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

The NIDDK Director, Dr. Griffin Rodgers, called to order the 199th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on September 9, 2015, in Building 31 on the NIH Campus.
(**Note**: the order of presentations at the meeting differed slightly from the original agenda.)

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Sharon Anderson
Dr. Gopal Badlani
Dr. Joseph Bonventre
Dr. Eugene Chang
Dr. Mark Donowitz
Dr. Cindy Hahn
Dr. Lee Kaplan
Dr. Kenneth Kaushansky
Dr. David Klurfeld
Ms. Ellen Leake
Dr. Jerry Palmer
Dr. Craig Peters
Dr. Alan Saltiel
Dr. Jean Schaffer
Dr. Alan Shuldiner
Dr. Irving Smokler
Dr. John Walsh

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
Abraham, Kristin – NIDDK
Akolkar, Beena – NIDDK
Andersen, Dana – NIDDK
Barnard, Michele – NIDDK
Bavendam, Tamara – NIDDK
Begum, Najma – NIDDK
Best, Carolyn – Amer. Urol. Assoc.
Bishop, Terry – NIDDK
Bleasdale, John – CSR
Blondel, Olivier – NIDDK
Bourque, Sharon – NIDDK
Bremer, Andrew – NIDDK
Buchanan, Sarah – NephCure
Burgess-Beusse, Bonnie – NIDDK
Calvo, Francisco – NIDDK
Camp, Dianne – NIDDK
Carrera, Krysten – NIDDK
Carrington, Jill – NIDDK
Castle Arthur – NIDDK
Cerio, Rebecca – NIDDK
Cheng, Clara – CSR
Chen, Hui – CSR
Christiansen, Dana
Chowdhury, Bratati – NIDDK
Connaughton, John – NIDDK
Copeland, Randy – NIDDK
Curtis, Leslie – NIDDK

Dayal, Sandeep – NIDDK
Densmore, Christine – NIDDK
Doherty, Dee – NIDDK
Donohue, Patrick – NIDDK
Drew, Devon – NIDDK
Duggan, Emily – NIDDK
Farishian, Richard – NIDDK
Fisher, Rachel – NIDDK
Flessner, Michael – NIDDK
Fonville, Olaf – NIDDK
Fradkin, Judith – NIDDK
Gallivan, Joanne – NIDDK
Gansheroff, Lisa – NIDDK
Gossett, Danny – NIDDK
Guo, Xiaodu – NIDDK
Haft, Carol – NIDDK
Hall, Sherry – NIDDK
Hamilton, Frank – NIDDK
Hardy, Evan
Hoff, Eleanor – NIDDK
Hubbard, Van – NIDDK
Hyde, James – NIDDK
Hoofnagle, Jay – NIDDK
Hoover, Camille – NIDDK
Hoshizaki Deborah – NIDDK
Ivins, Jonathan – CSR
James, Stephen – NIDDK
Jerkins, Ann – NIDDK
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Karimbakas, Joanne – NIDDK
Ketchum, Christian – NIDDK
Kimmel, Paul – NIDDK
Kirkali, Ziya – NIDDK
Krause, Michael – NIDDK
Kuczmarski, Robert – NIDDK
Kusek, John – NIDDK
Laakso, Joseph – Endocrine Society
Laughlin, Marin – NIDDK
Leschek, Ellen – NIDDK
Li, Yan – NIDDK
Linder, Barbara – NIDDK
Malik, Karl – NIDDK
Maruvada, Padma – NIDDK
Margolis, Ronald – NIDDK
Martey, Louis – NIDDK
Martinez, Winnie – NIDDK
McBryde, Kevin – NIDDK
Miller, David – NIDDK
Moxey-Mims Marva – NIDDK
Mullins, Christopher – NIDDK
Narva, Andrew – NIDDK
Nguyen, Van – NIDDK
Nurik, Jody – NIDDK
Olumi, Aria – Mass. Gen. Hosp.
Pawlyk, Aaron – NIDDK
Perrin, Peter – NIDDK
Perry-Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Pileggi, Antonello – CSR
Ramani, Rathna – NIDDK
Rankin, Tracy – NIDDK
Regan, Karen – NIDDK
Rivers, Robert – NIDDK
Roberts, Tibor – NIDDK
Rosenberg, Mary Kay – NIDDK
Rosendorf, Marilyn – NIDDK
Roy, Cindy – NIDDK
Rushing, Paul – NIDDK
Rys-Sikora, Krystyna – NIDDK
Sanovich, Elena – NIDDK
Saslowsky, David – NIDDK
Sato, Sheryl – NIDDK
Savage, Peter – NIDDK
Serrano, Jose – NIDDK
Sheets, Dana – NIDDK
Sherker, Averell – NIDDK
Shepherd, Aliecia – NIDDK
Sierra-Rivera, Elaine – CSR
Singh, Megan – NIDDK
Smith, Philip – NIDDK
Spain, Lisa – NIDDK
Star, Robert – NIDDK
Stephen, James – 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, Jeff – NIDDK
Wellner, Robert – NIDDK
Wilkerson, Anita – NIDDK
Yanovski, Susan – NIDDK
Yang, Jian – NIDDK

C. ANNOUNCEMENTS
Dr. Rodgers

Council Members Ending Their Four-Year Terms

Dr. Rodgers recognized and expressed appreciation to the following Council Members, who completed their four-year terms and are rotating off the Council after this meeting.

