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 200th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on January 27, 2016, in Building 31, Conference Room 10, the NIH Campus, Bethesda, Maryland.

## A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Sharon Anderson
Dr. David Brenner
Dr. Joseph Bonventre
Dr. Eugene Chang
Dr. Mark Donowitz
Dr. Joel Elmquist+
Ms. Cindy Luxhoj
Dr. Caren Heller
Dr. Steven Kahn
Dr. Lee Kaplan
Dr. David Klurfeld
Dr. Craig Peters
Dr. Alan Saltiel
Dr. Jean Schaffer
Dr. Linda Shortliffe+
Dr. Irving Smokler
Dr. Bruce Spiegelman
Ms. Pamela Taylor
Dr. Beverly Torok-Storb+*

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

*Attended via WebEx because of emergency weather conditions.
+Attended as an *ad hoc* member.

## B. NIDDK STAFF AND GUESTS

Abbott, Kevin – NIDDK
Agodoa, Lawrence – NIDDK
Andersen, Dana – NIDDK
Arreaza-Rubin, Guillermo – NIDDK
Barnard, Michele – NIDDK
Bavendam, Tamara – NIDDK
Begum, Najma – NIDDK*
Best, Carolyn – Am. Urol. Ass.
Bishop, Terry – NIDDK
Blondel, Olivier – NIDDK*
Bourque, Sharon – NIDDK
Burgess-Beusse, Bonnie – NIDDK
Camp, Dianne – NIDDK*
Carrington, Jill – NIDDK
Castle Arthur – NIDDK
Chowdhury, Bratati – NIDDK
Connaughton, John – NIDDK
Copeland, Randy – NIDDK*
Desiderio, Ulyana – Am. Soc. of Hem.
Dirks, Dale – NephCure
Doherty, Dee – NIDDK
Donohue, Patrick – NIDDK

Drew, Devon – NIDDK*
Duggan, Emily – NIDDK
Eggerman, Thomas – NIDDK*
Evans, Mary – NIDDK
Farishian, Richard – NIDDK
Fisher, Rachel – NIDDK
Fleischhacker, Sheila – NIDDK
Flessner, Michael – NIDDK*
Fonville, Olaf – NIDDK
Fradkin, Judith – NIDDK
Gallivan, Joanne – NIDDK
Gansheroff, Lisa – NIDDK
Gossett, Danny – NIDDK
Goter-Robinson, Carol – NIDDK
Guo, Xiaodu – NIDDK*
Haft, Carol – NIDDK
Hall, Sherry – NIDDK*
Hamilton, Frank – NIDDK*
Hanlon-Tilghman, Mary – NIDDK
Hill, Fred – The Hill Group
Hoff, Eleanor – NIDDK
Hoffert, Jason – NIDDK
Hyde, James – NIDDK*
Hoofnagle, Jay – NIDDK
Hoover, Camille – NIDDK
Hoshizaki Deborah – NIDDK*
Hunter, Christine – NIDDK*
James, Stephen – NIDDK
Jerkins, Ann – NIDDK*
Jones, Teresa – NIDDK*
Karp, Robert – NIDDK
Ketchum, Christian – NIDDK
Kimmel, Paul – NIDDK
Kirkali, Ziya – NIDDK
Kusek, John – NIDDK*
Laakso, Joseph – Endo. Soc.
Laughlin, Maren – NIDDK
Leschek, Ellen – NIDDK*
Li, Yan – NIDDK*
Linder, Barbara – NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Martey, Louis – NIDDK
Moxey-Mims Marva – NIDDK
Mullins, Christopher – NIDDK
Narva, Andrew – NIDDK
Newman, Eileen – NIDDK
Nguyen, Van – NIDDK*
Olumi, Aria – Am. Urol. Ass.
Pawlyk, Aaron – NIDDK
Perrin, Peter – NIDDK
Perry Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Rankin, Tracy – NIDDK
Rasooly, Rebekah – NIDDK
Regan, Karen – NIDDK*
Roberts, Tibor – NIDDK
Robinson, David – NIDDK*
Rosenberg, Mary Kay – NIDDK
Rosendorf, Marilyn – NIDDK*
Roy, Cindy – NIDDK
Rys-Sikora, Krystyna – NIDDK
Saslowsky, David – NIDDK*
Sato, Sheryl – NIDDK
Savage, Peter – NIDDK
Sechi, Salvatore – NIDDK
Serrano, Jose – NIDDK
Sheets, Dana – NIDDK
Shepherd, Aliecia – NIDDK
Silva, Corinne – NIDDK
Singh, Megan – NIDDK*
Smith, Philip – NIDDK
Spain, Lisa – NIDDK*
Star, Robert – NIDDK
Stoeckel, Luke – NIDDK
Surio, Priyanka – Crohns and Colitis F.
Tatham, Thomas– NIDDK
Teff, Karen – NIDDK
Tilghman, Robert – NIDDK*
Torrance, Rebecca – NIDDK*
Tuncer, Diane – NIDDK
Utama, Herman – NIDDK
Unalp-Arida, Aynur – NIDDK*
Van Raaphorst, Rebekah – NIDDK
Vinson, Terra – NIDDK
Wallace, Julie – NIDDK
Wellner, Robert – NIDDK*
Wilkens, Kenneth – NIDDK
Woynarowska, Barbara – NIDDK
Yanovski, Susan – NIDDK
Yang, Jian – NIDDK*

