDK  
Unalp-Arida, Aynur – NIDDK  
Van Raaphorst, Rebekah – NIDDK  
Vinson, Terra – NIDDK  
Wallace, Julie – NIDDK  
Weiner, Jeffry – NIDDK  
Yang, Jian – NIDDK

## C. ANNOUNCEMENTS

*Dr. Rodgers*

### New Council Member

Dr. Rodgers welcomed a new member to the Advisory Council:

*Dr. Beverly Torok-Storb*, joined the Kidney, Urologic, and Hematologic Diseases Sub-Council. Dr. Torok-Storb is a member of the clinical research division at the Fred Hutchinson Cancer Research Center in Seattle, WA. Her research focuses on the regulation of hematopoiesis. She earned her Ph.D. at the University of Pittsburgh and held a number of ascending positions at the University of Washington School of Medicine and the Fred Hutchinson Cancer Center.

### Extramural Awards and Other Announcements

Council member *Dr. Mark Donowitz* received the 2016 Distinguished Achievement Award in Basic Science from the American Gastroenterological Association (AGA). The award, established in 1968, recognizes a senior investigator whose major accomplishment in basic science research has significantly advanced the science and practice of gastroenterology.

NIDDK grantee *Dr. Jeffrey Friedman* of the Rockefeller University has received the Harrington Prize for Innovation in Medicine. The Harrington Prize was established by the Harrington Discovery Institute at the University Hospital at Case-Western Medical Center and the American Society for Clinical Investigation to honor scientists who have advanced discovery into clinical application. The award recognizes Dr. Friedman for the discovery of leptin and the leptin-mediated pathways that control feeding behavior. NIDDK and other NIH components have supported Dr. Friedman's work, and his work has provided a foundation for a deeper understanding of possible intervention strategies to address diseases related to obesity. Work on leptin in NIDDK's Intramural Program led to an FDA-approved treatment for patients with generalized lipodystrophy, a rare but life-threatening disorder for which there was previously no effective treatment.

*Dr. John Carethers*, John G. Searle Professor of Internal Medicine and Chair of the Department of Internal Medicine at the University of Michigan Medical School, was elected to the American Academy of Arts and Sciences in recognition of his leadership in academic medicine. A gastroenterologist, Dr. Carethers is an authority on the molecular basis of familial colorectal cancer as well as a leader in academic medicine. He received his first NIDDK grant in 1994 and continues a very active NIDDK- and NCI-funded research program focusing on mismatch repair genes in colorectal cancer in African Americans.

Another NIDDK grantee, *Dr. Richard Lifton*, will become the 11<sup>th</sup> president of Rockefeller University, succeeding Dr. Mark Tessier-Lavigne, who will be president of Stanford University. Dr. Lifton is currently Professor of Genetics and chair of the Department of Genetics at Yale University. Dr. Lifton is a pioneer in the use of genetics and genomics to understand

fundamental mechanisms underlying human disease, including cardiovascular disease, neoplasia, kidney disease, and osteoporosis. His work connecting mutations that affect renal salt reabsorption to blood pressure provided the scientific foundation for modulating salt balance to prevent and treat high blood pressure and informed public health efforts and therapeutic strategies that are used worldwide. He is one of the developers of exome sequencing, a method for rapidly and inexpensively sequencing the genome which is used to discover new genes as well as in clinical diagnosis. Dr. Lifton has served as an advisor to federal agencies, private foundations, universities, and biopharmaceutical companies and is currently a member of the Advisory Committee to the Director of the NIH. He is a member of the AAAS and serves on the Governing Council of the National Academy of Sciences and the National Academy of Medicine.

