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 211th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:26 a.m. on September 11, 2019, at the Natcher Conference Center, Conference Room E1/E2, the NIH Campus, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Ms. Tracey Brown
Dr. David D'Alessio*
Dr. Iain Drummond
Dr. Joel Elmquist
Dr. Lisa Guay-Woodford
Dr. Caren Heller
Dr. Barbara Kahn
Dr. David Klurfeld*
Mr. Richard Knight
Dr. Paul Lange
Mr. Thomas Nealon
Dr. Richard Peek
Dr. Jeffrey Pessin
Dr. Craig A. Peters +
Dr. Ronald Sokol
Ms. Lorraine Stiehl
Dr. Ian Stewart*
Dr. Beverly Torok-Storb
Dr. Gary Wu

Also Present:
Dr. Griffin P. Rodgers, Director, NIDDK and Chair of the NIDDK Advisory Council
Dr. Karl F. Malik, Executive Secretary, NIDDK Advisory Council
Dr. Gregory G. Germino, Deputy Director, NIDDK
Dr. William T. Cefalu, Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK
Dr. Stephen P. James, Director, Division of Digestive Diseases and Nutrition, NIDDK
Dr. Robert A. Star, Director, Division of Kidney, Urologic, and Hematologic Diseases, NIDDK

* *Ex Officio* member
+ Served as an *ad hoc* member for this meeting

B. NIDDK STAFF AND GUESTS

Abbott, Kevin – NIDDK
Abraham, Kristin – NIDDK
Agodoa, Lawrence – NIDDK
Akolkar, Beena – NIDDK
Anderson, Dana – NIDDK
Arreaza-Rubin, Guillermo – NIDDK
Banda, Jorge – Purdue University
Barthold, Julia – CSR
Bavendam, Tamara – NIDDK
Berti-Mattera, Liliana – CSR
Boerboom, Lawrence – CSR
Begum, Najma – NIDDK
Best, Carolyn – Amer. Urological Assoc.
Bishop, Terry – NIDDK
Blondel, Olivier – NIDDK
Bourque, Sharon – NIDDK
Burch, Henry – NIDDK
Burgess-Beusse, Bonnie – NIDDK
Camp, Dianne – NIDDK
Castle, Arthur – NIDDK
Cerio, Rebecca – NIDDK
Chan, Kevin – NIDDK
Chowdhury, Bratati – NIDDK
Connaughton, John – NIDDK
Curling, Mitchell – NIDDK
Davila-Bloom, Maria – NIDDK

Dayal, Sandeep – NIDDK
Denny, Alexis – PKD Foundation
Densmore, Christine – NIDDK
Doherty, Dee – NIDDK
Doo, Edward – NIDDK
Drew, Devon – NIDDK
Duggan, Emily – NIDDK
Eggerman, Thomas – NIDDK
Evans, Mary – NIDDK
Ferguson, Christopher – Booz Allen Hamilton
Fisher, Rachel – NIDDK
Fonville, Olaf – NIDDK
Gansheroff, Lisa – NIDDK
Gossett, Daniel – NIDDK
Greenwel, Patricia – NIDDK
Guo, Xiaodu – NIDDK
Haft, Carol – NIDDK
Hall, Sherry – NIDDK
Hamilton, Frank – NIDDK
Hanlon-Tilghman, Mary – NIDDK
Harley, Sheila – Betah Associates
Hein, Patrick – Purdue University
Herzog, Peter – Digestive Diseases Natl. Coalition
Hoff, Eleanor – NIDDK
Hoffert, Jason – NIDDK
Hoofnagle, Jay – NIDDK
Hoover, Elise – PKD Foundation
Hoshizaki, Deborah – NIDDK
Hyde, James – NIDDK
Jerkins, Ann – NIDDK
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Kasting, Monica – Purdue University
Ketchum, Christian – NIDDK
Kimmel, Paul – NIDDK
Kirkali, Ziya – NIDDK
Kozel, Peter – CSR
Kranzfelder, Kathy– NIDDK
Kuczmarski, Robert – NIDDK
Laakso, Joseph – Endocrine Society
Larkin, Jennie – NIDDK
Laughlin, Maren – NIDDK
Lee, Christine – NIDDK
Leschek, Ellen – NIDDK
Li, Yan – NIDDK
Linder, Barbara – NIDDK
Lynch, Christopher – NIDDK
Malozowski, Saul – NIDDK
Martey, Louis – NIDDK
Martinez, Winnie – NIDDK
Maruvada, Padma – NIDDK
Mendley, Susan – NIDDK
Morris, Ryan – NIDDK
Mullins, Christopher – NIDDK
Murray, Ryan – Am. Society of Nephrology
Norton, Jenna – NIDDK
Olumi, Aria – Amer. Urological Assoc.
Osganian, Voula – NIDDK
Otradovec, Heidi – NIDDK
Parsa, Afshin – NIDDK
Pawlyk, Aaron – NIDDK
Payne, January – NIDDK
Perrin, Peter – NIDDK
Perry-Jones, Aretina – NIDDK
Pileggi, Antonello – CSR
Portnoy, Matthew – NIDDK
Rabadan-Diehl, Christina – Westat
Ramani, Rathna – NIDDK
Rankin, Tracy – NIDDK
Regan, Karen – NIDDK
Repique, Charlene – NIDDK
Rieff, Heather – NIDDK
Rivers, Robert – NIDDK
Roberts, Tibor – NIDDK
Rosenberg, Mary Kay – NIDDK
Roy, Cindy – NIDDK
Sadusky, Anna – NIDDK
Sanovich, Elena – NIDDK
Saslowsky, David – NIDDK
Sato, Sheryl – NIDDK
Sechi, Salvatore – NIDDK
Serrano, Jose – NIDDK
Sheets, Dana – NIDDK
Shepherd, Aliecia – NIDDK
Sherker, Averell – NIDDK
Sierra-Rivera, Elaine – CSR
Silva, Corinne – NIDDK
Singh, Megan – NIDDK
Smith, Jaime – NIDDK
Smith, Philip – NIDDK
Smith, Thomas – NIDDK
Spain, Lisa – NIDDK
Spruance, Victoria – NIDDK
Stoeckel, Luke – NIDDK
Tenney, Susan – NICHD
Thornton, Pamela – NIDDK

Tian, Lan – NIDDK
Tilghman, Robert – NIDDK
Torrance, Rebecca – NIDDK
Unalp-Arida, Aynur – NIDDK
Van Raaphorst, Rebekah – NIDDK
Vinson, Terra – NIDDK
Voss, Alyssa – NIDDK
Wallace, Julie – NIDDK
Wang, Xujing – NIDDK
White, Vanessa – NIDDK
Wilkins, Kenneth – NIDDK
Woynarowska, Barbara – NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers

Council Member News

Dr. Rodgers recognized four Council Members completing their terms after this meeting: Drs. Caren Heller and Paul Lange, who served on the Digestive Diseases and Nutrition Subcommittee; Dr. Joel Elmquist, who served on the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee, and Dr. Beverly Torok-Storb, who served on the Kidney, Urologic, and Hematologic Diseases Subcommittee.

Dr. Rodgers reminded Council and staff members that a working group of the NIH Advisory Committee to the Director has recommended measures to ensure that NIH Institutes and Centers (ICs) follow a uniform process for vetting concepts for possible Funding Opportunity Announcements (FOAs). Henceforth, new concepts must receive clearance from an advisory committee constituted under the Federal Advisory Committee Act (FACA). NIDDK is adjusting its implementation plan so that all concepts are made available to Council Members in the Electronic Council Book prior to meetings, and that Council Members have the opportunity to discuss concepts in depth during open sessions of each subcommittee. These concepts will be briefly summarized in open sessions of the full Council and concepts for trans-NIDDK initiatives will be presented to and discussed by the full Council in open sessions. To accommodate this pilot process, a second open session has been added to the full Council agendas.