- *Dr. Alan Shuldiner,* John L. Whitehurst Professor of Medicine, University of Maryland School of Medicine, has contributed broad knowledge to the Council in many areas including clinical trials, and genetic/mechanistic studies. His focus on clinically important research questions has been especially valuable in helping to guide NIDDK research priorities. His expertise spans the Division of Diabetes, Endocrinology and Metabolic Diseases, and the Division of Digestive Diseases and Nutrition. Dr. Shuldiner has brought to the Council a thoughtful perspective on the NIH Precision Medicine Initiative because of his own research, which includes establishing APOC3 as a pharmaceutical target, and elucidating genetic variants affecting response to the drug metformin in type 2 diabetes. He has also played a leadership role in several NIDDK activities including sponsored workshops on topics such as clinical pharmacogenomics, and the leveraging of simple model organisms to understand human disease.

- *Mr. John Walsh,* President and CEO of the Alpha-1 Foundation, has served on the Council as a Public Member. He has contributed expertise regarding the perspectives and needs of patients and their participation in research. Since he co-founded the Alpha-1 Foundation in 1995, he has worked diligently for research and education programs to aid patients with alpha-1-antitrypsin deficiency, which can lead to emphysema, cirrhosis, and liver cancer. The Foundation has invested more than $50 million dollars in research, and in furthering access to care. While on the Council, Mr. Walsh has advised the NIDDK on many topics, including innovative approaches to clinical trials. He has a long history of support for and service to the NIH, including as a Member of the NIH Council of Councils and the NIH Director's Council of Public Representatives.

- *Dr. Kenneth Kaushansky,* Dean of Stony Brook University School of Medicine and Senior Vice President of Health Sciences at Stony Brook University, has contributed a broad perspective to Council deliberations. He has shared insights about national issues in biomedical research from his experiences as a leader in academic medicine. Dr. Kaushansky has been a tireless advocate for the training of junior investigators, with a particular interest in ensuring that future hematologists have skills, such as bioinformatics, essential for maintaining a rigorous and long-standing national hematology program. Dr. Kaushansky has advised on a number of NIDDK studies--including the program, "Stimulating Hematology Investigation: New Endeavors (SHINE)." He also played a key role in supporting the NIDDK's hematology program in developing an initiative on aging. As an NIDDK grantee for over 20 years, Dr. Kaushansky has many research accomplishments, including advancing knowledge of thrombopoietin.

***Ex Officio* Members Departing the Council**

Dr. Rodgers recognized two *ex officio* Members who are leaving the Council after serving for many years on the Diabetes, Endocrinology and Metabolic Diseases Subcouncil: Dr. Robert Vigersky, who represented the Department of Defense, and Dr. Jerry Palmer, who represented the Veterans Administration. Dr. Rodgers noted that Dr. Palmer served on NIDDK's Council for more than ten years and contributed expertise in the areas of beta cell biology and immunology. He has also played a role in major clinical trials on type 1 diabetes. During his time on the Council, Dr. Palmer received the American Diabetes Association's Outstanding Physician-Clinician Award.

Former and Current Council Members

Former NIDDK Advisory Council member *Dr. Nancy Andrews*, who is now Vice Chancellor and Dean of the Duke University School of Medicine, has been elected to the National Academy of Sciences. Her research has been continuously funded by NIH since 1993 and has led to important advances in understanding mammalian iron biology and human iron diseases.

Current NIDDK Advisory Council member *Dr. Bruce Spiegelman* received the InBev-Baillet Latour Health Prize, which is recognized as the most important international scientific Prize granted in Belgium. The Prize honors Dr. Spiegelman for his fundamental contributions to metabolic disorders research. The Prize cites his research as "*revolutionizing our knowledge of the function, the differentiation, and the pathophysiology of adipose tissue*."

"*In Memoriam*"

Dr. Jules Hirsch, a long time NIDDK grantee who served on the NIDDK's Advisory Council from 1989-1993, died in July 2015. Dr. Hirsch had a long career at the Rockefeller University, New York, as a physician scientist. His investigations into body weight regulation revolutionized thinking about obesity by helping to uncover its underlying biological processes. Early in his career, Dr. Hirsch observed that fat cells change with changes in weight, and that obese people generally have more and bigger fat cells than lean people. These discoveries eventually helped pave the way for investigations of signaling between fat cells and the brain. Work by Dr. Hirsch and others subsequently helped establish that people tend toward a set weight. Dr. Hirsch chaired an NIH panel on obesity in 1985.

New Office of Nutrition Research at the NIDDK

On August 1, 2015, the NIDDK established the Office of Nutrition Research within the Institute's Office of the Director. The Office will replace the NIH Division of Nutrition Research Coordination (DNRC). Guided by an assessment of DNRC activities, the new Office will assist in leading a trans-NIH group to strategically plan new initiatives for NIH nutrition research. The Office will also be closely aligned with nutritional sciences grant funding programs across the NIDDK, which is the largest funder of nutrition research at the NIH. A search is underway for an individual to serve both as the Director of the new Office, and as Chief

of the Nutrition Research Branch in the NIDDK Division of Digestive Diseases and Nutrition.

This organizational change coincides with the planned retirement of Dr. Van Hubbard, Director of the DNRC. Dr. Hubbard has had a long and distinguished career at the NIH--starting in the intramural program in 1976; leading the NIDDK's extramural nutritional sciences research programs since 1983; and serving as a Senior Advisor on Obesity to the Secretary of Health and Human Services. He is also a retired Assistant Surgeon General and Rear Admiral in the U.S. Public Health Service. While recruitment of a Director for the new Office is ongoing, Dr. Stephen James, Director of the Division of Digestive Diseases and Nutrition, is serving as the Acting Director.

"Friends of the NIDDK"

Dr. Rodgers reported that he was pleased to speak at the inaugural event of the "Friends of NIDDK" in June 2015, which occurred at a Congressional reception. The "Friends" is a coalition of dozens of organizations with a shared commitment to research to improve the lives of people living with, or at risk for, diseases within NIDDK's research mission. In addition to working for their respective organizations, the Coalition Members speak with one voice to promote and sustain the vital research activities of the NIDDK. The collective interests of these organizations span the NIDDK research portfolio.