**Dr. Patrick Stover**, a 2012 NIDDK Merit Award winner, was elected to the National Academy of Sciences earlier this month. He was one of 84 new members and 21 foreign associates from 14 countries who were recognized for distinguish and continuing achievements in original research. A professor and director of nutritional sciences at Cornell University, Dr. Stover and his group have investigated the role of B vitamins, folate, and B12 on nuclear and mitochondrial 1-carbon metabolism as well as their downstream effects on methylation, gene expression, genome stability, and their role in preventing human pathology. On the Cornell Faculty since 1994, he received the Presidential Early Career Award for Scientists and Engineers in 1996 and became an AAAS fellow in 2004. He is currently president of the American Society of Nutrition.

### **NIDDK Staffing Update**

On April 30, 2016, **Dr. Jill Carrington** retired as program director in the Division of Digestive Diseases and Nutrition. Extremely effective in her position, she maintained a portfolio that included grants on gastrointestinal development, epithelia biology and gut barrier. She was a project scientist for the Intestinal Stem Cell Consortium and served as project team lead for the biology initiative Stimulating Peripheral Activities to Relative Conditions, or SPARC, an NIH Common Fund Program. Before joining NIDDK in 2007, Dr. Carrington was a program director at the National Institute on Aging and at the National Center for Research Resources. After a short break, she will be rejoining NIDDK on a part-time basis to continue work with both the Stem Cell Consortium and SPARC.

**Dr. Frank Calvo**, chief of NIDDK's Review Branch, will retire at the end of May after nearly 30 years with NIDDK. He served as program director in the Division of Diabetes, Endocrinology, and Metabolic Diseases before moving to the Review Branch in 1990. He rose up through the ranks before being appointed chief in 2000. Dr. Calvo has contributed not only to NIDDK, but also to NIH in the development of the loan repayment program and his efforts to ensure inclusion in recruiting and policy.

NIDDK welcomes **Dr. Christine Lee** as a program director of the Division of Diabetes, Endocrinology and Metabolic Diseases. She will manage translational research focused on improving outcomes for people with or at risk of developing diabetes. She will also develop research efforts on diabetes in older Americans. She comes to NIDDK from the VA Portland Healthcare System, where she was a staff physician. She was also assistant professor in the

Division of Endocrinology, Diabetes, and Clinical Nutrition at the School of Medicine at Oregon Health Science University.

**Dr. Daniel Gossett** has joined the Division of Kidney, Urologic, and Hematologic Diseases as program director. Dr. Gossett has previously helped with NIDDK's SBIR and STTR programs and has served on several NIDDK and trans-NIH working groups. He recently completed a 4-month detail at National Center ATS where he worked on the Bridging Interventional Development Gaps (BrIDGs) and Therapeutics for Rare and Neglected Diseases (TRND) initiatives. Dr. Gossett's portfolio at NIDDK will include small business technology development and translational research.

On February 21<sup>st</sup>, **Dr. Christopher Lynch** assumed the roles of director of the newly created Office of Nutritional Research and chief of NIDDK's Nutrition Branch. Dr. Lynch will facilitate nutrition research within NIDDK and across NIH. As part of his leadership role, Dr. Lynch has formed and is leading a trans-NIH nutrition research strategic planning working group. Dr. Lynch comes to NIH after 27 years at Pennsylvania State University's College of Medicine in Hershey, PA, where he was professor and vice chair of the Department of Cellular and Molecular Physiology. His research focused on how what we eat and drink influences processes leading to obesity and type 2 diabetes; the relationship between antipsychotic therapies and obesity in type 2 diabetes, and how gastric bypass surgery changes metabolism.

## **II. CONSIDERATION OF SUMMARY MINUTES OF THE 200<sup>th</sup> COUNCIL MEETING**

***Dr. Rodgers***

The Council approved, by voice vote, the Summary Minutes of the 200th Council meeting, which had been sent to them in advance for review.