**Attended via WebEx because of emergency weather conditions.*

## C. ANNOUNCEMENTS

### New Council Members

Dr. Rodgers welcomed two new Council members.

***Caren Heller, M.D., M.B.A.,*** is joining the Digestive Diseases and Nutrition Subcouncil as a Public Member. Dr. Heller is the Chief Scientific Officer of the Crohn's & Colitis Foundation of America (CCFA). She is responsible for all mission-related activities including research, patient/professional services, and advocacy. Dr. Heller has more than thirty years of professional experience within the pharmaceutical and healthcare industries and in academic medical centers. She previously worked for Weil Cornell Medical College, where she most recently served as Associate Dean of Intercampus and Industry Initiatives. Prior to Weil Cornell, Dr. Heller was at Athena Healthcare Consulting, where she worked with industry and academic centers regarding new product opportunities, new drug development, and clinical and translational research. Dr. Heller has worked with an FDA Advisory Committee and implemented clinical development plans resulting in drug approval. Dr. Heller received her M.D. from Columbia University and a Master of Business Administration degree from the University of Chicago.

***Joel Elmquist, D.V.M., Ph.D.,*** is joining the Diabetes, Endocrinology, and Metabolic Diseases Subcouncil. At the University of Texas, Southwestern, Dr. Elmquist is Professor of Internal Medicine, Pharmacology and Psychiatry; Maclin Family Distinguished Professor in Medical Science in Honor of Dr. Roy A. Brinkley; the Carl H. Westcott Distinguished Chair in Medical Science; and the Director of the Division of Hypothalamic Research. Dr. Elmquist's research focuses on the functional neuroanatomy of the mammalian hypothalamus. His laboratory works mainly on the regulation of body weight homeostasis, food intake, and control of the autonomic nervous system. Dr. Elmquist earned his D.V.M. and Ph.D. degrees at Iowa State University, followed by postdoctoral work at Harvard Medical School/Beth Israel Deaconess Medical Center. In 2014, he received the American Diabetes Association's Outstanding Scientific Achievement Award, and the National Postdoctoral Association Mentor of the Year Award. He has served as both a member and chair of NIH Study Sections, and currently serves on the editorial boards of four scientific journals.

### *Ad Hoc* Members

Dr. Rodgers announced the participation of three *ad hoc* Council members.

***Steven Kahn, M.B., Ch.B.,*** is a Professor within the Division of Metabolism, Endocrinology and Nutrition at the University of Washington, and is affiliated with the Veterans Affairs Puget Sound Health Care System. He is also Director of the NIDDK-funded Diabetes Research Center at the University of Washington. Dr. Kahn is an endocrinologist whose research focuses on the mechanisms responsible for the critical impairments in insulin secretion that lead to diabetes. With his colleagues, Dr. Kahn is also examining novel approaches to preventing and treating type 2 diabetes. Dr. Kahn

received his medical degree from the University of Cape Town, South Africa. In addition to postgraduate training in South Africa, he also did an internship and residency in internal medicine at Einstein Medical Center in Philadelphia.

***Linda M. Dairiki Shortliffe, M.D.,*** is the Stanley McCormick Memorial Professor of Urology at Stanford University. Dr. Shortliffe earned her M.D. from Stanford, and did most of her postgraduate training at Stanford University Medical Center. She then went on to build a very successful career in urology, especially pediatric urology--holding a number of ascending positions primarily at Stanford. Dr. Shortliffe has had a very active research career with support from the VA, NIH/NIDDK, foundations, and other non-government sources. The more recent focus of her research has been defining parameters that may be involved in urinary tract hydronephrosis (non-obstructive), urinary tract obstruction, vesicoureteral reflux, and infectious nephropathy.

***Beverly Torok-Storb, M.Ed., Ph.D.,*** is a member of the Clinical Research Division of the Fred Hutchinson Cancer Research Center in Seattle, Washington. She has a long-standing interest in the regulation of hematopoiesis. A current focus of her research is the balance between stem cell replication and differentiation. She is active in supervising pre- and post-doctoral scientists, and has also been involved in high school intern programs. Dr. Torok-Storb earned her Ph.D. at the University of Pittsburg and then held a number of ascending positions at the University of Washington School of Medicine and the Fred Hutchinson Cancer Research Center. She has regularly served as an NIH Study Section member or chair. She also served as a member of the trans-NIH "Peer Review Advisory Committee" from 2005-2008.