Dr. Rodgers continued with additional announcements.

The Presidential Early Career Awards for Scientists and Engineers (PECASE) is the highest honor bestowed by the U.S. government to scientists and engineers who show exceptional promise for leadership at the beginning of their research careers. Four in the latest cohort chosen were nominated by NIDDK:

- Dr. Zachary Knight, Associate Professor, University of California, San Francisco, received the award for his innovative approach to elucidating the underlying neuromechanisms that control and regulate energy expenditure, hunger, thirst, and thermoregulation; and increasing our understanding of obesity and the development of anti-obesity therapies.
- Dr. Melina Bellin, Associate Professor, University of Minnesota Medical School, received the award for her investigations into childhood diabetes and advancing treatment of children and adults with chronic pancreatitis.
- Dr. Sandeep Mallipatu, Associate Professor at Renaissance School of Medicine at Stonybrook University, received the award for advancing research into diabetic kidney disease by elucidating the role of Krűpel-like factor-6 (KLM-6) in regulating mitochondrial function and attenuating disease progression as well increasing

understanding of molecular mechanisms underlying mitochondrial injury in diabetic patients.

- Dr. Katherine McJunkin, Stadtman Tenure Track Investigator in the Laboratory of Cellular and Developmental Biology in NIDDK's Intramural Research Program, received the award for elucidating the mechanisms underlying microRNA turnover, and providing insights into novel therapeutic approaches for treating diseases resulting from microRNA dysregulation.

NIDDK Staff News

Dr. Rodgers reported the following staffing news:

Dr. Rodgers welcomed **Dr. William T. Cefalu** as Director of the Division of Diabetes, Endocrinology, and Metabolic Diseases (DEM). Dr. Cefalu will be responsible for setting scientific priorities and allocating the Division budget. He will interact with leadership of professional societies, lay organizations, and advocacy groups and will provide advice on congressional inquiries within the mission of the division. Dr. Cefalu earned his Bachelor of Science from Southeastern Louisiana University, and his Doctor of Medicine at LSU Health Sciences Center. He joins NIH after serving as the Chief Scientific, Medical, and Mission Officer at the American Diabetes Association (ADA). Dr. Cefalu has been active in both clinical and basic science research for diabetes and metabolic diseases and has received research support and served as a principal investigator on two NIH-funded research centers. In addition to his post at ADA, he served as Executive Director; and as the George A. Bray, Jr.-endowed Super Chair in Nutrition and as a professor at LSS's Pennington Biomedical Research Center in Baton Rouge, LA. He has also held academic appointments at Tulane University School of Medicine, Wake Forest University School of Medicine, and the University of Vermont College of Medicine.

Dr. Matthew Portnoy is the new Deputy Director of NIDDK's Division of Extramural Activities (DEA). He earned his doctorate in biochemistry and molecular biology from The Johns Hopkins University. After postdoctoral work in the laboratory of Dr. Eric Green at the National Human Genome Research Institute at NIH, Dr. Portnoy joined the National Institute of General Medical Sciences as program director. He went on to become Director, Division of Special Programs in the NIH Office of Extramural Research, serving as the Coordinator of the NIH/HHS Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs. He also oversaw NIH's Academic Research Enhancement Award and provided program management and oversight for conference grants (R-13s and U-13s), as well as the Extramural Staff Training Office. He has served as Acting *NIH Guide* Director, overseeing the publication process for Funding Opportunity Announcements.

Dr. Andy Narva, Program Director for the National Kidney Disease Education Program, has retired from NIDDK's Kidney, Urologic and Hematologic Diseases (KUH) division. During his 13 years at NIDDK, Dr. Narva served as program scientist for the Chronic Renal Insufficiency Cohort Study, as Chief Clinical Consultant for Nephrology for the Indian Health Service, and Chair for the Kidney Interagency Coordinating Committee. He also managed a grant portfolio focused on chronic kidney disease, end-stage renal disease, dialysis, population health and pragmatic trials. He was dedicated to reducing the burden of chronic kidney disease, particularly in underserved communities with an elevated risk for the condition. His expertise on pragmatic trials has contributed to the Institute's understanding of chronic kidney disease and the impact of patient education on results. Dr. Narva earned his M.D. at Harvard Medical School, and prior to

his career at NIH served as a medical officer with the U.S. Public Health Service Commissioned Corps for the Indian Health Service, and Chief Clinical Consultant for Nephrology for the Indian Health Service.

Dr. Rodgers congratulated **Dr. Paul Kimmel**, program director for the Acute Kidney Injury program and Kidney HIV/AIDS program, who received an honorary fellowship on behalf of the Royal College of Physicians of London, a prestigious accolade held by some of the most innovative and exceptional physicians in the world.

NIDDK Strategic Planning Process

Dr. Germino gave an update on the NIDDK institute-wide strategic planning required by the 21st Century Cures Act. This institute-wide plan will have a five-year horizon and will complement disease-specific planning.

The process will include consulting with past and present Council Members as well as reviewing past NIDDK strategic plans and strategic plans of other organizations with shared research interests. The objective will be to identify common themes for advancing progress in all NIDDK mission areas. NIDDK will also reach out to the broader research and patient communities for input on scientific opportunities, challenges and future directions. This process will take place during 2020, which coincidentally marks NIDDK's 70th anniversary.

Dr. Germino introduced a draft framework that will guide requests for input. Some of the broad areas to be covered include:

- Advancing understanding of biological pathways and environmental contributors to health and disease,
- Supporting pivotal clinical studies and clinical trials,
- Funding research to evaluate promising prevention and treatment strategies in diverse, real-world settings,
- Biomedical research workforce development and training, and
- Diversity.

He explained that the report would contain a high-level discussion of these issues with an emphasis on cross-cutting themes with a final length of 50 to 60 pages. Advisory Council Members will be receiving a copy of the framework soon with an invitation to share their insights over the course of the next year.

Dr. Heller asked if the strategic plan will be linked to funding decisions. Dr. Rodgers answered that budget discussion may be more relevant to disease-specific or organ-specific strategic planning rather than this higher-level discussion of cross-cutting themes, especially considering frequent uncertainties surrounding budgets when looking at a five-year horizon. Dr. Germino added that the 21st Century Cures Act requires the strategic plan to include metrics by which progress can be assessed.

Dr. Rodgers explained that in 2018, NIH released its first Strategic Plan for Data Science, which noted that accessible, well-organized and secure data resources may accelerate the pace of biomedical discoveries for better health outcomes. To advance data resources relevant to NIDDK, the Institute has acquired funds from the HHS Assistant Secretary for Planning and

Evaluation to develop data standards for care planning for people with multiple chronic conditions, including kidney disease, type 2 diabetes, cardiovascular disease, and chronic pain. To inform this work, NIDDK plans to develop a working group that will include Council Members, patients and family members, informaticists and data scientists, and researchers and clinicians with expertise in the diseases of interest, social determinants of health, and patient-centered outcomes research, among other areas. The data elements and standards developed through this work will become part of the NIH Common Data Element Repository.

Mr. Richard Knight and Dr. Ian Stewart have agreed to serve as Council representatives on this working group, and they will report their recommendations to Council for consideration before action is taken. A motion was made and approved by voice vote to establish the working group.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 210th COUNCIL MEETING

Dr. Rodgers

The Council approved, by voice vote, the Summary Minutes of the 210th Council meeting, which had been sent to them in advance for review.