## **III. FUTURE COUNCIL DATES**

### **2016**

September 7-8 (Wednesday and Thursday)

*Building 31, Conference Rooms 10, 6 and 7*

### **2017**

February 1-2 (Wednesday and Thursday)

*Building 31, Conference Rooms 10, 6 and 7*

May 10-11 (Wednesday and Thursday)

*Building 31, Conference Rooms 10, 6 and 7*

September 6-7 (Wednesday and Thursday)

*Natcher Conference Center (Building 45)*

*Conference Rooms E1/E2, D and F1/F2*

Most meetings are expected to be a single day. However, the NIDDK asks Council members to reserve two days for each meeting should a situation arise where a longer meeting is required.

#### IV. ANNOUNCEMENTS

*Dr. Karl Malik*

##### **Confidentiality**

Standing in for Dr. Brent Stanfield, who was not present for the first part of the meeting, Dr. Malik reminded the 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. Malik reminded the 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 the Member does not participate in, and is not present during, the 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. A statement is provided for the signature of the Member, and this statement becomes a part of the meeting file. Dr. Malik directed each Council Member to a statement in his or her meeting folder regarding the conflict of interest in review of applications. He asked each Council Member to read it carefully, sign it, and return it to NIDDK before leaving the meeting.

Dr. Malik pointed out 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.

Regarding multi-campus institutions of higher education, Dr. Malik 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.

## V. REPORT FROM THE NIDDK DIRECTOR

*Dr. Rodgers*

### **Budget Update**

On February 9, shortly after the January Advisory Council meeting, President Obama released his fiscal year 2017 budget for all government agencies. The President requested \$33.14 billion for NIH, an increase of \$825 million or 2.55% over fiscal year 2016. The 2016 NIH budget was \$2 billion over the 2015 budget for an increase of 6.6 percent.

Dr. Rodgers pointed out that the President's 2017 budget has two important distinguishing features:

- **The President's request for 2017 replaces \$1 billion in discretionary funds with \$1.825 billion in mandatory funds.** NIH funding has always come from funds labeled "discretionary" within the Department of Health and Human Services. However, in the two-year budget agreement made in December 2015, Congress capped discretionary spending for 2016 and 2017. In order to provide agencies with program increases, the President has made heavy use of mandatory funds. While appropriators voiced support for an NIH funding increase at the House and Senate appropriations hearings for NIH held on March 16 and April 7, they also opposed the shift from discretionary to mandatory funding. The appropriations subcommittee chairman maintained that the final NIH appropriations would not include this shift.
- **The additional \$825 million in the President's request for 2017 includes three targeted areas.** NCI would receive a \$680 million increase for National Cancer Moonshot. The Common Fund would receive \$100 million for the Precision Medicine Initiative Cohort, and the Office of the Director would get \$45 million for the BRAIN Initiative. ICs other than NCI will not receive a funding increase under the President's request.

Congress ultimately determines the budget and how the NIH's appropriation is divided, but as of right now NIDDK's budget would remain at \$1.966 billion, including the \$150 million special diabetes program.

The House Republican leaders have started bringing spending bills to the floor, but there has been no announcement of when the Labor/HHS bill—which includes NIH—will be considered. With only 45 legislative days before the start of the next fiscal year, many believe a continuing resolution will be needed to continue to fund the government beyond October 1. Under a continuing resolution agencies would operate under current fiscal 2016 funding levels.

Dr. Rodgers noted that this situation means that the budget is uncertain and the national election may add to the uncertainty. He expressed hope that there will be more encouraging news at the next Council meeting in September.