## Extramural Awards

***Dr. C. Ronald Kahn*** has received the 2016 Wolf Prize in Medicine in recognition of his discoveries in the insulin signaling network in people with diabetes and/or obesity. He served on the Council from 1998-2002. Dr. Kahn began his research career in the NIDDK Intramural Program. He is currently the Chief Academic Officer, Joslin Diabetes Center, Boston, and has considerable research support from the NIDDK and the NIH.

## "In Memoriam"

***Dr. Tim Bartness***--a long-time NIDDK grantee and MERIT awardee--passed away in late September 2015. Dr. Bartness had a very productive research career, primarily at Georgia State University. He contributed substantially to knowledge in a number of areas, including white and brown adipose tissue sympathetic and sensory nervous system innervation; neural control of white adipose tissue lipolysis and brown adipose tissue thermogenesis; obesity reversal; and photoperiodism/melatonin receptor signaling. A highly regarded scientist, he regularly served on NIH peer review groups. He was also a dedicated mentor and strong advocate for early career investigators.

## New NIDDK Staff

***Charles Niebylski, Ph.D., J.D.,*** was selected and is now serving as Director of the NIDDK Technology Advancement Office (TAO). He was TAO's senior intellectual property advisor from 2011 to 2013, until joining the NIH National Center for Advancing Translational Sciences as Strategic Alliances Manager. In addition to his experience as a biotech patent attorney, Dr. Niebylski has worked as a scientist in basic, applied and clinical research areas. As TAO Director, he will collaborate with NIDDK scientists and senior management to identify and further new technologies and strategies.

**NIDDK Recent Advances and Emerging Opportunities**

This latest NIDDK research compendium is posted in the "Strategic Plans and Reports" section of the NIDDK website (http://www.niddk.nih.gov/about-niddk/strategic-plans-reports/Pages/NIDDK-recent-advances-emerging-opportunities-2016.aspx).
The report provides examples of NIDDK-supported research advances published in Fiscal Year 2015. It also includes longer-term "Stories of Discovery;" summaries of scientific presentations made at Council meetings during 2015; and updated data on NIDDK funding trends and support of the Institute's core values. There is a section about the new "Friends of NIDDK" coalition. The NIDDK Office of Scientific Program and Policy Analysis developed the report, with input and guidance from the Divisions.

## II. CONSIDERATION OF SUMMARY MINUTES OF THE 199th COUNCIL MEETING

***Dr. Rodgers***

Following a motion, the Council approved by voice vote the summary minutes of the 199th Council meeting, which had been sent to them in advance for review.

## III. FUTURE COUNCIL DATES

***Dr. Rodgers***

Dr. Rodgers reminded the Council members of upcoming meeting dates. Meetings are expected to be only one day, but members are asked to reserve two days for each meeting should a situation arise where a longer meeting is required.

**2016 Council Meeting Dates**
May 18-19 (Wednesday and Thursday)
September 7-8 (Wednesday and Thursday)
***Meetings in 2016 will be held in Building 31, Conference Rooms 10, 6 and 7***

**2017 Council Meeting Dates**

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***

## 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 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 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. Stanfield directed the Council members to a statement in their folders regarding the conflict of interest in their review of applications. He asked each Council member to read it carefully, sign it, and return it to the NIDDK before leaving the meeting. Dr. Stanfield 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. 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.

**Annual Approval of the Council Operating Procedures**

The Council approved by voice vote its 2016 Operating Procedures, which had been sent to them in advance for review. The Procedures are essentially identical to those for 2015.

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

**Budget and Appropriations Update**

Dr. Rodgers reported that the President signed the Consolidated Appropriations Act of 2016 (H.R. 2029) on December 15, 2015. Continuing resolutions had kept the NIH and other agencies operational from the start of the fiscal year until that date. The Consolidated Appropriations Act has provided the NIH with the largest budget increase in many years--reflecting strong bi-partisan support for the agency. The NIH received 32.31 billion, which is a total program increase of $2 billion, or 6.6 percent, over the comparable Fiscal Year 2015 level. The NIDDK received $1.968 billion in total program funds. That amount reflects an increase of $69 million provided through the regular appropriations process, as well as $150 million in Special Statutory Program for Type 1 Diabetes Research that NIDDK manages for NIH.