At the event, welcoming remarks were given by Ms. Shereen Arent of the American Diabetes Association. Senator Dick Durbin of Illinois spoke of his legislative work to promote biomedical research, and of the new bipartisan Senate NIH Caucus, which he co-launched with Senator Lindsey Graham of South Carolina in 2015. Senator Jeanne Shaheen of New Hampshire, who had extended the invitation to this event, also spoke of the many benefits of research. Representative Robin Kelly of Illinois expressed her support for research, particularly with respect to health disparities--a topic relevant to many of the diseases within the NIDDK research mission. Dr. Rodgers had the opportunity to highlight some of the NIDDK's program efforts for the Members of Congress and the Congressional staff in attendance.

NIDDK Staff

Dr. Ron Margolis is retiring after 26 years with the NIDDK. He has had a major scientific impact by skillfully fostering nuclear receptor signaling research, and is widely known and respected in the endocrinology research community. He led the creation of the Nuclear Receptor Signaling Atlas (NURSA), and the NIDDK Information Network (dkNET). He has also made significant contributions NIH-wide to the Molecular Libraries and Big Data initiatives. Dr. Margolis helped recruit and mentor numerous extramural staff within the Division of Diabetes, Endocrinology and Metabolic Disease. He was also the lead in developing an outstanding training program for new extramural staff members. His accomplishments have been recognized five times with the NIH Director's Award, and he has received the Endocrine Society's Sidney H. Ingbar Award for Distinguished Service.

Dr. Bonnie Burgess-Beusse is the new Director of the Cell and Molecular Biology of the Liver Program, and also the Developmental Biology and Regeneration Program, in the Division of Digestive Diseases and Nutrition. She earned her Ph.D. in molecular and human genetics at Baylor College of Medicine while studying transcriptional regulation of the hepatic acute phase response to inflammation and the regulation of transcription factors in the liver. She conducted postdoctoral research in the NIDDK Laboratory of Molecular Biology, where she studied vertebrate chromatin insulator elements. For the past 10 years, she served as a Scientific Review Officer within the Digestive, Kidney, and Urological Systems Integrated Review Group at the NIH Center for Scientific Review.

Dr. David Saslowsky is the new Director of the Career Development and Training Program in the Division of Digestive Diseases and Nutrition. He received his Ph.D. in Cellular and Molecular Biology from Virginia Tech. He conducted postdoctoral research with Robert Henderson in the Department of Pharmacology at the University of Cambridge, United Kingdom, and with Wayne Lencer in the Division of Gastroenterology and Nutrition at Boston Children's Hospital. Previously, he was Director of the Harvard Digestive Diseases Center Confocal Microscopy Core at Boston Children's Hospital, and an Assistant Professor at Harvard Medical School. A former NIDDK K01 grant awardee, Dr. Saslowsky has focused his research on the ways that microbial toxins interact with enterocyte membranes to elicit host cell signaling and immunomodulatory responses. He also has a strong interest in mentoring early-stage investigators.

Dr. Rob Rivers has joined the NIDDK Office of Minority Health Research Coordination (OMHRC) as a Program Director. He completed his Ph.D. in Chemistry at the University of Cambridge in the laboratory of Professor Christopher M. Dobson. His doctoral research focused on elucidating the structure and aggregation propensities of alpha and beta synuclein. He later served as a community developer and outreach organizer in Lima, Peru, where he tutored students and gave research-related talks to community groups. Dr. Rivers joined the National Institutes of Health as an AAAS Science and Technology Policy Fellow in the Office of Cancer Clinical Proteomics Research at the National Cancer Institute (NCI). There, he supported efforts to help build an interdisciplinary analysis pipeline, through the Clinical Proteomic Tumor Analysis Program, to link cancer genomics with cancer proteomics. Additionally, he served as a liaison to the NCI Center To Reduce Cancer Health Disparities--working to expand training opportunities in areas of emerging technologies to students from underrepresented populations. At the NIDDK, his primary focus will be directing the Short-Term Research Experience for Underrepresented Persons Program for both high school and undergraduate students, in addition to leading the NIH-National Medical Association Fellows Academic Careers Travel Awards Program.

Federal Plan To Update/Revise the Common Rule That Governs Human Subject Protections in Research

The proposed update was presented in a Notice of Proposed Rulemaking (NPRM) published in the *Federal Register*. The major reforms propose to: (1) calibrate oversight to level of risk; (2) enhance respect for research participants; (3) facilitate broad participation in research; (4) increase privacy and security safeguards for research with biospecimens and data; (5) simplify consent documents; and (6) streamline review by Institutional Review Boards (IRBs). Dr. Rodgers encouraged NIDDK stakeholders to take the opportunity to engage in modernizing the Common Rule by reading the Notice closely and participating in the comment process. (https://www.federalregister.gov/articles/2015/09/08/2015-21756/federal-policy-for-the-protection-of-human-subjects)

II. CONSIDERATION OF SUMMARY MINUTES OF THE 198th COUNCIL MEETING

Dr. Rodgers

The Council approved, by voice vote, the Summary Minutes of the 198th Council meeting, which had been sent to them in advance for review.

III. FUTURE COUNCIL DATES

2016

January 27-28 (Wednesday and Thursday)
May 18-19 (Wednesday and Thursday)
September 7-8 (Wednesday and Thursday)
All meetings in 2016 will be held in 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. UPDATE FROM THE NIH DEPUTY DIRECTOR: Developing the NIH-Wide Strategic Plan

Dr. Lawrence A. Tabak, Principal Deputy Director, NIH

Dr. Rodgers welcomed and introduced to the Council Lawrence A. Tabak, D.D.S, Ph.D., the Principal Deputy Director of the NIH. Dr. Tabak was appointed to that position in 2010. He previously served as Acting Deputy Director, NIH, from November 2008 through August 2009, and as Director of the National Institute of Dental and Craniofacial Research (NIDCR) from September 2000 through August 2010. Prior to joining the NIH, Dr. Tabak served as the Senior Associate Dean for Research, and Professor of Dentistry and Biochemistry and Biophysics, in the School of Medicine and Dentistry, University of Rochester, New York. A former NIH MERIT Award recipient, Dr. Tabak has received honors and awards for his research including election as a Member of the Institute of Medicine of the National Academies. He has also received teaching awards for his work with both graduate and medical students.