## **VI. UPDATE FROM THE DIRECTOR, FOGERTY INTERNATIONAL CENTER: Dr. Roger Glass**

*Director Rodgers introduced Roger Glass, M.D., Ph.D., who has served as the Director of the Fogarty International Center and Associate Director of Global Health for NIH since 2006. The Fogarty Center, established in 1968, is the arm of NIH specifically devoted to supporting and facilitating global health research. About 5,000 scientists have received significant research training through the Center.*

*Dr. Glass holds an M.D. from Harvard Medical School, an M.P.H. from the Harvard School of Public Health, and a doctorate from the University of Göteborg in Sweden. His research interests are in the prevention of gastroenteritis from rotaviruses and noroviruses through the application of novel scientific research. He has maintained field studies in India, Bangladesh, Brazil, Mexico, Israel, Russia, Vietnam, China, and elsewhere. His research has been targeted toward epidemiologic studies to anticipate the introduction of rotavirus vaccines. He has received numerous awards including the prestigious Charles C. Shepard Lifetime Scientific Achievement Award presented by the CDC in recognition of his 30-year career of scientific research application and leadership, and the Dr. Charles Merieux Award from the National Foundation for Infectious Diseases for his work on rotavirus vaccines in the developing world. He is a member of the Institute of Medicine, the American Academy of Microbiology, the American Society of Microbiology, the American Association for the Advancement of Science, the American Society of Virology, and the American Epidemiological Society. He is also a fellow in the Infectious Disease Society and the American College of Epidemiology, and has co-authored more than 600 research papers and chapters.*

Dr. Glass focused his remarks on how funding for research in global health can not only address health crises in developing nations but also translate into major advances in health care in the U. S. and globally. He said the NIH, and the NIDDK in particular, can accelerate global research into problems affecting the U.S. as well as other countries. He proposed a number of avenues: funding U.S. researchers to develop research programs in other countries, working cooperatively with foreign funding agencies, and borrowing ideas and technologies developed in other countries to address chronic disease challenges in the U.S.

### **Leveraging Global Health Research Opportunities**

Dr. Glass said the return on global health investments can be spectacular. He used his own history as an illustration of the principle. Early in his career, the CDC funded him for two years to conduct a trial of a cholera vaccine in Bangladesh. His research there yielded an understanding of how to do effective oral rehydration therapy to treat children with diarrhea. Dr. Glass estimated that the original research funding for oral rehydration therapy was \$10 million or less. Such therapy, through products such as Pedialyte, represents a \$100 million a year industry in the U.S. alone and is the standard of care for children with diarrhea anywhere in the world. It has saved millions of lives. The CDC's initial investment in Dr. Glass's work also led to his own 30-year career, and allowed him to train others to recognize rotavirus and work on vaccine development.

Another example is the AIDS International Training and Research Program (AITRP), begun in 1988 near the beginning of the AIDS epidemic, which linked U.S. and foreign institutions to train investigators. The early cohorts of AITRP researchers now lead HIV research all over the world, Dr. Glass said. Dr. Glass advocated for a similar focused program for NIDDK, to fund investigators to study diabetes in the developing world. Dr. Glass observed that while Americans have the highest prevalence of diabetes, the sub-populations that suffer most are of African, Hispanic, and Asian origin. Researchers might be able to make important discoveries about diabetes and other diseases by studying founder populations.

A global approach might also yield opportunities and insights about strategies to combat obesity. For example, Mexico recently enacted a national tax on sugar-sweetened drinks that reduced consumption significantly. Monitoring health trends in countries that have enacted sugar taxes and other public health-related taxes may help the U.S. and its states determine which strategies are most effective.

Dr. Glass observed that the diabetes epidemic worldwide is impairing efforts to address tuberculosis infections because diabetes compromises the immune system and makes tuberculosis more virulent and harder to control. He recommended that research be conducted in countries like India and Mexico where the two conditions frequently co-occur, to investigate the link and ways to address it.

The Fogarty Center is supporting a diabetes expert from Rwanda to work at NIDDK for two years to begin exploring research collaborations to combat the global diabetes epidemic. Dr. Glass made an appeal for the NIDDK to consider how it could make strides in its research mission by considering global health possibilities beyond diabetes, such as support of collaborators in Central America to study Mesoamerican nephropathy.