Dr. Rodgers said that the Institute will post its FY 2016 funding policies on the NIDDK website shortly (http://www.niddk.nih.gov/research-funding/process/award-funding-policy/Pages/award-funding-policy.aspx). He gave a few highlights. R01 grants requesting less than $500 thousand will have a payline of the 13$^{th}$ percentile. Those requesting higher amounts will have a more stringent payline of the 8$^{th}$ percentile. Early Stage Investigators (ESIs) will again receive a more generous 18$^{th}$ percentile payline. The NIDDK will fully fund non-competing renewals (Type 5s). The nominal payline will be the 15$^{th}$ percentile for first competitive renewal applications for R01 awards to researchers who were ESIs when they competed for their initial NIDDK Type 1 R01 grant. Those R01 applications received in response to Funding Opportunity Announcements (FOAs) and to Program Announcements with special receipt, referral and/or review considerations (PARs) will not automatically be considered for funding based on payline/percentile ranking. Scores and additional programmatic factors will be weighed when considering those applications.

Dr. Rodgers said that the NIH has posted its FY 2016 funding policies on its website (http://grants.nih.gov/grants/financial/index.htm). He noted that there are several major priority areas in the final NIH budget, all of which were emphasis areas in the earlier President's Budget Request and the House and Senate bills. The Precision Medicine Initiative received $200 million, with $130 million going to the NIH Common Fund and $70 million going to the National Cancer Institute. An increase of $100 million was

provided to the NIAID to combat antimicrobial resistance. An increase of $85 million was provided for the NIH BRAIN initiative, which will be available to NIH institutes and centers. There was also a very large increase for Alzheimer's disease research.

**Fiscal Year 2017 President's Budget**

The President's Budget Request for Fiscal Year 2017 is scheduled to be released on February 9, 2016. Until then, the NIH is not permitted to discuss any details. However, it is recognized that there is still a spending cap for non-defense discretionary programs such as the NIH. The NIDDK will post information on its website when it is released.

Dr. Rodgers said that House Speaker Paul Ryan has signaled his goal for the House to pass all 12 appropriations bills for federal agencies by the end of March. That would mean that appropriations hearings would need to start very soon.

## VI. UPDATE FROM THE DIRECTOR, NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES (NIMHD)
***Eliseo J. Pérez-Stable, M.D.***

*Dr. Rodgers welcomed Eliseo J. Pérez-Stable, M.D., the new Director of the NIMHD. He has joined the NIH following a 37-year career as a research clinician and educator at the University of California, San Francisco (UCSF). He will direct the NIMHD's $270 million annual budget to conduct and support research, research training, research capacity and infrastructure development, and public education and information dissemination programs to improve minority health and reduce health disparities. Dr. Pérez-Stable received his M.D. from the University of Miami School of Medicine. He completed his primary care internal medicine residency and research fellowship at UCSF, where he was a Professor of Medicine, Chief of the Division of General Internal Medicine, and Director of the Center for Aging in Diverse Communities. Recognized as a leader in Latino health care and disparities research, Dr. Pérez-Stable spent more than 30 years leading research on smoking cessation and tobacco control policy in Latino populations in the United States and Latin America, including collaborations with researchers and public health advocates in Argentina. Dr. Pérez-Stable has received many honors and awards throughout his career, including the UCSF's Kaiser Award for Excellence in Teaching; the Society of General Internal Medicine's John M. Eisenberg National Award for Career Achievement in Research; and election to the National Academy of Medicine of the National Academy of Sciences. He was honored with the UCSF Lifetime Achievement in Mentoring Award in 2015.*

Dr. Pérez-Stable described the NIMHD, some of his goals as its new Director, and areas of mutual research interest between the NIMHD and the NIDDK. The NIMHD was established as an NIH Institute in 2010, after having been a grant-awarding "Center," and prior to that, an "Office" within the Office of the NIH Director. The NIMHD mission includes supporting research on minority health, as defined by racial/ethnic groups in U.S. Census. The NIMHD also supports research to understand the causes of and reduce health disparities in specific populations. Related efforts include the training of a diverse

scientific workforce, as part of broader NIH efforts, and the translation and dissemination of research information. The NIMHD also fosters innovative collaborations and partnerships.

Dr. Pérez-Stable said that one of his major goals in 2016 is to complete, to a large extent, a review of the NIH portfolio on minority health and health disparities research. This review is important for strategic planning across the NIH. While some planning efforts have been undertaken in the past, the development of a new NIH Strategic Plan for minority health and health disparities has been mandated by the Congress.

**Definitions**

Dr. Pérez-Stable said that greater clarity is needed regarding the terms "minority health" and "health disparities." Defining these terms appropriately is essential to the formulation of meaningful strategic plans, program development, and the tracking and reporting of research progress. He said that the terms are often incorrectly treated as synonyms. The terms are also confused with the inclusion of minorities in clinical research studies and trials, which he believes should be reported separately.