III. FUTURE COUNCIL DATES

Dr. Rodgers

2020

January 30 (Thursday)
Natcher Conference Center (Building 45)
Rooms E1/E2, D, and F1/F2

May 20-21 (Wednesday and Thursday)*
Building 31, C-Wing 6th Floor
Conference Center, Rooms 6, 7, and 10
*Subsequent to the Council meeting the date and location for this meeting was changed to May 12-13 at the Porter Neuroscience Research Center (Building 35), Rooms 610-640

September 9-10 (Wednesday and Thursday)
Building 31, C-Wing 6th Floor
Conference Center, Rooms 6, 7, and 10

2021

January 20-21 (Wednesday and Thursday)
Building 31, C-Wing 6th Floor
Conference Center, Rooms 6, 7, and 10
*Subsequent to the Council meeting the date and location for this meeting was changed to September 21-22.

May 12-13 (Wednesday and Thursday)
Natcher Conference Center, (Building 45)
Rooms E1/E2, D, and F1/F2

September 1-2 (Wednesday and Thursday)
Natcher Conference Center, (Building 45)
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 for which a longer meeting is required.

Dr. Rodgers noted that renovations on the Building 31 conference center have met with some delays and this may require adjustments to planned Council meeting dates. Advisory Council Members will be informed as soon as possible if changes are needed, and others should check the NIDDK website for updated information.

IV. ANNOUNCEMENTS
Dr. Malik

Confidentiality

Dr. Malik 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. Malik reminded the Council Members that advisors and consultants serving as Members of public advisory committees, such as the NIDDK Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur.

Responsible NIDDK staff shall assist Council Members to help ensure that a 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, or partner (including close professional associates), or an organization with which the Member is connected.

To ensure that a Member does not participate in the discussion of, nor vote on, an application in which he/she is in conflict, a written certification is required. A statement is provided for the signature of the Member, and this statement becomes a part of the meeting file. Dr. Malik directed each Council Member to a statement in his or her meeting folder regarding the conflict of interest in review of applications. He asked each Council Member to read it carefully, sign it, and return it to NIDDK before leaving the meeting.

Dr. Malik pointed out that when the Council reviews applications in groups without discussion—also called "*en bloc*" actions—all Council Members may be present and may participate. The vote of an individual Member in such instances does not apply to applications for which the Member might be in conflict.

Regarding multi-campus institutions of higher education, Dr. Malik said that an employee at one campus may participate in any particular matter affecting another campus, if the employee's financial interest is solely at one campus and the employee has no multi-campus responsibilities.

V. REPORT FROM THE NIDDK DIRECTOR

Dr. Rodgers

Budget Update

Dr. Rodgers updated the Council on the status of NIH's appropriation for Fiscal Year (FY) 2020, noting that the President's 2020 budget was released in March. The total request for NIH is just under $34 billion, which represents an overall 13.3 percent cut from FY 2019 levels and an approximate return to the level of the FY 2017 budget.

This decrease in budget would mean that the number of research grants made by NIH would drop from 11,700 to 7,900. For NIDDK specifically, the President's 2020 budget would mean a reduction of $283 million, or 14 percent.

Dr. Rodgers accompanied Dr. Collins when he testified before the Senate Labor-HHS-Education appropriations subcommittee hearing in April, and the consensus was that the hearing went smoothly, and that NIH still enjoys strong bipartisan support in congress.

The House Labor-HHS-Education appropriations subcommittee and full House Appropriations Committee made changes to the President's Budget Request in April and May 2019. The resulting bill increased the NIH budget by 5.1 percent and NIDDK's budget by 4.9 percent. The House passed the bill as part of a multi-bill ("minibus") package that also included funding for Defense, State, Foreign Operations, and Energy and Water. Dr. Rodgers noted that discretionary spending in this bill far exceeded spending limits prescribed under the 2011 deficit law, but those caps were raised and, the limits on public debt were suspended as part of the bipartisan Budget Act signed into law on August 2, 2019. He noted that this agreement doesn't affect mandatory spending caps, which affects NIDDK as the Special Diabetes Program receives mandatory funding. The Office of Management and Budget will determine whether this mandatory funding will be subject to sequester, as it was in 2013, 2014, and 2017.

The Senate Labor-HHS-Education Subcommittee on Appropriations had been scheduled to take up their version of the bill on September 10, but that process was postponed. With three weeks until the end of the current fiscal year, a continuing resolution (CR) now appears to be a possibility, as does a federal shutdown should a CR not be passed and signed by the President. To keep governmental operations going, the Senate must pass some version of the minibus and then their version, if modified, must go back to the House for consideration and vote, and then the President must sign it.

Dr. Rodgers noted that the appropriations bills that have it made through the House committees so far—including the Labor—HHS-Education bill—used a non-defense discretionary cap $15 billion higher than that agreed to in the 2019 Budget Act. This means that adjustments will have to be made, and the amount marked by the House for NIH may decrease. He concluded by saying the budget was a work-in-progress and that he remained hopeful that a new appropriations bill will be passed before September 30.

Dr. Rodgers also reported on NIDDK's participation in some recent congressional activities. The biennial Children's Congress, organized by the Juvenile Diabetes Research Foundation, took place as part of a three-day event JDRF held to highlight efforts to combat type 1 diabetes. At least 2 children with type 1 diabetes from each of the 50 states came to Washington, DC to speak with Senators and House Members about the importance of reauthorizing the Special Diabetes Program (SDP), which is due to expire on September 30, 2019.

On July 10, 2019, Dr. Rodgers testified before the Senate Special Committee on Aging hearing on type 1 diabetes research and the renewal of the SDP. He briefed the Committee on research supported by NIH and NIDDK, especially studies funded by the SDP. Advocates from the type 1 diabetes research community joined Dr. Rodgers, including actor Victor Garber, JDRF President and CEO Aaron Kowalski, and two children who have type 1 diabetes. Present at the hearing was former NFL tight end, Isaiah Stanback, and his daughter, who has type 1 diabetes. The SDP has been continually funded for more than 20 years, and the hope is that this important funding and the research it supports will continue.

NIDDK representatives have had several congressional meetings and briefings, with one more scheduled for later in September. Meetings have taken place with Representatives Diana DeGette (co-chair of the House Diabetes Caucus), Bobby Rush, Joe Kennedy, and Bill Foster. and an additional meeting is scheduled with Representative Ed Case to discuss NIDDK's program for underrepresented minorities, especially as it relates to Representative Case's home state of Hawaii. Dr. Rodgers noted that he continues conversations with representatives on both sides of the aisle, including during the Children's Congress and at briefings hosted by the American Diabetes Association.

VI. PATIENT ENGAGEMENT IN NIDDK RESEARCH

Dr. Paul K. Kimmel
Ms. Tracey D. Brown
Dr. Caren Heller
Dr. Richard Knight

Dr. Rodgers emphasized that both NIDDK and NIH recognize the importance of patient perspective and insights in determining research priorities. He turned the floor over to NIDDK Program Director Dr. Paul Kimmel to introduce the presentation on patient engagement in NIDDK research.

Dr. Kimmel explained that NIDDK has made a major commitment to community and patient engagement in large clinical studies and is in many ways a leader among NIH Institutes and Centers (ICs). For this presentation, the Advisory Council heard from three fellow Council Members who represent NIDDK's advocacy partners about the state of patient engagement in clinical studies and prospects for the future as well as two additional Council Members who will give their thoughts on the topic. After this, the floor will be open for discussion of the full Council.