### **Fogarty Center Strategic Plan**

Dr. Glass outlined the following goals under the strategic plan for the Center:

- Build research capacity of individuals; institutions, and networks to meet future and evolving global health challenges;
- Stimulate innovation in the development and evaluation of technologies to address global health problems;
- Support research and research training in implementation science;
- Advance research on prevention and control of the dual burden of communicable and non-communicable diseases and disability; and
- Build and strengthen partnerships to advance global health research and research capacity.

Dr. Glass emphasized that the Fogarty Center works to bolster the pipeline for investing in global health careers through programs targeting trainees (domestic and foreign), institutions, networks and foreign funders.

The Center funds five consortia, which include 20 universities, for five-year programs that link interested students with research mentorships in their institutions and in the developing world. It also supports medical students, post-doctoral students, and other early-career investigators with fellowships and small grants. Dr. Glass commented that the Center supports researchers from a wide range of disciplines, including genetics, veterinary science, dentistry, nephrology, cardiology and oncology. Recipients typically spend substantial time in developing countries, building up lasting partnerships with the local research community.

The Center has also developed relationships with foreign funding bodies. In addition, the Center participates in the Global Alliance for Chronic Disease, which brings together funding agencies from around the world to coordinate funding calls and develop research networks. To date the consortium has funded work in hypertension, diabetes, and environmental lung disease, representing about \$100 million in funding for non-communicable diseases.

Dr. Glass urged NIDDK to extend its scope outside the U.S., to areas that have unusual genetic mixes, diets, exercise patterns, toxin exposure, and specific public health interventions like the sugar tax. In addition, some national health systems, such as China's, may be better suited than the U.S. to handle large clinical trials and cohort studies.

Dr. Glass observed that the U.S. shares many health problems with other countries, and can benefit from research cooperation globally, and from innovations developed abroad. He finds particular promise in "frugal innovations," such as India's development of \$30 cataract surgery that meets U.S. standards.

### **Council Questions and Discussion**

*Is the Fogarty Center working with the Gates Foundation (which works to combat disease in developing countries, and specifically on rotaviruses and vaccines)?*

Mr. Gates and members of the Foundation have met several times with representatives of NIH including the Fogarty Center during the past three years. The two organizations are collaborating on 10 programs, and together account for 60 percent of the total worldwide funding for global health research. Dr. Glass specifically mentioned a collaboration on developing and testing a one-dose vaccine for human papilloma virus.

*Does the Fogarty Center have any programs, or plans for programs, to offer opportunities to high school students?*

The Center does not have specific programs geared toward younger students, and Dr. Glass said such programs are beyond the reach of NIH and the Fogarty Center. However, he encouraged universities and other local organizations to try to develop such programs, to engage students early.

*Is the Fogarty Center doing any work on surgical innovations in areas such as cataract treatment and limb replacement, which could yield results that can be applied in the U.S. to reduce overall healthcare costs?*

Through its Fellows and Scholars Program, the center has sent 10 to 12 surgeons to do their third and fourth years of residency in countries such as Rwanda. It has also funded surgical research. Dr. Glass gave the example of a shunt for hydrocephalus developed by a Harvard pediatric neurosurgeon as part of his work in the CURE Hospital in Uganda, and which he has now brought back the U.S. He said that the NIGMS supports some surgical research, and the NIDDK might also have some areas of interest that could yield surgical research initiatives appropriate for global action.

## **VII. UPDATE FROM THE NIH OFFICE OF EXTRAMURAL RESEARCH**

***Dr. Michael Lauer, Deputy Director for Extramural Research, National Institutes of Health***

*Director Rodgers introduced Michael Lauer, M.D., Deputy Director for Extramural Research at NIH. Dr. Lauer serves as a principal scientific leader and advisor to the Director of the NIH on all matters related to substance, quality, and effectiveness of NIH's extramural research programs and administration.*