Dr. Tabak described ongoing efforts to develop a new NIH-wide Strategic Plan. (http://www.nih.gov/about/strategic-plan/) Current law requires the NIH to submit a Strategic Plan to the Congress by mid-December 2015. Moreover, the pending 21st Century Cures Act would also require a Strategic Plan.

The five-year Plan will outline a vision for biomedical research that underscores NIH's commitment to the pursuit of fundamental knowledge, and its application to extend healthy life and reduce illness and disability. Dr. Tabak emphasized that the NIH has pursued an interactive process to develop a conceptual framework for the Plan. This process will continue in the future to incorporate new discoveries and opportunities into NIH strategic planning efforts.

Dr. Tabak presented current thinking about goals for the Plan, in terms of what the document should and should not be. The NIH believes that the Strategic Plan: (a) should be a dynamic "living document" that would help guide the agency in fulfilling its mission, (b) should articulate approaches and opportunities that are forward-looking and inspirational, and (c) should identify major trans-NIH themes and opportunities that would advance biomedical research. On the other hand, the NIH Strategic Plan should not describe all the many important things that NIH does and would do in the future. Otherwise, the document would be too voluminous to be useful. Also, the NIH Strategic Plan should not address all the research priorities and emphases of the individual Institutes, Centers, and Offices. Each of the NIH components has its own strategic plan, which would be referenced in the NIH-wide document. The NIH believes that agreement on these principles would help to avoid unrealistic expectations.

Strategic Planning Process and Framework

The new NIH strategic planning process began with discussions among the senior NIH leadership. A working group was then formed with representatives from the various NIH components, including the NIDDK. These representatives have been instrumental in providing input and feedback to the NIH leadership regarding the possible architecture and contents of the Plan. Dr. Tabak has made presentations about the Strategic Plan's development to the Advisory

Committee to the Director, NIH (ACD) and received feedback, including positive comments on the most recent version of the framework. The ACD has advocated for additional emphasis on the interconnected nature of research, and for inclusion of the topics of clinical methodologies, data science, and workforce retention. The NIH is also aware of congressional emphasis areas such as pediatric research and rare diseases. The Plan is still a work in progress, and its structure and contents are likely to be refined further as additional comments are received and processed. The NIH Director is monitoring the strategic planning process carefully and will oversee the final document.

Dr. Tabak described the following organizational framework envisioned for the Strategic Plan. He touched on some concepts that would likely be woven into the document, along with examples of research advances ("call outs").

Overview: This part of the Plan would underscore the NIH mission, as well as the current landscape of NIH research and the compelling opportunities and challenges that exist. The Plan would make clear that biomedical research is at a unique moment of opportunity because it can build upon a remarkable body of advances in scientific knowledge coupled with new technologies. At the same time, however, the research community faces constraints due to lost purchasing power.

Areas of Opportunity: The Plan would succinctly describe and provide examples of emerging opportunities in the following three areas, and describe the ways that further progress could be realized: fundamental science; health promotion/disease prevention; and treatments/cures. The Plan would stress that progress in one of these areas fuels the other areas on a continuing basis. These areas of opportunity apply across biomedicine, and align with the Strategic Plan of the Department of Health and Human Services. The NIH plays a unique role in exploiting existing and emerging opportunities in these areas.

- *Fundamental Science:* The NIH would emphasize its continuing commitment to fundamental science as an essential foundation for progress in understanding, treating and preventing diseases and maintaining health. Data science would continue to play a key role in increasing the efficiency and impact of research, and in propelling the translation of laboratory findings to the clinic. Examples would show how fundamental discoveries and technologies can catalyze and propel clinical discoveries. For instance, basic research on the gut microbiome is providing insights into immune system development and disease processes. The Plan would also point out that the consequences of basic research are often unpredictable, but many times revolutionary in their importance. For example, by studying fundamental questions regarding microbial diversity, scientists have made serendipitous discoveries, such as identifying the bacterial defense mechanisms that led to a new genome editing technology that has enormous impacts on science and health.

- *Health Promotion/Disease Prevention:* The Plan would illustrate that improvements in the early diagnosis and detection of disease could provide enormous health benefits. New knowledge could also be gained from studies of healthy individuals. Evidence-based approaches could be instrumental in reducing and eliminating health disparities. Vital

contributions could come from the NIH's global leadership in vaccine development. For example, the NIH Vaccine Treatment and Evaluation Units include a clinical trials network for rapid testing and evaluation of promising vaccine candidates to counteract emerging public health issues.

- *Treatments and Cures:* The Plan would highlight therapeutic opportunities arising from new knowledge about biological processes at the molecular level. Moreover, interdisciplinary research is overcoming the limitations of traditional, disease-focused research categories. For example, cancer is no longer exclusively regarded in an anatomical way. Instead, new insights have been gained about commonalities in biologic pathways and processes that lead to abnormal tissue growth in various cancer types. This knowledge has led to a variety of new interventions; for instance, cancer immunotherapy approaches.

Unifying Principles: The Plan would conclude by describing NIH-wide efforts to further biomedical research, including the following:

- *Setting Priorities:* The NIH would seek to foster scientific opportunity and progress in a nimble way. Disease burden would be an important consideration in program development and resource allocation, but not the only factor. Combating rare and pediatric diseases would remain important objectives. The NIH Clinical Center would be emphasized as a research hub for facilitating intramural-extramural collaborations, and for accelerating new therapeutic discoveries. The challenges and value of permanently eradicating a pandemic would be considered.