***Minority Health:*** Dr. Pérez-Stable pointed out that "minority health" is the distinctive health characteristics and attributes of the principal minority racial and/or ethnic groups in America--as defined in the U.S. Census. For federal research programs, the U.S. Office of Management and Budget has identified minority health populations as including those who are: African American or Black, Asian American, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, and Latino or Hispanic. Although demographics may change in the future, these are the groups that are currently the focus of minority health research, which investigates the health of these groups. Dr. Pérez-Stable noted that a common theme among these groups is that they are often disadvantaged socially or in some other way, often subject to discrimination, and/or under-represented in biomedical research and the scientific workforce.

***Health Disparities:*** Dr. Pérez-Stable said that a "health disparity" is a health difference that adversely affects disadvantaged populations, based on one or more health outcomes. Health disparities research is devoted to advancing scientific knowledge about the influence of health determinants and health-defining mechanisms, and how this knowledge is translated into interventions to reduce health disparities.

Dr. Pérez-Stable elaborated on differences in outcomes or events that can indicate a health disparity in a disadvantaged population relative to other populations or the general population. These include: (a) higher disease incidence and prevalence, such as disease morbidity with specific diagnosis; (b) poorer survival outcomes (mortality); (c) worse quality of life, self-reported symptoms, or function using standardized measures; (d) higher/lower rates of hospitalization, emergency department visits, or use of appropriate services; and/or (e) more incident events that affect health (such as dialysis); and/or Disability-Adjusted Life Years (DALYs). These and other possible indicators of health disparities are under discussion at the NIH.

Dr. Pérez-Stable said that research on the minority disparity population looks at the reasons for adverse or beneficial health outcomes, defines the contributing mechanisms, and identifies interventions to improve health, reduce health disparities, and establish the science base, which taps into the constructs of basic, clinical and population science. The health disparity population includes at least two groups. The first is outlined in the classification system used by the U.S. Office of Management and Budget for minority racial/ethnic groups, which includes poor and rural groups. The second is whatever metric one uses to define socioeconomic status. The Agency for Healthcare Research and Quality (AHRQ) is expected to collaborate in defining the health disparity population. AHRQ has identified as priority groups: women, urban poor, children/adolescents, sexual/gender minorities, immigrants/migrants, and special needs populations--including disabled, chronic care, end-of-life, medically underserved, disadvantaged, and very elderly groups. Dr. Pérez-Stable believes that race/ethnicity and socioeconomic status are really the pillars of the topic--with subgroups that could reflect different regions or conditions as appropriate.

Some of the questions that need to be addressed in health disparity research are: How does a difference in risk factors translate into a health disparity; for example, what role does genetics play in more aggressive biological forms of disease in certain populations? What social determinants interact with behavior, environment, and biology to result in a health disparity? Why do more aggressive biological forms of disease exist in some populations? How, when, and where does one intervene? What defines better health outcomes among traditionally disadvantaged groups?

With respect to the role of health determinants, Dr. Pérez-Stable pointed out a new strategy that is focused on a multidisciplinary systems-approach across the lifespan. He presented a "Minority Health and Health Disparities Research Framework" that depicted the way that, over the life-course, biological/behavioral factors, the physical/sociocultural environment, and the health care system interact with and influence health at the individual, interpersonal, community, and societal levels. Mechanisms that can lead to or contribute to health disparities include: earlier age of onset; faster progression of disease; later diagnosis due to access barriers; and/or different treatment results.

**Shared Research Concerns**

Dr. Pérez-Stable commented on several health disparities of mutual concern to the NIMHD and the NIDDK. These include: higher rates of diabetes and pre-diabetes in all racial/ethnic minorities and low socioeconomic status (SES); variations in normal body mass index (BMI) by race/ethnicity; the influence of the *APOL1* gene on the progression of chronic kidney disease (CKD); and liver diseases--including hepatitis B and C, fatty liver, chronic liver disease, and liver cancer. He also mentioned recent NIMHD grants relevant to NIDDK research areas such as diabetes and kidney disease. Both the NIMHD and the NIDDK support Historically Black Colleges and Universities (HBCUs).

**Looking Forward**

Dr. Pérez-Stable expressed his commitment to advancing the science of minority health and health disparities, and to ensuring that the best scientific strategies are included in the NIMHD and NIH strategic planning processes. In addition, he will emphasize: (a) promoting innovation from extramural scientists in population/clinical sciences; (b) establishing a program on health services and research in clinical settings; (c) promoting diversity in the workforce; and (d) funding fewer and more outstanding Centers of Excellence. The NIMHD currently funds about 50 such centers, and Dr. Pérez-Stable plans to free up some of that funding to support R01 grants in a transition that could take about two years. In the NIMHD Intramural Program, he will place emphasis on: (a) population science, especially clinical components; (b) recruitment of a scientific director and senior scientist--ideally with expertise in epidemiology and in social/behavioral and clinical research; (c) undertaking a possible new cohort study; and (d) networking with other Institutes and Centers to further mutual scientific interests.