*Dr. Lauer received his M.D. degree from Albany Medical College and interned in internal medicine at the Massachusetts General Hospital and Harvard Medical School. After a residency in medicine at Massachusetts General, he had a clinical fellowship in cardiology at Harvard and Beth Israel Hospital in Boston. He also served as a research fellow in the Framingham Heart Study. He spent 14 years at Cleveland Clinic as Professor of Medicine, Epidemiology, and Biostatistics. During his tenure there, he led a federally funded internationally renowned clinical epidemiology program that applied big data from large-scale electronic health platforms to questions regarding the diagnosis and management of cardiovascular disease. From 2007 to 2015 he served as a Division Director at the National Heart, Lung, and Blood Institute, where he promoted efforts to leverage big data infrastructure to enable high-efficiency population and clinical research, as well as the adoption of a research funding culture that reflects data-driven policy. He has received numerous awards, including the NIH Equal Employment Opportunity Award of the Year and the Arthur S. Flemming Award for Exceptional Federal Service in recognition of his efforts to grow a culture of learning and accountability.*

Dr. Lauer focused his talk on the question of how to maximize the benefit of the diminishing research dollars available through the federal government, by changing the metrics by which the value of research is measured. He said too much attention is paid to levels of funding, and not enough to measuring whether that funding furthers the research agenda in measurable ways.

Drawing a parallel with Southwest Airlines, he observed that the airline doesn't measure its success by how much fuel it burns, but by whether it gets passengers where they want to go, on time, as well as several other metrics that are objective, quantifiable, verifiable, and meaningful.

Dr. Lauer discussed a new "finish line" for research grants, based on outputs such as patents,

publications, new forms of delivering health care, new devices, new molecules, and, ultimately, better health care and better health.

### **Stagnant Funding for Research**

Dr. Lauer offered evidence that by several measures, the U.S. spends substantially less on research than it once did, and less as a share of GDP than other countries. The U.S. currently spends about \$120 billion per year on biomedical research, including federal, nonprofit, and industrial sources—about half what was spent in 1994. While overall funding grew at a healthy 6+ percent per year up until 2002, it has stagnated since and now grows less than one percent per year. NIH research funding, specifically, has actually been shrinking over the past 10 years, about 2 percent per year. The U.S. spends between 2.5 and 3 percent of its GDP on research, less than South Korea, Japan, Sweden, Finland, and Israel. The federal government spent 8 percent of its 1970 budget on research, and now spends 3 percent. This is at a time when many other countries are increasing their research budgets.

### **NIH Applicants and Investigators**

Transitioning from a focus on dollars spent, Dr. Lauer explored trends associated with the numbers of investigators NIH supports and the numbers of applicants seeking NIH funding. Jon Lorsch, the Director of the National Institute of General Medical Sciences, has pointed out that the number of investigators is an important metric for NIH to monitor (see Lorsch, JR. *Mol. Biol. Cell* 2015; 26: 1578-82).

In fiscal year 2015 about 27,500 unique investigators had at least one research project grant from NIH, up about 10 percent from 25,000 in 2003. However, the number of unique investigators seeking funding rose almost 50 percent during that same period, from 60,000 in the five year window associated with fiscal year 2003 to 89,000 in a five year window associated with fiscal year 2015. During this time period the cumulative investigator rate (percentage supported by NIH) fell from 45% to 32%.

Focusing on just R01 dynamics, the number of unique investigators who have at least one R01 has dropped. In the five year window associated with fiscal year 2003, about 21,000 unique investigators had an R01, while in the five year window associated with 2015 it was 20,500. The number peaked around fiscal year 2011, when approximately 21,500 unique investigators had at least one R01 award. Then, over the last five years, there has been a 5 percent decline. Meanwhile, the number of unique applicants has increased from about 45,000 to 60,000, and so the cumulative investigator rates have gone down accordingly.

Dr. Lauer referenced a 2014 article in the *Proceedings of the National Academy of Science* (see Alberts B. et al. *PNAS*. 2014;111:5773-7 ) which, he reported, points out that the fundamental problem is that the system has become hypercompetitive. Dr. Lauer stated that the authors argue that this is an unsustainable state, a recipe for long-term decline and, hence they argue that we need to rethink some fundamental features of the U.S. biomedical

research system.