- *Enhancing Stewardship:* The NIH would maintain the public trust in its stewardship in several ways that also align with the Department's Strategic Plan. It would seek to recruit and retain an outstanding research workforce, enhance workforce diversity, encourage innovation, optimize approaches to inform funding decisions, enhance research impacts through partnerships, and ensure rigor and reproducibility of research. Strategies for reducing administrative burdens and improving risk management would also be presented. One example is the Accelerating Medicines Partnership (AMP) involving the NIH, the FDA, a group of pharmaceutical companies, and several not-for-profit organizations. The goal is to develop new diagnostics and treatments by identifying and validating promising biological targets in several areas of opportunity, including type 2 diabetes.

The NIH is actively soliciting input regarding development of the Strategic Plan. Over 450 comments, mostly positive, were received in response to a Request for Information that closed in August 2015. Among the many suggestions were to emphasize implementation science, interdisciplinary approaches, and improvements in peer review. Other suggestions were to promote the use of Big Data, and underscore population health. Disease-focused suggestions were also submitted. The NIH has conducted three webinars with the community that were led by members of the ACD, NIH. The webinars engendered comments regarding the need to emphasize topics such as workforce training, the role of patients as partners in research, the behavioral and social sciences, systems approaches, and interdisciplinary research. The NIH is also making presentations to and seeking input from the various National Advisory Councils. Dr.

Tabak is particularly interested in the views of Council members about the benefits and drawbacks of the current framework for the Strategic Plan with regard to overall structure and content, whether the framework is compatible with the broad scope of the NIH mission, whether any major trans-NIH themes are missing, and whether additional research opportunities need to be included. Feedback from all sources will be considered as the NIH moves forward to complete the Plan and submit it to the Congress by mid-December 2015.

Council Questions and Discussion

How will the Strategic Plan address workforce retention issues? Dr. Tabak responded that the Plan would likely give a few examples regarding efforts the NIH has made to put incentives in place for recruiting and retaining talented scientists in research careers, especially physician scientists. The agency is already looking at new ways to encourage retention through early career development programs. Gaps in the career development pipeline need to be closed because they create vulnerable periods when scientists may leave research. The NIH is also considering ways to recruit and retain M.D.s who do not have a Ph.D. Another idea being explored through modeling is to see whether the NIH could give special consideration to applicants applying for their first competitive renewal grants, because that is also a time when investigators tend to drop out of research.

While most scientists would likely agree with the general principles and directions of the Strategic Plan as outlined thus far, its success would largely depend on the details. How would the recommendations be implemented? How would research initiatives grow over time? What metrics would be used to assess the impact and success of a research program or area? Dr. Tabak replied that some areas, such as stewardship, lend themselves to measurement and accountability. Assessing progress in areas of scientific opportunity would be more difficult, especially with regard to fundamental science. He noted that industry does not typically set benchmarks for accomplishments in basic research. Rather, investment levels are established to support serendipitous work. Regarding implementation, Dr. Tabak said that parts of the Plan would be implemented in different ways. He is hopeful that a common, flexible, general framework would emerge from discussions with the Institutes, Centers, and Offices on stewardship and priority setting. On issues of optimizing innovation and partnerships, Dr. Tabak said the Plan is intended to lay out principles and opportunities that can be fostered by NIH components, but that it would not constrain them from pursuing their respective strategic missions. An example would be the NIH microbiome initiative, which has gained broad support across the NIH because of its relevance to the individual missions of NIH components. Dr. Tabak said that topics in the Plan that are NIH-specific would likely be addressed in greater operational detail, whereas those that align with other components of the Department of Health and Human Services may be presented in terms of broader principles.

Given that research institutions are generally organized in terms of specific Departments having individual R01 grant activity, how would the NIH encourage the creation of new partnerships and interdisciplinary team science? Dr. Tabak commented that, as part of its stewardship, the NIH would seek to make it easier for research institutions to cut through their organizational silos to support cross-cutting scientific areas more efficiently. The NIH could foster creation and

support of partnerships for interdisciplinary research, particularly in the framing of research applications and in peer review. The NIH clearly recognizes the trend toward more interdisciplinary, team-centered approaches to science. These approaches need to be incorporated into the NIH portfolio, along with traditional R01 grants initiated by individual investigators.

What is the thinking in the NIH Director's Office regarding the agency's role in implementation science? Dr. Tabak responded that the NIH dovetails with other agencies within the Department of Health and Human Services on this issue. The NIH has met with the leadership of sister agencies to develop a better understanding of each agency's portfolio, constituencies, interests, and strengths. These communications will help the agencies avoid duplicative efforts and promote interagency partnerships.

The Strategic Plan may help garner increased resources for the NIH by making the agency's contributions more visible to the public and the Congress. What in the Strategic Plan would actually be implemented with respect to the relationship between the NIH and the FDA? Dr. Tabak commented that the NIH would use the Strategic Plan to renew and underscore the benefits of a productive relationship between the NIH and the FDA. The document would likely point out some past successes in that regard, and perhaps make some suggestions for optimizing interactions in the future.

Is consideration being given to garnering more private sector support for NIH research, especially through foundations? Dr. Tabak responded that the NIH is continuing to work productively with foundations, and welcomes specific ideas for expanding partnerships with foundations and other voluntary health organizations. The NIH wants to catalyze funding support for research from all possible sources.