Ms. Brown, CEO of the American Diabetes Association, explained that while patient engagement has been a topic of discussion since the early 1990s, the concept has become even more relevant as health care shifts to a value model. In terms of research, patient engagement means that instead of doing research *on* people, we're doing it *with* them as collaborators. But language shifts are not enough; the larger challenge is forging connections with patients and

involving them in every step of the research cycle, from identifying and prioritizing research questions to commissioning, designing, managing, and undertaking clinical trials; disseminating results; implementing programs, and evaluating the impact.

She pointed out that the basis of meaningful engagement is trust, and a large portion of Americans do not trust scientific information or scientific experts. A study from the Pew Research Center shows that about a third of Americans have "a great deal" of trust in science. That figure has increased from 2016 but is still significant enough to affect the adoption of clinical breakthroughs. This lack of belief in science, she said, is not based on facts or findings, but on people's values. Patient engagement requires finding common values. To find common values, we need to see, hear, and understand the communities of patients with which we are trying to connect. Patient engagement, Ms. Brown said, is an unwritten democratic right as well as fundamental to helping reduce health disparities.

She explained that most people who engage in clinical research do so not only for their own personal reasons, but also to connect to something bigger. If they are not engaging, it may be that they don't feel invited, that the process is not clear, that they do not feel a connection, or that no empathy was involved.

Since the discussion on patient engagement started in the 1990s, the country has undergone a shift and understanding that shift is key to engaging with patients in clinical research. To explore this shift, the ADA has used a methodology called the Q™ Proprietary System that tracks and evaluates thousands of cultural signals. ADA has identified 25 elements of culture that relate to engagement, connection, health care, research, and chronic diseases. These elements help elucidate the four health care delivery networks: hospitals, doctors' offices, urgent care centers, and community-based care. Understanding this "fourth network" is critical to patient engagement.

Community-based care breaks down into three areas: infrastructure, accessibility, and socialization. Ms. Brown highlighted some examples of how communities are leveraging these areas to deliver health care in communities. She pointed to clinics set up in firehouses and blood pressure tests in barbershops, both examples of taking advantage of trusted community resources to deliver needed care. She also pointed to programs that increase access to care by combining health care delivery with health information delivery and introducing health care to the retail environment, such as CVS or Walmart, meeting people where they are. Socialization also plays a role, as in those who are using smart watches and other devices to track their health data, learn healthy habits, and share that with others. A community in Wisconsin has provided training to residents and businesses to make their area more welcoming to people with dementia.

What these programs have in common, she pointed out, is their use of connection to improve the health of communities. This same principle, she said, should be applied to the clinical research cycle.

Ms. Brown concluded with three pieces of advice for NIDDK:

- Meet people where they are.
- Make the research process simple and frictionless for participants.
- Replace "involvement" with real connection.

Dr. Caren Heller, Chief Scientific Officer of the Crohn's & Colitis foundation, followed, reporting on her organization's experience with patient-centricity in research, particularly in setting priorities and funding decisions.

The mission of the Crohn's and Colitis Foundation is to find new therapies and a cure for these diseases and to improve the quality of life of patients and families. To do this, the organization must ensure that research efforts are headed towards goals that are meaningful for patients, because then patients are more likely to adopt and use these new diagnostics and therapies. The key to this is to involve patients as early as possible in the process so that they can help build a trial in which patients will enroll. Enrollment can be a major hurdle in research, she pointed out. The Foundation does not want to waste money on trials that don't get enough enrollment or in trials that don't address what's important to patients.

Patient engagement in clinical research can only work if there is mutual respect between researchers and patients, she said, including the belief that patients have the necessary authority to become contributing partners. She chooses the term "patient-centric" rather than "patient-focused" because the former means that patients are involved in all activities.

As Chief Scientific Officer, Dr. Heller is responsible for the Foundation's research and education efforts as well as the evaluation of those efforts. She looks at the research funding continuum as having three steps: setting research priorities, developing proposals, and reviewing proposals. She reported that patients and caregivers serve on all grant/proposal review committees, including basic science, translational research, clinical research, quality of care, and patient-facing (surveys). They also participate in the organization's venture philanthropy program that funds entrepreneurial efforts and its data repository for bio-samples. Patients and caregivers have recently been added to the committees reviewing senior research awards, career development awards, research fellowship awards and clinical research networks.

She explained that projects are scored on significance (whether it addresses an unmet clinical need or bridges a research gap) and innovation (whether it addresses the problem in a new way or improves current solutions). In the event of a "tie" between projects, the patient/caregiver score becomes the deciding factor. Any feedback from patients/caregivers is also given to the research applicants to further their understanding of the patient perspective. She pointed out that the organization has recruited patients and caregivers who are scientists as well as lay patients.

Looking ahead for the organization, she said that they will be exploring ways to improve the information exchange and open the dialogue to identify research questions that resonate with both researchers and patients/caregivers. A grant from PCORI is funding this work in clinical research, and the organization intends to do something similar for basic and translational research. Eventually, they may consider requiring researchers to engage with patient volunteers at the letter of intent stage.

She concluded with the following recommendations for NIDDK:

- Include patient advocacy groups in NIDDK strategic planning initiatives (which NIDDK already does).
- Design a process to include patients/caregivers in research review committees, perhaps starting first with clinical research proposals.

- Work with patient advocacy groups to develop evaluation criteria that reflect patient values and build mutual respect between researchers and patients for reviewing basic/translational/clinical research proposals.

Mr. Richard Knight, President of the American Association of Kidney Patients (AAKP), summarized patient engagement with the phrase, "Nothing about us without us." Patients speak for themselves and researchers and those making decisions about research need to speak directly to patients, not through a third party.

He explained that his association recently celebrated its 50th anniversary. Its mission is to educate and advocate for kidney patients. Mr. Knight and his organization define patient engagement as a substantive means to impact policy and health outcomes.

He reviewed some of the benefits and challenges of patient engagement in clinical research as revealed by a PCORI systematic review of 142 studies. A small number of the studies described potential harms, such as patient frustration with the length of the process, the need for additional time, funding needs, and the hypothetical potential of treating patients as "tokens" and for "scope creep" in terms of research questions. He said that with proper management, these situations should not occur. For example, funding for patient engagement should be included in the initial costs of projects.

He pointed out that patient engagement depends on commitment from leadership. As an example, he pointed to the NIDDK's Kidney Precision Medicine Project (KPMP) led by Drs. Robert Star and Jonathan Himmelfarb. They stated from the beginning of the project that they wanted patients involved all along the way. Patients served on the steering committee and helped develop the informed consent process, draft agreement, protocol development, and determine the transparency of research results. Mr. Knight has attended many scientific webinars and other research project activities, which have given him insights into the challenges and scope of this large-scale, long-term project.

He clarified that his organization is a nonprofit advocacy group, not a lobbying organization, but does get involved with speaking as patients to make the case for funding for NIDDK.

In addition to the KPMP project, he mentioned APOLLO-APOL1, which looked at kidney disease in African-Americans, who lose their kidneys four-times as often as Caucasians. Patients were not involved in the beginning of the project, but a Community Advisory Council was formed, and their subsequent input has had significant impact on the project.

He closed with a few recommendations to improve results from KUH clinical trials:

- Work with the kidney community to improve lives of kidney patients.
- Focus on patient-centered outcomes: Ask how the research impacts patients and use that information to inform priorities.
- Clarify research costs.
- Mitigate potential harms by improving recruitment techniques and working with appropriate patient organizations to help with recruitment.
- Collaborate with AAKP (as NIDDK already does) through their National Patient Meeting, targeted events, and workshops that help patients understand the specifics of clinical trials.

Following Mr. Knight's presentation, Ms. Stiehl was asked to comment on the overall content. She started by introducing herself as the spouse of someone with type 1 diabetes who has herself been involved with NIDDK and the kidney community for more than 20 years. She has worked directly with patients, recruiting for NIDDK-sponsored trials through TrialNet.org.