## Measuring Research Productivity

Dr. Lauer observed that there is no widely accepted standard for determining the impact of research. For example, one measure of impact is how frequently a paper is cited. However, the citation rate varies dramatically depending on the field.

Dr. Lauer presented regression analysis data indicating that when publications are binned by topic or field, the best predictor of highly cited papers among research project grants was project duration. The grant mechanism, funding level, and first fiscal year of funding had comparatively modest predictive value, and other factors (e.g., whether the project was a “Human” or Animal” study or whether the research was conducted by a “New Investigator”) were poor predictors.

Dr. Lauer then showed several follow up charts with transformed axes in part to introduce a point regarding a well-studied phenomenon referred to as "power law" which holds that output is associated with a power of the input. Dr. Lauer stated that this means that output does not follow a simple normal distribution but rather a log normal distribution and this is not just a mathematical curiosity. Dr. Lauer referenced an article entitled, "Power Laws in Economics" (see Gabaix X. *J Econ Persp.* 2016;30:185-206). He explained that the author, a professor of finance at New York University, argues these power laws are not just in economics. They're also in, for example, publication and citation data. In his article, Dr. Gabaix makes the case that...”One implication of the [power] law is that there are many more extreme events than would occur if the distribution were Gaussian” (Gabaix X. *J Econ Persp* 2016;30:185-206). Dr. Lauer then discussed arguments by Nassim Nicholas Taleb (see Taleb N. *Antifragile: Things That Gain from Disorder*; 2012 Random House), where, following the power law, many projects produce no or limited results, but a few projects produce such remarkable results that they more than make up for the larger number of projects that do not have large impact. Using power law as a guide, the correct approach is to fund as large a number of projects as possible, to increase the chances of a few large payoffs. Dr. Lauer suggested that perhaps the "finish line" for funding agencies should ultimately be those extreme or transformative events—a revolutionary finding or new drug—rather than the amount of funding, the number of projects funded, or the number of resulting publications and citations.

Dr. Lauer presented two diagrams that appeared in the journal *Cell* in September 2015 (see Sanders Williams R. et al. *Cell* 2015;163:21-23), illustrating the thousands of scientists, institutions, publications, trials, and patents that lay behind the blockbuster cystic fibrosis drug, Ivacaftor, and the LDL-reduction drug Repatha. He suggested doing the same type of analysis for other transformative events to identifying which elements are related to work funded by the NIH. With this approach, patterns may emerge that could help NIH understand where funding dollars are having the most impact and perhaps help us focus our funding policies to enhance the number of transformative events.

## **The NIH Strategic Plan**

Dr. Lauer briefly outlined the NIH strategic plan first presented in December 2015, drawing particular attention to managing by results. He said the underlying goal is to move towards a system that is focused on "evidence-based funding."

### Council Questions and Discussion

*Should the NIH consider adopting a policy of funding investigators, as the Howard Hughes Medical Institute does, as opposed to funding projects?*

Dr. Lauer said that one comparison of investigator-based funding and project-based funding, conducted by the National Bureau of Economic Research, matched a group of researchers who had gotten NIH project-based awards with a comparable group of awardees who received investigator-based funding from HHMI. Over time, the HHMI group published more highly cited papers and were more likely to do "innovative work" that helped them move into different fields of study.

Several institutes, including NIGMS, NCI, NINDS, and NHLBI, are experimenting with an investigator-based funding program called the R35, where investigators are funded based on their track record, rather than a detailed project proposal.

Dr. Griffin Rodgers added that NIDDK is considering adopting an investigator-funding program, but is waiting to see the results of pilot programs at other Institutes.