What new approaches to funding, within and outside of NIH, are being considered? Dr. Tabak said that, in the absence of major funding increases from the Congress, new approaches are needed for allocating available resources. One suggestion is to give greater priority to programs such as the MERIT Award, which provides long-term grant support to investigators whose research competence and productivity are broadly recognized as being distinctly superior, and who are highly likely to continue to perform in an outstanding manner. However, a parallel strategy would be needed for new investigators who lack the track records of established scientists. Another suggestion is to extend the length of time for awards so that investigators are not constantly writing grant applications and worrying about the stability of their funding. New approaches are also needed in the peer review system, where the clustering of scores makes differential funding decisions difficult. Dr. Tabak said that other ideas would be welcome.

Should the NIH take steps to break down the silos that exist among its own components? Dr. Tabak replied that silos do exist, but the NIH is furthering research efforts that transcend organizational lines. The NIH Common Fund has promoted that type of cooperation and laid a foundation for other cross-agency efforts. For example, the "Environmental Influences on Child Health Outcomes (ECHO)" study involves multiple Institutes and Centers. Through effective stewardship, the NIH can establish and refine cross-cutting programs based on successful models.

What role is envisioned for patients and the groups that advocate for them? Dr. Tabak noted that patients are empowered with new information, and a desire to participate more fully in furthering research. The NIH recognizes the need to involve patients as full participants in research. Their insights can help in the development of studies, and their feedback can help strengthen future research efforts. For example, patients can be involved more fully in planning efforts and at various advisory meetings. Likewise, patient advocacy groups have enormous energy and knowledge to contribute. The important role of patients is being underscored in the NIH Precision Medicine Initiative, which can be a model for patient engagement. Suggestions on this topic and others are welcome.

V. ANNOUNCEMENTS
Dr. Stanfield

Confidentiality

Dr. Stanfield 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. Stanfield 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. Stanfield 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. 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. Regarding 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.

VI. REPORT FROM THE NIDDK DIRECTOR
Dr. Rodgers

FY 2016 Budget Prospects

Dr. Rodgers reported on Congressional actions relative to FY 2016 funding. In the Spring, the full House and Senate appropriations committees passed all 12 of their respective appropriations bills. For the NIH, the House allowance is $31.41 billion, and the Senate allowance is $32.31 billion. These allowances exceed the President's Budget request and the current FY 2015 spending level for the NIH.

For the NIDDK, the House allowance is $1.92 billion and the Senate allowance is $1.975 billion. These allowances include the Special Statutory Funding Program for Type 1 Diabetes Research. Dr. Rodgers noted that the House and Senate committees targeted substantial funds for the following areas highlighted in the President's Budget request: the new NIH Precision Medicine Initiative, the NIAID's Antimicrobial Resistance Program, the ongoing NIH BRAIN Initiative, and the Alzheimer's disease efforts of the National Institute on Aging. The amount targeted for Alzheimer's disease substantially exceeds the amount proposed in the President's budget. Under the House allowance, the funding levels for several Institutes, including the NIDDK, are below the President's request.

The House and Senate have not yet negotiated a joint bill that would resolve their differences. Often, the Congress sets a final appropriation level for an agency by "splitting the difference" between the two Chambers. This is one possible scenario for FY 2016. However, if a regular appropriations bill is not enacted before the new fiscal year begins on October 1, 2015, then a Continuing Resolution would likely be needed to maintain operations. That mechanism has been used many times in the past to provide funds for a set period of time, pending further Congressional action. Several pending issues may impact the final FY 2016 funding level for the NIH. For example, the Congress is still working under a cap for total discretionary spending, whereas the President's budget proposes removing that cap and ending sequestration. If the latter steps are taken, the Congress could act with greater flexibility in making funding decisions. Although the final FY 2016 funding level for the NIH has not yet been determined, the Congressional actions to date reflect bipartisan support for increasing the NIH budget.

Congressional Hearing on Type 1 Diabetes in Conjunction with "Children's Congress"

Dr. Rodgers said he had the pleasure of testifying about progress in type 1 diabetes research before the Senate Special Committee on Aging on July 15, 2015. Senator Susan Collins of Maine

is the Chair of the Committee, and Senator Claire McCaskill of Missouri is the Ranking Member.

The hearing on "Diabetes Research: Improving Lives on the Path to a Cure" was held in conjunction with the "Children's Congress" of the Juvenile Diabetes Research Foundation (JDRF). Every two years, more than 150 children living with type 1 diabetes gather in Washington, D.C. for this event, which lets them meet face-to-face with some of the top decision-makers in the U.S. government. The children represent all 50 states and the District of Columbia. They help Members of Congress understand what life with type 1 diabetes is like and why research is critically important. Dr. Rodgers said he testified on a panel with type 1 diabetes patients, and with an NIDDK grantee from the University of Missouri, Dr. Habib Zaghouani, who is studying the role of T cells in type 1 diabetes. A major theme of the patients' testimony was the importance of continuous glucose monitors to their health and well-being, and the need for medical coverage for this technology while research continues to seek a cure for the disease. This goal is being pursued legislatively by Senator Collins.

Dr. Rodgers testified regarding recent advances and future opportunities in type 1 diabetes research funded by the NIDDK/NIH. He described research supported by the Special Statutory Funding Program for Type 1 Diabetes Research, which was recently renewed by the Congress through Fiscal Year 2017. Dr. Rodgers highlighted clinical trials testing approaches to delay or prevent type 1 diabetes, development of artificial pancreas technologies, islet transplantation as a treatment approach for people with difficult-to-control type 1 diabetes, and recent progress toward producing large quantities of insulin-producing beta cells in the laboratory.