She pointed out that many of the young people who participated in the JDRF's Children's Congress have participated in NIDDK clinical trials and even have been diagnosed through the Institute's TrialNet trial. She has been involved in selecting the young people to participate in the Children's Congress, and that selection process is very difficult because they all have such compelling stories that point out that patient engagement starts even when patients are young.

Ms. Steihl said Ms. Brown's comments about the "fourth network" resonated with her. Working only with academic institutions limits outreach to patients. One model to look at is NIH's current *All of Us* study. They are working with a consulting firm, HCM Strategists, to help them spread the word about the study through retirement and senior communities, AARP, churches, Pride organizations, and in the Hispanic and African-American communities. She suggested that NIDDK look at ways to partner with *All of Us*, which just received another $9.1 million to pursue outreach efforts.

Mr. Nealon, CFO of the American Liver Foundation, commented on the presentations from the perspective of liver disease, which now affects more than 100 million Americans. Liver diseases include non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, and viral hepatitis, which affect huge numbers of patients, including some children, and other liver diseases, like biliary atresia, Wilson's disease, or progressive familial intrahepatic cholestasis, which affect less than 20,000 people in the U.S.

Despite the large numbers of people with liver disease, people don't talk about it, he said. Primary care physicians may be poorly informed about the disease. As a result, there are probably many more people who have liver disease and are unaware. Finding a way to empower patients to come forward and be engaged in the research process is a further challenge.

His organization is working to elevate the patient voice and advocate for liver health and wellness by developing patient cohorts and recruiting people with liver disease to speak out about the challenges of the disease, including paying for treatment, understanding clinical trials, or getting other information. He pointed out that there is a severe shortage of livers. Of the 8,000 transplants done in 2018, 400 were transplants from living donors. That number will have to expand to meet the needs of the 14,000 people currently on the transplant list.

Next, Dr. Lange commented based on his experience as a principal investigator as well as a prostate cancer patient. He noted that when he wrote the grant application for the Prostate SPORT trial, he looked at the patient engagement section and the patient engagement committee as a burden he had to go through to get the grant. As chair of the committee, he went from skepticism to shock at how patient engagement activities helped prioritize, conceive, and develop research direction as well asimprove focus, relevancy and patient acceptance, all of which assisted in the development of the clinical trial. He said that the process took patience, listening, and developing better patient skills to convey respect and build trust.

He also pointed to the application of the internet and social networking to patient engagement activities. For a study on bladder cancer, his team developed a patient survey network that now has more than 1,000 patients involved and has resulted in better and faster prioritization of research goals. Crowdsourcing—the practice of obtaining services, ideas or advice from large groups of people, typically the general public, in an online community—has also been helpful. His team used Amazon's Mechanical Turk platform to assess surgical skills and found that results were as accurate as and faster than more cumbersome physician panels. He recommended that the research community delve in to this exciting and complex world to interface with patients.

Council Questions and Discussion

To start the discussion, Dr. Kimmel asked the group to think about the idea of patient participation in NIH grant reviews.

Dr. Torok-Storb commented that patient engagement is unquestionably important. However, most patients need more understanding of the research process so that they can participate more fully. She gave the example of a study she worked on in which they wanted to engage Hispanic migrant workers. The researchers went to the community with a giant inflatable colon that people could walk through and better understand the disease under study.

Dr. Cefalu pointed out there are different degrees of patient engagement based on the research level and that patient involvement in basic science review may present challenges.

Dr. Heller explained that the Crohn's & Colitis Foundation has changed their procedure for this. They originally combined patient/caregiver review scores with the scientific scores, which caused issues when the patient scored the proposal very poorly and the scientists scored it highly. It resulted in a lot of peer pressure for patients to change their score. Now, the science is evaluated by scientists and the patient/caregiver score is used as a priority score. Both sets of comments are fed back to the researchers so that they understand the patient/caregiver perspective and appreciate the impact science has on their care. They also hired an Associate Director for Digital Health and Patient Engagement who will be leading an effort to look at better evaluation criteria that resonate for both patient and researcher. The timeline to impact for basic research is going to be longer than for translational or clinical research.

Ms. Brown agreed that the value of hearing from patients in basic science reviews comes from understanding the connection to problems patients have or a solution they're seeking. They may not know the science, but they know what they are living, and that information can help researchers identify the right question.

Dr. Wu pointed out that if scientists know that patients and caregivers will have input on their projects, it would influence their science and encourage them to think about relevance and real-world experience. It also increases patient understanding of basic science and how it fits in the research process. He also commented on Ms. Brown's mention of the large proportion of the U.S. population that doesn't entirely trust science. Is there an opportunity to partner with patient advocacy organizations and use crowdsourcing methods to help educate the public about the value of science?

Dr. Guay-Woodford highlighted two takeaways from the presentations. For studies that involve patient recruitment, integrating the patient voice in the development of the study can help address the challenges involved in patient recruitment—such as transportation and access to care. Also, support for basic science from patient foundations like the Crohn's & Colitis Foundation helps make the point that this research has value for patients. This bi-directionality is necessary to advance our knowledge and enhance the lives of patients.

Dr. Star wondered if altering the grant application might address some of the challenges of engaging patients in basic science review. In addition to the general significance section, perhaps a "Summary for the Patient" section is needed on significance for the patient, similar to the "Public Health Implications" section.

Dr. Drummond amplified Dr. Guay-Woodford's point about needing guidance from patients on what is important for their lives. Patients, basic scientists, and physicians were asked to rank criteria for success for the Kidney Health Initiative and the patients put all the quality-of-life and access to care criteria at the top, while the physicians put all the clinical criteria at the top. The patients helped define goals that were in some cases easier to achieve.

Dr. Pessin believed that the issue is more complicated than presented in relation to basic science. Some studies may have no apparent direct application today and unclear implications for future patient outcomes, and yet go on to become fundamental, award-winning findings. The lay person may not be able to appreciate this. Patients should be involved in clinical research, he said, but it may be a mistake to involve patients in decisions about basic research.

Dr. Rodgers ended the discussion by thanking the speakers for their presentations and the discussants for their comments, which will help inform NIDDK's strategic planning efforts.

VII. SUBCOMMITTEE MEETINGS

VIII. CONCEPT CLEARANCE

Presentation of Concepts

To comply with new recommendations from the NIH Advisory Committee to the Director, NIDDK adopted a new process in May 2019 for clearing concepts for Funding Opportunity Awards (FOA) prior to publication. After in-depth discussion in the subcommittees, NIDDK staff presented brief concept summaries to the full Council.

Trans-NIDDK Concepts

Dr. Christopher Lynch and Dr. Rob Rivers presented concepts that span the mission area of NIDDK:

- **GI Sampling and Monitoring Tools or Devices for Diet and Host-Microbiome Interactions** addresses the need for new tools and devices to enable monitoring and sampling *in situ* of chyme and mucosa in various regions of the GI tract without disrupting normal gut physiology or host-microbiota interactions. The project will support development of multifunctional smart technologies to make them more accessible for clinical research and clinical care. This concept is part of a broader nutrition research task force effort related to precision nutrition and microbiome research.