**Council Questions and Comments**

*Will the NIMHD and the NIDDK work together with increased synergy to explore diseases of mutual interest?* Dr. Pérez-Stable said that the Program Directors of NIH Institutes and Centers tend to share information and goals across organizational lines to advance science. For example, if the NIDDK has a meritorious grant application on minority health or health disparities that is not within its payline, the NIMHD could step forward to fund it. However, it is unlikely that the NIMHD would support much in the way of animal studies or very basic research given its perspective on health disparities. Clinical, translational, or population studies are more likely to be relevant to the NIMHD mission and goals.

*What is the NIMHD's philosophy about reporting on the inclusion of minority populations in the clinical trials done by other Institutes?* Dr. Pérez-Stable recognized the importance of such inclusion, but he thinks these clinical trials should be reported separately from research on minority health and on health disparities.

*Will the NIMHD promote collaborations? For example, will it seek resources from private foundations? What about partnering with the NIDDK's medical student program?* Dr. Pérez-Stable said that the NIMHD is interested in collaborative ideas, and has been approached by the Robert Wood Johnson Foundation in that regard.

## VII. UPDATE FROM THE DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

***Walter J. Koroshetz, M.D.***

*Dr. Rodgers welcomed Dr. Koroshetz, who was selected Director of the NINDS in June 2015. He had previously served as Deputy Director since 2007. Prior to joining the NINDS, he served as Vice Chair of the neurology service and Director of stroke and neurointensive care services at Massachusetts General Hospital (MGH). He was a Professor of Neurology at Harvard Medical School and he led neurology resident training at MGH between 1990 and 2007. Dr. Koroshetz has held leadership roles in a number of NIH and NINDS programs including the NIH BRAIN Initiative; the Traumatic Brain Injury Center collaborative effort between the NIH intramural program and the Uniformed Health Services University; and the multi-year work to develop and establish the NIH Office of Emergency Care Research to coordinate research and research training in that field. Dr. Koroshetz received his M.D. from the University of Chicago. He trained in internal medicine at the University of Chicago and Massachusetts General Hospital (MGH). He trained in neurology at MGH, after which he did post-doctoral studies in cellular neurophysiology at MGH.*

Dr. Koroshetz described the extent of neuroscience research across the NIH, the leadership role of the NINDS, and collaborations among the Institutes, including between the NINDS and the NIDDK. In 2014, the NIH investment in neuroscience research was approximately $5.5 billion--involving most components of the NIH. The funds expended on neuroscience research exceeded those for cancer, for infectious diseases, and for cardiovascular diseases. Moreover, the number of neuroscience Ph.D.s among NIH trainees and fellows has outstripped those in several other fields.

The growth in neurosciences research at the NIH has been driven largely by investigator-initiated research. Scientists have been attracted to the field because of its impressive scientific advances and opportunities. The development of sophisticated neuroimaging techniques has helped fuel the expansion of neuroscience. One of the challenges of the NINDS is to find ways to optimize this burgeoning portfolio of neuroscience research across the many Institutes that support it. That goal is furthered by the "Blueprint for Neuroscience Research," through which many Institutes contribute funds and work together to support trans-NIH efforts. One of the accomplishments of the "Blueprint" was the development of a new technology for visualizing white matter connections in the brain. This technology has permitted new insights regarding many brain functions.

**Snapshot of the NINDS**

The NINDS research mission is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological diseases. To that end, the NINDS employs multiple strategies, including: (a) investing across the full spectrum of basic, translational, and clinical research; (b) establishing a data-driven process to identify unmet scientific opportunities and public health needs within and across neurological diseases; (c) supporting research resources and technical advances that catalyze new discoveries; (d) communicating and collaborating with the public and with others involved in biomedical research--including many different patient advocacy groups; (e) training a robust and diverse neuroscience research workforce; and (f) adopting a culture of evaluation and continuous improvement across all NINDS

programs. Dr. Koroshetz is hopeful that research can uncover commonalities among the hundreds of diseases addressed by the NINDS. For example, a common thread in neurodegeneration may be the inability of cells to handle the metabolism of proteins. The identification of such common disease mechanisms might speed the development of broadly applicable therapies.

In Fiscal Year 2015, the NINDS achieved a success rate of 20.5 percent and a payline of 14 percent. Dr. Koroshetz hopes to maintain at least a 14 percent payline going forward. Emphasis is placed on funding Early-Stage Investigators. The NINDS organizational structure is lean and can respond quickly to new research needs and opportunities.