VII. UPDATE FROM THE DIRECTOR, NATIONAL INSTITUTE ON AGING: Current Efforts on Alzheimer's Disease and Possible Interactions with the NIDDK
Dr. Richard J. Hodes

Dr. Rodgers introduced Richard Hodes, M.D., the Director of the National Institute on Aging (NIA). The NIA is the principal Federal funding agency for studies of the basic, clinical, epidemiological, and social aspects of aging. Named Director of the Institute in 1993, Dr. Hodes also directs and conducts research in the Immune Regulation Section of the National Cancer Institute, a laboratory devoted to studying regulation of the immune system. Dr. Hodes received his B.A. from Yale University and his M.D. from Harvard Medical School. He is a Diplomat of the American Board of Internal Medicine. In 1995, Dr. Hodes was elected as a Member of The Dana Alliance for Brain Initiatives; in 1997, he was elected as a Fellow of the American Association for the Advancement of Science; and, in 1999, he was elected to Membership in the Institute of Medicine of the National Academy of Sciences. He has authored more than 250 research papers.

Dr. Hodes focused most of his remarks on the Alzheimer's Disease component of the NIH Accelerating Medicines Partnership (AMP) and on some other collaborative efforts relevant to aging research. The AMP has been orchestrated by the NIH Director, Dr. Francis Collins, to speed the pace at which discoveries are being translated into effective therapeutic interventions. To that end, Dr. Collins assembled a group of leaders from the NIH and the private sector to

identify areas of scientific promise that would be particularly well-suited for public-private partnerships that include intellectual and funding collaborations. Alzheimer's disease was one of the areas selected, along with Type 2 diabetes and autoimmune diseases.

For Alzheimer's disease, NIA and the National Institute of Neurological Disorders and Stroke (NINDS) were assigned lead responsibility for developing a partnership under the auspices of the AMP. (https://www.nia.nih.gov/alzheimers/amp-ad) Over five years, it is expected that more than $90 million will be expended on the AMP-AD partnership, with about $69 million of that coming from the NIH and close to $22 million from industry, along with about $40 million of in-kind contributions from industry. There are two major components: (1) a biomarkers project, and (2) a project aimed at target discovery and preclinical validation.

Biomarkers Project

The Project on "Biomarkers for Treatment Responsiveness and Disease Progression" (AMP-AD Project A) aims to identify measurable indicators of Alzheimer's disease, the way it progresses, and its responsiveness to therapeutic interventions. (https://www.nia.nih.gov/alzheimers/amp-ad-biomarkers-project) Such biomarkers would advance research efforts to find ways to intervene in the disease process before irreparable damage to the brain occurs from the abnormal accumulation of amyloid and tau proteins. The Project may also identify factors that are protective against the development of Alzheimer's disease in those at risk. Researchers are approaching Alzheimer's disease at an early clinical/translational level in the hope of achieving progress not attained in previous clinical trials that were centered on late-stage disease. The Biomarkers Project includes a consortium of three NIA-supported Phase II and Phase III secondary prevention trials that are testing several anti-amyloid therapies in different study populations. The AMP-AD is enabling the supplementation of existing research methods with novel fluid biomarkers and with tau imaging using Positron Emission Tomography (PET). Baseline data from the trials will be made broadly available through the collaborative platform (GAINN) of the Alzheimer's Association.

Target Discovery and Preclinical Validation Project

Dr. Hodes drew the Council's attention to the complexity of Alzheimer's disease as illustrated in a 2013 *Cell* article that shows how gene expression profiles can elucidate the disease. (Zhang B, *et al.* "Integrated Systems Approach Identifies Genetic Nodes and Networks in Late-Onset Alzheimer's Disease." *Cell* 2013, Vol. 153, Issue 3, pp. 707-720). This research approach illustrates a major avenue of AD research, and is an underpinning of the Project on "Target Discovery and Preclinical Validation" (AMP-AD Project B). (https://www.nia.nih.gov/alzheimers/amp-ad-target-discovery-and-preclinical-validation-project)

The goals of this Project are: (1) to discover novel therapeutic targets for Alzheimer's disease; (2) to gain a systems-level understanding of the gene, protein, and metabolic networks in human brains within which these novel targets operate; (3) to expand the application of integrated network analysis (both RNA and proteomic studies) in human AD brain samples to identify

biologic nodes and networks that are linked to the development or progression of AD, and (4) to evaluate their drugability in multiple model organisms.

Dr. Hodes described the AMP-AD Target Drug Consortium, which is a public-private partnership that facilitates pre-competitive scientific interactions among the participants. The consortium is applying cutting-edge systems and network biology approaches for integrating multidimensional human "omics" data with clinical and pathological data. Researchers are working to discover, select, and characterize novel therapeutic targets for AD and to build predictive models. Two new studies have been added since the beginning of the Project: "Metabolic Networks and Pathways in Alzheimer's Disease," and "Targeting a Novel Regulator of Brain Aging and Alzheimer's Disease."

There is rapid and broad sharing of data and analytical/ research tools prior to publication of research results. Activities are coordinated by Sage Bionetworks through its collaborative data platform, Synapse. In March 2015, the AMP-AD Knowledge Portal was launched and the first wave of data was released.

NIA Collaborations with the NIDDK

Dr. Hodes noted the research benefits derived from NIDDK-NIA collaborations on the Diabetes Prevention Program (DPP) and Look Ahead clinical trials. For example, the NIA gained new insights from the positive response to the DPP's lifestyle intervention in older adults at risk for type 2 diabetes. Regarding additional opportunities for collaboration, Dr. Hodes pointed out that risk factors for AD include diabetes, hypertension, and cardiovascular disease. It would therefore be useful if studies of those diseases included markers for cognitive function, and in some cases, brain imaging. He said that the NIA is currently interested in the possibility that the drug metformin may have a role across a series of metabolically relevant pathways, and may affect age-related conditions, beyond its effects in diabetes. This concept is being discussed by the NIDDK, the NIA, and the FDA.