- **Advanced Tools for Continuous Monitoring of Nutrients and Metabolites** aims to develop tools that can continuously monitor a broader range of nutrients (beyond glucose) in clinical studies. Solid-state analytical techniques are becoming increasingly miniaturized, creating opportunities to expand sensing to metabolites such as peptides. This concept is part of a broader nutrition research task force effort.
- **Summer Research Experiences Utilizing SPARC-generated Resources** (Stimulating Peripheral Activity to Relieve Conditions) is an NIH Common Fund program that attempts to map the peripheral nervous system and a variety of organs to develop effective bioelectronic therapies for a wide range of diseases. This concept leverages NIDDK's current partnership with SPARC to provide short-term training opportunities in computation, physiology, anatomy, and neurobiology to doctoral students and postdocs in NIDDK focus areas.
- **Short-Term Research Program for Underrepresented Persons (STEP-UP)** is an existing NIDDK program that provides diverse high school and undergraduate students with summer research experiences. Programmatic analysis shows that the majority of STEP-UP participants go on to complete degrees in STEM fields and some have gone on to receive independent NIH funding. NIDDK coordinating centers will receive funds to use novel interventions to reach younger students in a one-year pilot project that will evaluate young students' continuing interest and participation in science.
- **Study Coordinators Supplement** is a pilot to increase the gender, racial, and ethnic diversity of front-line clinical trial workers to correspond with that of their communities. This pilot will also address the need to recruit new clinical trial coordinators as older workers retire. Supplemental funding will be available to NIDDK clinical research studies that target underrepresented communities to recruit potential study coordinators from those communities.

Council Questions and Discussion

What are the evaluation criteria for the STEP-UP program? Are the students given a stipend?
Dr. Rivers explained that there is an external evaluation of the program that looks at how long student participants stay involved in biomedical research and whether they stay involved in areas of interest to NIDDK. The idea is to determine whether the program increases interest in science among these students. Students are paid a stipend to encourage participation in the program.

Special Diabetes Program (SDP)

Dr. Philip Smith preceded his summary of the Special Diabetes Program's concept clearance remarks by reminding Council about the Program's unusual funding structure. It is separate from NIH's regular appropriation and is part of the government's nondiscretionary (i.e., mandatory) funding pool. Beginning in 2008, the program started receiving infusions of one-year money, which compromised the ability to fund long-term projects like clinical trials. Staff successfully developed funding mechanisms that were approved for use only by the Special Diabetes Program to allow for the consolidation of multi-year funding into an upfront award.

Dr. Smith explained that, with the mission of funding potentially high-risk, high-reward large initiatives to study the prevention, treatment, and cure of type 1 diabetes, the Program has deployed about $2.7 billion since its inception. Nearly $1 billion of that has been allocated to pre-clinical research, including a large number of staff-managed research consortia.

Special Diabetes Program funds can be deployed to any agency in the Department of Health and Human Services. In particular, the Centers for Disease Control and Prevention has received funds.

The Diabetes Mellitus Interagency Coordinating Committee (DMICC) is composed of many government agencies, including the Veterans Administration, Centers for Medicare & Medicaid Services, U.S. Department of Agriculture, and the Department of Defense. This committee meets regularly to discuss diabetes research and to oversee the process of soliciting and reviewing concepts for consideration. For example, 33 concepts were considered at the most recent committee meeting in May 2019.

Legislation is currently pending in Congress to renew this program, making planning for the future difficult. However, the NIDDK has chosen the following approved concepts for immediate initiative development if Congress renews the Program's funding:

1. **Artificial Pancreas:** In addition to continuing work on the data coordinating center, NIDDK plans to address behavioral and other factors that influence adoption and effective use of these technologies in real-life situations. The four concepts in this area include:
   - Continuation of the Data Coordinating Center for Advanced Clinical Trials to Test Artificial Pancreas Devices for Type 1 Diabetes Management
   - Clinical, Behavioral, and Physiological Studies of Open- and Closed-Loop Systems
   - Development and Integration of Novel Components for Open- and Closed-Loop Hormone Replacement Therapy
   - Development and Integration of Novel Components for Open- and Closed-Loop Hormone Replacement Therapy (Small Business Innovation Research (SBIR) program)

2. **Pancreatic Pathobiology:** Concepts under this topic include an examination of the relationship between acute pancreatitis and the development of type 1 diabetes, including a specific model of pancreatitis associated with cystic fibrosis.
   - Type 1 Diabetes and Acute Pancreatitis Consortium
   - Type 1 Diabetes and Acute Pancreatitis Data Coordinating Center

3. **Beta Cells: Assessment and Therapies:** This area includes several studies using data from a large human islet research network to look at aspects of human pancreatic pathophysiology. Initiatives will look at using immune cells to deliver therapeutic or mutagenic agents to islet cells, early signs of dysfunction in beta cells, and new cell replacement technologies. The Human Islet Research Network has proposed a type of gateway award that will link mentors from within the consortium with early stage investigators (ESIs) to increase the workforce addressing type 1 diabetes research. Components of this concept include:
   - Immune System Engineering for Targeted Tolerance and Disease Monitoring in Type 1 Diabetes
   - Discovery of Early Type 1 Diabetes Disease Processes in the Human Pancreas
   - Development and Testing of New Technologies and Bioengineering Solutions for the Advancement of Cell Replacement Therapies for Type 1 Diabetes (SBIR)
   - New Investigator Gateway Awards for Collaborative Type 1 Diabetes Research

4. **Diabetes Complications:** This topic area looks at complications associated with diabetes, applying methodologies used in other diseases to diabetes wound healing.
    - Biomarkers for Diabetic Foot Ulcers through the Diabetic Foot Consortium
    - Building a Cellular and Molecular Atlas of the Diabetic Foot Ulcer Niche

5. **Autoimmune Etiology, Epidemiology, and Clinical Trials:** This collection of initiatives will examine biological pathways and the new chemistry of autoantigens and neoantigens to increase understanding of autoimmune diseases. Other projects include closing out the current SEARCH cohort study and formulating a new plan to address more effectively the issues raised by that study, as well as an initiative to target diabetic distress and improve glycemic outcomes. The last concept in this category is the continuation of the TrialNet Coordinating Center that has helped redefine type 1 diabetes and resulted in an effective pipeline for diabetes research.
    - Mechanisms Underlying the Contribution of Type 1 Diabetes-associated Variants
    - Autoantigens and Neoantigens' Role in Etiology and Pathophysiology of Type 1 Diabetes
    - SEARCH cohort study closeout
    - Treating Diabetes Distress to Improve Glycemic Outcomes in Type 1 Diabetes
    - Continuation of the TrialNet Coordinating Center

Dr. Malik reminded Council that the next group of concepts has received full discussion in subcommittee meetings and that write-ups of these concepts are available in the electronic council book.

Digestive Diseases and Nutrition Subcommittee
Dr. James gave the report from the Digestive Diseases and Nutrition Subcommittee:

- **Liver Cirrhosis Network:** This new initiative will focus on the fundamental pathophysiology of cirrhosis of the liver, which is the common final pathway for many different etiologies of liver disease and is a common cause of death in people 25-65 and in those with HIV. This initiative would establish a Liver Cirrhosis Network focused on clinical and translational science challenges through state-of-the-science techniques and approaches.
- **Pediatric Acute Liver Failure Immune Response Network (PALF IRN):** Pediatric acute liver failure (PALF) is complex, rapidly progressive, and potentially devastating clinical syndrome that can occur as a result of many acute liver diseases in children and for which transplantation may be the only available therapy. A single Multi-Centered Clinical Study Implementation Planning Cooperative Agreement proposed in 2018 and subsequently funded established the PALF Immune Responsive Network (to conduct an immune modulation intervention clinical trial for indeterminant PALF. The intent of this initiative would be to support a clinical trial cooperative agreement application that would allow the transition from the study implementation planning phase to the initiation of the active clinical trial.
- **Catalyst Award in Digestive Diseases, Liver, Nutrition, and Obesity Research:** Most NIDDK-funded research consists of hypothesis-driven R01 awards that are submitted and reviewed by standard study sections in the Center for Scientific Review (CSR) and

NIDDK. Following the success of a similar high-risk, high-reward, high-impact award developed by DEM, DDDN proposes this catalyst concept to create an opportunity for highly creative investigators to perform Division of Digestive Diseases and Nutrition (DDDN) mission-specific research that accepts risk in order to achieve innovative at the highest level.