In Fiscal Year 2016, the NINDS budget is nearly $1.7 billion, which includes nearly $80 million in special funds the Institute received under the NIH BRAIN Initiative. With its budget, the Institute supports a multifaceted body of research, including studies of many rare diseases. The NINDS is analyzing its research portfolio so that it can better understand trends and undertake changes or new initiatives as needed. For example:

***Basic Research:*** Because fundamental research is an essential foundation for clinical progress, the NINDS is taking steps to remedy a decline in basic research, which represents about 25 percent of the Institute's budget. To that end, the NINDS is stimulating studies with several other Institutes to address fundamental questions in the neurosciences--with a total funding goal of $5 million.

***New Research Program Awards:*** The NINDS has a new program that will provide up to $20 million annually to support meritorious Research Program Awards (R35s) that give investigators the freedom to pursue long range, innovative, or high-risk research.

***Preclinical Research:*** Another initiative addresses the growing research challenges across research areas. Emphasis will be placed on issues in preclinical research, such as optimizing the reliability and predictive value of research data through rigor and transparency. Pre-clinical research findings need to be tested under different conditions to ensure that they are robust before they are used as the foundation for major, costly clinical trials. Dr. Koroshetz stressed that the reproducibility in research findings is essential for maintaining credibility with the Congress. Issues that may need to be addressed to ensure reproducible results include the mastery and consistent application of new techniques and technologies by investigators; the proper randomization of animals for study; the acquisition of the quantitative skills needed to deal with vast amounts of research data; and the removal of unconscious biases.

## NINDS Translational Research

Dr. Koroshetz elaborated on the Institute's translational research. These efforts are particularly important because industry has become reluctant to support clinical trials in neurologic diseases. Unfortunately, investments in the 1990s did not meet expectations for the successful commercialization of new drugs. The NINDS Office of Translational

Research (OTR) is therefore working to propel laboratory discoveries into clinical testing that could regain industry's support of major clinical trials.

Some initiatives include: Innovation Grants to Nurture Initial Translational Efforts (IGNITE); a Blueprint Neurotherapeutics Network (BPN) for small molecules; and Cooperative Research to Enable and Advance Translational Enterprises (CREATE). These programs are milestone-driven, and offer multiple entry points and a seamless path of support across the therapy-development pipeline. The NINDS has established a "Fail Early, Fail Fast" approach in which grants that do not meet milestones are discontinued and their resources re-deployed. There are also other translational research efforts, including CounterACT, which will develop FDA-approved therapeutics and diagnostic technologies to reduce mortality and morbidity during and after chemical emergency events.

To speed the translation of laboratory findings into clinical studies, the NINDS has awarded more than 220 exploratory/developmental research grants and 80 cooperative grants over the past 10 years--several of which have produced ground-breaking peer-reviewed publications. In 2014, NINDS-funded investigators filed at least five Investigational New Drug Applications with the FDA. These include applications for the clinical testing of a small molecule that may prove beneficial in Alzheimer's disease; gene therapy approaches for glioblastoma; and the possible therapeutic use of gene therapy and antisense oligonucleotides for muscular dystrophy.

Dr. Koroshetz underscored the importance of finding ways to identify and validate measures of "target engagement" so that researchers can determine at an early point in clinical testing whether a drug is working at the dose and for the duration given. To that end, the Institute has developed the NeuroNEXT Program--the Network for Excellence in Neuroscience Phase 2 Clinical Trials. Comprised of a network of 25 sites across the country, this program provides a robust, standardized, and accessible infrastructure to conduct studies of treatments for neurological diseases. The Network creates and leverages partnerships with academia, private foundations, and industry, and increases the efficiency of clinical trials. It supports scientifically sound, possibly biomarker-informed, exploratory clinical trials that provide data for clear go/no-go decisions regarding whether to move forward toward larger clinical trials.

## NINDS and NIDDK Mutual Interests

The NINDS shares research interests with the NIDDK in such areas as diabetic neuropathy; insulin resistance and brain structure; obesity and stroke; and brain glycolysis. Both Institutes have a strong interest in combating stroke, which affects about 750,000 people each year in the U.S. and can be a major complication of diabetes. Describing research progress in stroke, Dr. Koroshetz noted that, for example, the results of clinical trials have contributed to declining stroke risk in America. Also, the administration of tissue plasminogen activator (tPA) following a stroke has revolutionized stroke management. Dr. Koroshetz described some important clinical trials.