The NIA also joined with the NIDDK to investigate the impact on humans of caloric restriction unrelated to weight loss or obesity. This research built on the long history of observations in aging research that caloric input below the usual *ad libitum* eating behavior (i.e., eating food as desired) has a strong impact on extending life span in many species, including many mice and rat strains. To study this issue in humans, the NIDDK and the NIA supported a clinical trial, "Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy" (CALERIE). Among the results obtained, there was a significant lowering of risk factors for cardiovascular disease and diabetes, without prohibitive side effects, thus laying the groundwork for mechanistic studies. (https://www.nia.nih.gov/newsroom/2015/09/nih-study-finds-calorie-restriction-lowers-some-risk-factors-age-related-diseases)

Dr. Hodes noted that a Geroscience Interest Group has been formed at the NIH--including scientists from the NIA, the NIDDK, and many other Institutes and Centers. The Group is looking at the ways that basic, underlying biologic processes may be relevant to translational research efforts. A better understanding of common age-related metabolic changes would help

researchers develop interventions that not only treat a single disease--such as diabetes, cancer or cardiovascular disease--but that may also have broader impacts on health.

In closing, Dr. Hodes underscored the need to remove impediments to research. For example, if certain animal models are needed for research to advance, then they need to be developed, maintained and made available. For some time, the NIA has been maintaining aged rodents, and has subsidized the cost of making them available to the NIDDK and other Institutes. A recent NIA initiative involves cost-sharing for the application of current disease-focused research to age-appropriate models. The goal is to facilitate the inclusion of aging as a relevant variable in research.

Council Questions and Discussion

It is an important step forward that biomarkers can predict risk of developing Alzheimer's disease, but what will be the interventions for those at risk? Can biomarkers be used as surrogates for determining the efficacy or promise of a particular therapeutic agent? Dr. Hodes said that the AMP-AD projects are aimed at therapeutic progress; however, there are no interventions to date that can effectively alter the disease course and the progression of symptoms. The first step is to identify biomarkers that can be used to predict disease risk and track disease progression, and to monitor those biomarkers during clinical interventions. If the interventions don't work, important insights will be gained as to whether they have engaged the target.

Are there differences in changes in the body in Alzheimer's disease vs. normal aging--for example, with respect to bladder and bowel functions? Dr. Hodes said that there are changes that occur in the body with aging that are independent of Alzheimer's disease, and distinct from its underlying pathology. Interventions for cognitive decline with aging may turn out to be quite different from those for Alzheimer's disease, which has been largely focused on targeting the amyloid pathway.

To what extent has the NIA been actively exploring the beneficial effects of physical activity in normal aging and in Alzheimer's disease? Dr. Hodes said that a remarkable confluence of animal studies show the beneficial effects of physical activity on aging parameters, such as cardiovascular and musculoskeletal function. Such effects have also been seen in animals with respect to the number of new neurons formed in certain areas of the brain, including the area critical to memory. In humans, studies are showing the positive impact of physical activity in reducing cardiovascular risk. Very recently, the NIA and collaborators carried out the "LIFE" study, which reported beneficial effects of a physical activity regimen in preventing disability in aging. The NIA is interested in looking at exercise and lifestyle interventions for prevention of cognitive decline with aging, as well as potentially for dementia. A related issue is insulin metabolism. One intervention currently being studied experimentally for Alzheimer's disease is intranasal insulin. This study is based on findings that there is altered insulin tolerance within the brain, as well as in glial and neuronal cells, in Alzheimer's disease.

Does caloric restriction push the body below where it wants to be or should be? Dr. Hodes said the answer is not yet known. Relative to obesity, caloric restriction is considered positive, but its value is unknown relative to a "normal" state, which has not yet been defined. It is thought that the mechanism by which caloric restriction works is stress-related. In some studies, caloric restriction has been practiced intermittently--only a few days a week or month--and researchers have observed positive metabolic consequences, such as increased insulin sensitivity.

Is there a specific diet to be followed in caloric restriction studies? Dr. Hodes replied that there are subtleties involved, and approaches can vary among researchers. In the CALERIE trial, care was taken to maintain important nutrients, while giving the study participants the flexibility to self-select other dietary components in order to further their adherence to caloric restriction. He noted that the earlier NIDDK DPP and Look Ahead trials provided insights into designing caloric restriction studies.

VIII. SCIENTIFIC PRESENTATION: Molecular Machines in DNA Biology

Dr. Wei Yang, Chief, Mechanism of DNA Repair, Replication, and Recombination Section, Laboratory of Molecular Biology, NIDDK Intramural Research Program

Dr. Rodgers introduced Dr. Yang, whose research focuses on the study of DNA recombination, repair, and replication. Her lab uses x-ray crystallography, molecular biology, and various biochemical and biophysical approaches to discover the molecular mechanisms underpinning complex biological processes. Dr. Yang earned her Ph.D. in Biochemistry and Molecular Biology at Columbia University. She then did post-doctoral work at both Columbia and Yale. She joined the NIDDK Intramural Research Program in 1995 and was tenured in 2000. Among her many honors, she has been a Fellow of the American Association for the Advancement of Science (AAAS) since 2012, and was elected as a Member of the National Academy of Sciences in 2013.

IX. ANNUAL UPDATE ON THE NIDDK INTRAMURAL RESEARCH PROGRAM

Dr. Michael Krause, NIDDK Scientific Director, and Director, Intramural Research Program

The Council entered Executive Session for Dr. Krause's presentation. NIH policy requires that the Scientific Director, the leader of the NIDDK Intramural Research Program, report to the NIDDK Council once each year on the recent activities of the NIDDK Board of Scientific Counselors, which reviews the Program.

X. CONSIDERATION OF APPLICATIONS

A total of 1436 grant applications (402 primary and 1034 dual), requesting support of $443,740,929 were reviewed for consideration at the September 9, 2015 meeting. An additional 335 Common Fund applications requesting $157,667,198 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1284 applications requesting $409,737,663 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level.

XI. 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 199th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m. on September 9, 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