*Why hasn't the supply of investigators and projects adjusted to the reduced levels of research funding? And what is happening to the researchers who are unable to get funding?*

Dr. Lauer said some research has shown that there is a surplus of scientists in biomedical research. Salaries of Ph.D.s in computer science and engineering are substantially higher than the salaries of Ph.D.s in biomedical research, which may suggest a surplus of scientists. Others would dispute this analysis, he admitted.

The NIH's Common Fund has a program called Broadening Experiences in Scientific Training (BEST) that helps graduate programs train their students for careers other than tenure-track faculty and ensure graduates are equipped to fill the full range of positions available in biomedical, behavioral, social and clinical research.

*It seems that there may be differences in productivity depending on the type of grant someone applies for and receives—for example between the R01 and P01. Is this a team sciences outcome? Can you comment on that?*

Dr. Lauer indicated that he has been reviewing data on R01 versus P01s across several different institutes. One issue is that the P01 is a collection of smaller projects and each is expected to have a certain amount of productivity, and it might be expected that when you put all the projects together you may generate more productivity than one big project. Another observation is that

P01s appear to be a bit more productive than R01s within a fairly tight window. However, there are a fair number of R01s that are not very productive and few that are wildly productive, way above P01s. One way to think about this is to consider the R01 as a much smaller investment—to use a cliché, high risk and high reward. A greater number of them wind up not being particularly productive, but a few of them are much more so. A problem with a direct comparison is that the phenotypes of the R01 and P01 are different and Dr. Lauer is trying different things to make the comparisons as comparable to see if it is possible to tease out the effect of mechanism.

*Do R01 grants defeat the purpose of generating collaborative science, because of their focus on individual innovation?*

Dr. Rodgers and Dr. Lauer discussed the "fail but fail fast" approach sometimes used in business. Dr. Lauer said that this type of approach helps protect money to pay for success. He indicated that science is inherently unpredictable and we don't know where the next great success is going to be. One area outside of traditional innovation is clinical trials and he described a two-phase award process used by some components of NIH. The first phase of the award includes study design, infrastructure development and perhaps some enrollment. After the first phase there is a rigorous administrative review to assess whether the trial is likely to be successful, and funding is withdrawn if success seems unlikely. In this way, if it appears the trial will fail then money is freed up to do something else.

*How do you assess the effectiveness of program center grants?*

Dr. Lauer said his office is still studying the question, but would like to look at how the grants are distributed, how the content of their work may overlap with each other, and their geographic distribution.

## **VIII. SCIENTIFIC PRESENTATION: Inflammatory Links Between Obesity and Type 2 Diabetes**

*Dr. Saltiel*

*Dr. Alan Saltiel is a professor at University of California at San Diego School of Medicine and the director of its new Comprehensive Diabetes Center. He is a cell biologist who researches insulin and how it relates to obesity, diabetes, and other metabolic disorders. He holds a Ph.D. in biochemistry from the University of North Carolina. He has worked in both academia and the pharmaceutical industry. He holds 18 patents, has published more than 280 original papers, and has developed drugs for diabetes and cancer. Dr. Saltiel has received numerous awards including the Rosalyn Yalow Research and Development Award from the American Diabetes Association, the Herschel Award, and the John Jacob Abel and the Goldman and Gilman awards in experimental therapeutics from the American Society of Pharmacology. He's a member of the National Academy of Medicine and a fellow of the American Association for the Advancement of Science.*

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

A total of 1098 grant applications (328 primary and 770 dual), requesting support of \$363,048,497 were reviewed for consideration at the May 18, 2016 meeting. An additional 1160 Common Fund applications requesting \$2,087,031,491 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1380 applications requesting \$417,090,040 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 May 18, 2016 meeting.

## **X. ADJOURNMENT**

*Dr. Rodgers*

Dr. Rodgers expressed appreciation on behalf of the NIDDK to the Council members, presenters, and other participants. He thanked the Council members for their valuable input. There being no other business, the 201th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m. on May 18, 2015.

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