*Systolic Blood Pressure Intervention Trial (SPRINT):* This trial sought to determine whether maintaining a blood pressure level that is lower than current medical standards can help to decrease myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes. Promising results in older, non-diabetic Americans were published in the *New England Journal of Medicine* in November 2015 ("A Randomized Trial of Intensive versus Standard Blood-Pressure Control." http://www.nejm.org/doi/full/10.1056/NEJMoa1511939)

*Stroke Hyperglycemia Insulin Network Effort (SHINE):* This trial is assessing the benefits of delivering insulin to manage glucose levels during a stroke event. (http://www.ninds.nih.gov/disorders/clinical_trials/NCT01369069.htm)

*Insulin Resistance Intervention in Stroke (IRIS):* This trial was designed to test the effectiveness of reducing insulin resistance following a stroke. Promising results were announced shortly after the January 27, 2016 Council meeting. (http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_IRIS_trial_02172016.htm)

The NINDS and the NIDDK also share an interest in vascular disease, which can be involved in both stroke and diabetes. Dr. Koroshetz said that the NINDS is very interested in small blood vessel disease and its contribution to dementia. He noted that hypertension--in addition to being the primary driver of stroke--can lead to "diffuse white matter disease" in which small blood vessels that supply the center of the brain are compromised. One NIH collaborative effort is identifying ongoing cohort studies that could be leveraged or enhanced to support additional research on vascular contributions to cognitive impairment and dementia. Research has suggested that the control of blood pressure to prevent strokes and heart attacks may also help prevent cognitive decline with aging. Dr. Koroshetz noted that this message will be part of the collaborative "Mind Your Risks" educational effort. (http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_mindyourrisks_02022016.htm)

**The Evolving NIH Blueprint for Neuroscience**

The NIH Blueprint for Neuroscience Research (http://neuroscienceblueprint.nih.gov/) grew out a Presidential Initiative known as BRAIN--the "Brain Research through Advancing Innovative Neurotechnologies®" Initiative. (http://www.braininitiative.nih.gov/) He pointed out that the NIH Blueprint has changed over time. Early efforts centered mainly on the creation of resources and training activities that could be used by awardees of the participating NIH components. Starting in Fiscal Year 2010, the focus shifted to "Grand Challenges" to catalyze research with the potential to transform basic understanding of the brain and approaches to treating brain disorders. Three major projects were: the Human Connectome Project, the Grand Challenge in Chronic Pain, and the Blueprint Neurotherapeutics Network.

NIH BRAIN investments are being directed toward: (a) research on the delivery of targeted electrical pulses to the brain to treat illnesses such as traumatic brain injury and epilepsy; (b) studies of ultrasound to image the brain with higher resolution, (c) collaborations with physicists to build non-invasive tools that peer deep into the brain to observe neural activity with unprecedented spatial detail; (d) technological advances in large-scale recordings of neural activity; and (e) short courses to educate neuroscientists, as well as scientists from other disciplines, about cutting edge neuroscience tools and the analysis of enormous, complex data sets. There will be a continuing emphasis on the development and application of research tools to elucidate the ways that brain circuits and networks help to generate thoughts and actions.

**Council Questions and Comments**

*What can be done to address situations in which Study Sections don't perceive the relevance of an NIDDK area of science, such as mitochondrial biology, to research on the brain? Could the NINDS issue RFAs to help to address this issue?* Dr. Koroshetz responded that research can indeed fall through the cracks in Study Sections. However, when the budget is relatively flat, it is difficult for an Institute to issue RFAs unless funds are freed-up from other areas.

## VIII. SCIENTIFIC PRESENTATION:

**The Kidney Repair Shop**

***Joseph Bonventre, M.D., Ph.D.***

*Dr. Rodgers introduced, Dr. Joseph Bonventre, the Samuel A. Levine Professor of Medicine at Harvard Medical School. He is also Chief of the Renal Unit and Director of the Bioengineering Division at Brigham and Women's Hospital. Dr. Bonventre has had a long-standing interest in various aspects of cellular injury and repair mechanisms in the kidney, with a special emphasis on the role of inflammation, biomarkers, and stem cells. He has established the origin of the epithelial cells that repair the kidney after injury. An internationally recognized scientist and scholar with an extensive list of honors and prizes, Dr. Bonventre has a long history of research support from the NIDDK. He serves on the editorial boards of several national and international journals, and has regularly served as a peer reviewer for the NIH and other biomedical research organizations. Dr. Bonventre earned his M.D. and Ph.D. from Harvard Medical School. He then did his internship, residency and fellowships at Massachusetts General Hospital.*

## IX. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1179 grant applications (268 primary and 911 dual), requesting support of $373,627,431 were reviewed for consideration at the January 27, 2016 meeting. An additional 26 Common Fund applications requesting $8,090,889 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1330 applications requesting $376,536,344 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 January 27, 2016 meeting.

## X. ADJOURNMENT
***Dr. Rodgers***

Dr. Rodgers expressed appreciation on behalf of the NIDDK to the presenters and other participants. He thanked the Council members for their attendance and valuable input. There being no other business, the 200th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m. on January 27, 2016.

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