- **Dietary Biomarkers of Intake and Exposure:** Nutritional epidemiological studies rely heavily on dietary intake assessment based on self-reported recalls, food diaries, and Food Frequency Questionnaires. These instruments suffer from a variety of systematic, inherent and random errors and poses a serious limitation for establishing causal relations between dietary intervention and health outcomes. There is a critical need for ideal biological markers that provide independent assessment of intake and nutrient status. The purpose of this initiative is to support the advancement of metabolomics-based dietary biomarkers research.
- **Continued NIDDK participation in the National Collaborative for Childhood Obesity Research (NCCOR):** NCCOR is a public-private partnership bringing together four major research funders: the CDC, NIH, USDA, and Robert Wood Johnson Foundation, to accelerate progress in reducing childhood obesity in America. Several NIH Institutes, Centers, and Offices participate in NCCOR, with NIH scientific staff serving in leadership positions for workgroups and projects. NCCOR identifies research gaps and opportunities, develops tools and resources for the research and public health communities, and brings together stakeholders to explore opportunities to work synergistically across agencies to enhance high-quality research. NIDDK plans to continue membership in and support of NCCOR for the next four years.
- **Continued NIDDK Participation in ASA-24, Self-Administered 24hr Dietary recall:** Several years ago, NCI developed an electronic, self-administered 24-hour recall tool (ASA-24), which can be completed anywhere with web access without an interviewer needed, making it less expensive and more convenient. About 600 NIH grants have used this platform for studies that require dietary recall data. NIDDK, along with other ICs, contribute to support that continued development of this platform. This initiative requests co-funding to support this NCI contract for maintenance of ASA-24 system.
- **Continuation of the Gastroparesis Clinical Research Consortium (GpCRC):** In its twelfth year of funding, the GPCRC is a multisite, multi-PI consortium with the goal of advancing understanding of the pathophysiology of gastroparesis and seeking effective treatments. The intent of the continuation of this consortium is to better define pathophysiologic signatures in GP and develop effective therapeutic targets.
- **Continuation of Action for Health in Diabetes (Look AHEAD):** Since the early 2000s, the Look AHEAD clinical trial has followed overweight/obese people with type 2 diabetes to study the long-term health effects of an intensive lifestyle intervention (ILI) compared to a less intensive program of diabetes education and support (DSE). The study ended in 2013, and long-term observational follow-up on this cohort has continued, shifting focus from cardiovascular disease to other complications of aging, overall mortality, economic costs, and other issues that overlap with the mission of the National Institute on Aging, which co-funds the study. This renewal proposal would continue follow-up of participants for longer-term effects of the ILI vs DSE condition on outcomes associated with aging (including decline in cognitive, psychological, physical, and other functions), accumulation and burden of multi-morbidity associated with chronic diseases, and healthcare costs and utilization.

Diabetes, Endocrinology, and Metabolic Diseases Subcommittee
Dr. Smith introduced the concepts from DEM:

- **Pilot and Feasibility Program for Emerging Physician Scientists:** The declining number of M.D.s conducting clinical research in diabetes and related metabolic diseases points to a need for additional avenues of support for emerging physician-scientists. The proposed program is intended to allow emerging physician-scientists to expand their clinical research experience and productivity to help them transition beyond their clinical training to the next stage of their research careers as physician-scientists. The program would provide matching funds to the DDEMD Centers to co-support research within the scope of a Center-funded, patient-oriented clinical research pilot and feasibility project.
- **Expansion of the SEARCH Registry to Increase Geographic and Ethnic Diversity:** The SEARCH Registry was started in 2000 by CDC (with NIDDK co-funding) to provide U.S. population-based statistics on diabetes in youth (<19 years of age). It has been a key vehicle for understanding incidence and prevalence of both type 1 and type 2 diabetes in youth, showing that rates are increasing, especially in minority groups. The five sites currently participating are generally representative of the U.S. population, but have some gaps in geographic and race/ethnic coverage. Current national surveillance efforts also have gaps related to type 1 diabetes. This proposal would add sites to expand surveillance of diabetes in youth and by type to fill these gaps.
- **Diabetes Prevention Program Outcomes Study (DPPOS) Extension:** DPPOS, going into its 29th year, demonstrated that metformin and intensive lifestyle are effective in preventing or delaying the development of type 2 diabetes in individuals at high risk, and long-term follow of the cohort has demonstrated durability of diabetes prevention and cost-effectiveness of interventions. Retention during the last 17 years of DPPOS is outstanding: 99 percent of surviving cohort consented in the current phase with no differential loss in treatment arms. The current phase, which examined primarily metformin's effect on cancer rates, ends in one year, and results at this point are unknown. Like Look AHEAD, this has become an aging study in which other partners (such as NCI) may be interested. Continued follow-up for an additional year would allow researchers to lock data and conduct initial analyses and consider compelling, unique questions.
- **Centers for Diabetes Translation Research:** The renewal of this existing program will focus on addressing high priority areas for NIDDK: health equity, health disparities, social determinants of health, and dissemination research.
- **dkNET New Investigator Pilot Award in Bioinformatics:** dkNET is an existing program that supports NIDDK researchers with a central information source about research resources. With an expertise in bioinformatics and key understanding of diabetes research, they are well positioned to develop a pilot program to develop a DDEM-focused bioinformatics work force. The pilot will allow us to assess the interest of the community and gauge the effectiveness of the strategy.

Council Questions and Discussion

Are MDs or PhDs the focus on this workforce development pilot?

The program will focus on researchers who are emerging from fellowship programs and have not received a grant before. The goal will be to provide them more research expertise so that they

can compete for a K grant. KUH takes a slightly different approach in their pilots; the idea is to test several different approaches to see which is most effective.

Is the goal of the Pilot Award in Bioinformatics to bring expertise in high-dimensional multi-omic analysis or will it focus on disseminating already existing database information?

The purpose is to build a workforce in the NIDDK disease areas. dkNet already works to disseminate resources, and the Council has voiced a need for more repositories for data.

Kidney, Urologic, and Hematologic Diseases Subcommittee
New Initiatives
Dr. Star introduced 13 initiatives from this subcommittee. The first 6 are new initiatives:

- **Interventions to Improve Outcomes After AKI:** This initiative will fund a clinical trial to test whether a multimodal set of outpatient care services can improve outcomes after 3 years (death, renal function, physical functioning) in patients with acute kidney injury who survive initial hospitalization. (Dr. Star noted that this is an instance where scientists in the group had a different initial idea that was redirected with input from patients.)
- **Understanding Chronic Kidney Diseases of Uncertain Etiology (CKDu) in Agricultural Communities:** CKDu causes end-stage kidney failure in rural areas of many low- and middle-income countries and may contribute to end-stage renal disease in the United States. Environmental exposures are suspected, but there is a lack of compelling evidence for any specific agent. Family and geographic clustering raise the possibility of an unrecognized genetic susceptibility. Finding an etiology and treatment for CKDu would save many lives and offer insights into mechanisms of progressive kidney disease.
- **Cooperative Agreement for Transplanting Hepatitis C+ Kidneys into Hepatitis C- Recipients:** Kidney transplantation is the preferred treatment for end-stage kidney disease but is limited by a severe scarcity of donor organs (100,000 currently on the waiting list vs.12,000 procedures annually). Transplantation of kidneys from patients with hepatitis C followed by antiviral drugs would increase the number of available kidneys, and preliminary research shows promising results. NIDDK proposes an investigator-initiated, multicenter, larger scale (N=200) prospective clinical study of this procedure followed by direct acting antiviral therapy shortly after transplant. Participants would be followed for outcomes of viral transmission and organ function/clinical outcomes and data needed for insurance companies to cover antiviral treatment before official diagnosis with hepatitis C.
- **KUH Innovative Science ACcelerator (ISAC) Awards:** This initiative aims to establish a new program to fund small pilot projects via a streamlined application and review process to support cutting-edge research and accelerate true innovation in areas of science of interest to the Kidney, Urology, and Hematology research communities.
- **Development of Enabling Tools for Biomedical, Behavioral, and Clinical Research in Kidney, Urologic, and Hematologic Diseases:** This initiative promotes the development of enabling tools and technologies in the areas of kidney, urologic, and hematologic diseases. The initiative will support pilot projects to advance innovative concepts and seed larger biomedical, behavioral, and clinical research efforts.
- **Institutional Training Network Award:** The KUH division aims to reshape and refocus its Institutional Training Award Program. New awards will cultivate a dynamic network of multi-disciplinary trainees, including F/T/K awardees and alumni; coordinate training and career development activities across an institution (Peer to Peer Networking); develop

novel teaching tools and curriculum for trainees and mentors; and hold an annual T32 trainee face-to-face national meeting and community outreach activities,

Kidney, Urologic, and Hematologic Diseases Subcommittee
Renewals
Dr. Star explained that the remaining 7 initiatives are recompetitions, reconfigurations, and an extension of an existing trial:

- **Re-competition of GUDMAP – Lower Urinary Tract Develop Molecular Anatomy Project:** The purpose of the GenitoUrinary Development Molecular Anatomy Project (GUDMAP) is to provide fundamental information necessary to guide new strategies for repair or replacement of damaged organs; to generate new insights into pathologic processes underlying developmental defects and disease; and to provide a thorough understanding of organogenesis so congenital malformations might be prevented and treated. This GUDMAP initiative focuses on the lower urinary tract to identify new cell types and establish cell signatures, categorize developmental events, and interrogate a well-chosen set of murine disease or injury models for kidney and lower urinary tract to define disease-associated cell signatures. Recognizing the importance of getting data out quickly, this project makes validated data available through a shareable database before publication.
- **Reconfiguration of GUDMAP/RBK Data Hub:** The NIDDK supports two consortia, GenitoUrinary Development Molecular Anatomy Project (GUDMAP) and the ReBuilding a Kidney (RBK), in which the data is shared with the research community upon validation. This initiative consolidates the data hubs for the GUDMAP and RBK. The single data hub will facilitate activities of both consortia by serving as a central data and resource repository using FAIR (findable, accessible, interoperable and reusable) principles, and will function as an administrative hub, and will manage a single Opportunity Pool program.
- **Extension of USDRN Prevention of Urinary Stones with Hydration (PUSH) Study:** This randomized clinical trial to investigate the effects of a multi-component program of behavioral interventions to encourage increased intake of water, which can prevent development of kidney stones. The study is the first ever to assess the impact of financial incentives on a person-centric health outcome (kidney stone event) and involves novel features such has participant choice of interventions and gradual tapering financial incentives.
- **Re-competition of the George M. O'Brien Urology and Development Centers Program and Interactions Core:** This renewal of these Centers Programs allows continued advances in understanding the underlying mechanisms of urologic disorders and further supports the development of new prevention and clinical management strategies, as well as ensuring a strong and diverse urologic research community. Critical to these broad goals is the ability to promote productive interactions between the various Centers, associated Career Development Programs, and the broader urology research and clinical communities. To address this need, a solicitation for a Urology Centers Program Interactions Core (U24) is also proposed.
- **Re-competition of Institutional Career Development for Epidemiology of Urologic Diseases (UroEpi):** This renewal continues support to mentor and develop a cohort of proficient and self-sustaining investigators who can conduct epidemiologic research in

benign urological diseases and conditions. This program serves as a parallel resource to existing projects for chronic and end stage kidney disease within KUH, and for diabetes and digestive diseases within NIDDK.

- **Stimulating Hematology Investigation: New Endeavors (SHINE) Topic: Bioinformatic Exploration of Hematology Cohort Data:** The SHINE program was started in FY2010 as a pool of revolving funds to support emerging fields in hematology research. The purpose of this renewal—the project currently has funding through FY2020—is to announce plans to hold a workshop and introduce a new topic, "Tools for Mining Cohort Data." The goal of the workshop is to develop new partnerships between data science investigators and investigators curating clinical cohorts. Participants will discuss state of the art tools for identification of disease pathways, especially in non-malignant hematologic diseases, and identify the limitations inherent in existing tools. The development of new tools for genotype-phenotype analyses and disease pathway prediction will provide unique insights into a range of inherited and acquired underlying diseases including the hemoglobinopathies, porphyrias, hereditary hemochromatosis and bone marrow failure disorders.
- **Predoctoral to Postdoctoral Fellow Transition Award:** Interdisciplinary research is increasingly being recognized as the foundation for the development of new scientific knowledge and discovery. However, exposure to interdisciplinary education is limited. One potential approach to address the current gap in interdisciplinary education is to create a program that would engage truly outstanding graduate students from a variety of fields, including but not limited to engineering, statistics, data science, imaging, biochemistry and genetics, and recruit them to pursue a career as an independent researcher in kidney, urologic, or hematologic disease.

Council Questions and Discussion

Could the concept of transplanting kidneys from people with hepatitis C be applied to other organs?

Yes. At a federal workshop on August 27, HRSA members met to discuss this in reference to all transplants, including liver, heart and others. This initiative will focus on kidney transplantation.

How are we prioritizing funding in these three subgroups (KUH, DDN, DEM)?

Funding allocation follows priorities set out in the NIDDK Strategic Plan, adjusted up or down depending on scientific opportunities.

Dr. Malik opened the floor to general questions about initiatives and concepts presented or about the concept clearance process. Balancing other Council business with presenting concepts is a challenge, and NIDDK has included materials about the concepts in the electronic Council book as a way of addressing those challenges.

What happens to the concepts after presentation? Are the concepts competing for funds with each other and across divisions?

Dr. Rodgers explained that some ideas will move forward because they represent unique funding opportunities and fill gaps in emerging areas of science. Limitations in funding—and the fact that the NIDDK budget has not kept up with the inflation rate—affect the Institute's ability for

fund projects. In the future, we will be looking at concepts two years in advance. Some of the questions that factor into funding decision include: Is it a good scientific opportunity? Is it filling a particular void in research? Does the project fit with other priorities of the Institute? Can we partner with other Institutes with similar interests?

While everything is, in a sense, competing when there are limited funds, competition is more in terms of opportunity and scientific considerations. Fully funding one project gives it a better chance of success than partially funding multiple projects.

Dr. Rodgers concluded the discussion of concept clearance and adjourned to Closed Session at 3:45 pm.

IX. CONSIDERATION OF GRANT APPLICATIONS

Dr. Malik

A total of 1,420 grant applications (386 primary and 1,034 dual), requesting support of $536,081,454 were reviewed for consideration at the September 11, 2019, meeting. An additional 40 Common Fund applications requesting $14,514,846 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1,165 applications requesting $408,813,283 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the September 11, 2019, meeting.

X. ADJOURNMENT

Dr. Rodgers

Dr. Rodgers expressed appreciation on behalf of the NIDDK to the Council Members, presenters, and other participants. He thanked the Council Members for their valuable input. There being no other business, the 211th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m.

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 Chair, National Diabetes and Digestive and Kidney Diseases Advisory Council