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 202st meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on September 7, 2016, in Building 31, Conference Room 10, the NIH Campus, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

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

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
Agodoa, Lawrence – NIDDK
Akolkar, Beena – NIDDK
Andersen, Dana – NIDDK
Arreaza-Rubin, Guillermo – NIDDK
Baker, Jenna – NIDDK
Barnard, Michele – NIDDK
Bavendam, Tamara – NIDDK
Best, Caroline – Am. Urol. Assoc.
Bishop, Terry – NIDDK
Blondel, Olivier – NIDDK
Bourque, Sharon – NIDDK
Bremer, Andrew – NIDDK
Buchanan, Sarah – CCFA
Burgess-Beusse, Bonnie – NIDDK
Camp, Dianne – NIDDK
Carrera, Krysten – NIDDK
Carrington, Jill – NIDDK
Cerio, Rebecca – NIDDK
Cheng, Clara – CSR
Chowdhury, Bratati – NIDDK
Civillico, Gene – NIH/OD
Connaughton, John – NIDDK
Copeland, Randy – NIDDK
Cowie, Catherine – NIDDK
Curtis, Leslie – NIDDK
Dayal, Sandeep – NIDDK
Densmore, Christine – NIDDK
Doherty, Dee – NIDDK
Donohue, Patrick – NIDDK
Drew, Devon – NIDDK
Duggan, Emily – NIDDK
Eggerman, Thomas – NIDDK
Evans, Mary – NIDDK
Fisher, Rachel – NIDDK
Fleischhacker, Sheila – NIDDK
Flessner, Michael – NIDDK
Fonville, Olaf – NIDDK
Fradkin, Judith – NIDDK
Gallant, Kathleen Hill – Purdue Univ.
Gansheroff, Lisa – NIDDK
Garcia, Martha – CSR
Goglas, Philip – NephCure Kidney Intern.
Gossett, Danny – NIDDK
Goter-Robinson, Carol – NIDDK
Greenwel, Patricia – NIDDK
Guo, Xiaodu – NIDDK
Haft, Carol – NIDDK
Hall, Sherry – NIDDK
Hamilton, Frank – NIDDK
Hanlon, Mary – NIDDK
Hoff, Eleanor – NIDDK
Hoofnagle, Jay – NIDDK
Hu, Jianxin – CSR
Hunter, Christine – NIDDK
Hyde, James – NIDDK
Ivins, Jonathan – CSR
James, Stephen – NIDDK
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Kent, Bridgett – NIDDK
Ketchum, Christian – NIDDK
Kimmel, Paul – NIDDK
Kirkali, Ziya – NIDDK
Kirkham, Perry – Perdue Univ.
Kranzfelder, Kathy – NIDDK
Kuczmarski, Robert – NIDDK
Kusek, John – NIDDK
Laughlin, Maren – NIDDK
Lee, Christine – NIDDK
Leschek, Ellen – NIDDK
Li, Yan – NIDDK
Linder, Barbara – NIDDK
Lynch, Christopher – NIDDK
Malik, Karl – NIDDK
Malozowski, Saul – NIDDK
Martey, Louis – NIDDK
Maruvada, Padma – NIDDK
Moxey-Mims Marva – NIDDK
Mullins, Christopher – NIDDK
Narva, Andrew – NIDDK
Newman, Eileen – NIDDK
Niebylski, Charles – NIDDK
Norton, Jenna – NIDDK
Nurik, Jody – NIDDK
Olumi, Aria – Am. Urol. Ass.
Osganian, Voula – NIDDK
Pawlyk, Aaron – NIDDK
Perrin, Peter – NIDDK
Perry-Jones, Aretina – NIDDK
Pike, Robert – NIDDK
Pileggi, Antonello – CSR
Ramani, Rathna – NIDDK
Ramesh, Ganesan – CSR
Rankin, Tracy – NIDDK
Rasooly, Rebekah – NIDDK
Reiter, Amy – NIDDK
Riley, William – NIH/OD/OBSSR
Rojas, Raul – CSR
Rosenberg, Mary Kay – NIDDK
Roy, Cindy – NIDDK

Rushing, Paul – NIDDK
Rys-Sikora, Krystyna – NIDDK
Sanovich, Elena – NIDDK
Saslowsky, David – NIDDK
Sato, Sheryl – NIDDK
Serrano, Jose – NIDDK
Sheets, Dana – NIDDK
Shepherd, Aliecia – NIDDK
Sherker, Averell – NIDDK
Sierra- Rivera, Elaine – CSR
Silva, Corinne – NIDDK
Smith, Jaime – NIDDK
Smith, Philip – NIDDK
Spain, Lisa – NIDDK
Star, Robert – NIDDK
Stoeckel, Luke – NIDDK
Tatham, Thomas– NIDDK
Teff, Karen – NIDDK
Tilghman, Robert – NIDDK
Torrance, Rebecca – NIDDK
Tuncer, Diane – NIDDK
Unalp-Arida, Aynur – NIDDK
Utama, Herman– NIDDK
Van Raaphorst, Rebekah – NIDDK
Vinson, Terra – NIDDK
Wallace, Julie – NIDDK
Wellner, Robert – NIDDK
Wilkerson, Anita – NIDDK
Woynarowska, Barbara – NIDDK
Xia, Ashley – NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers

Outgoing Council Members

Dr. Rodgers recognized five Council members who complete their terms with this meeting: Cindy Luxhoj, who served on the Digestive Diseases and Nutrition Subcommittee; Dr. Sharon Anderson, Dr. Gopal Badlani, and Dr. Irving Smokler, who served on the Kidney, Urology, and Hematology Subcommittee; and Dr. Bruce Spiegelman who has served on the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee.

New Council Member

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

Dr. Ian J. Stewart will serve as an ex-officio member representing the Department of Defense. He will serve on a Kidney, Urology, and Hematology Subcommittee. Dr. Stewart is a major in the Medical Corps of the United States Air Force, currently stationed at David Grant Medical Center at Travis Air Force Base near Fairfield, CA. He is chief of Combat Casualty Care Research at the Clinical Investigations Facility. He is also assistant professor of medicine at the Uniformed Services University of Health Sciences. Dr. Stewart earned his M.D. from the University of Southern California's Keck School of Medicine, did his residency in internal medicine at San Antonio Uniformed Services Health Education Consortium and did a fellowship in nephrology at the University of Texas Health Science Center, also in San Antonio. Dr. Stewart's military experience includes serving as an intensive care unit physician at the Craig Joint Theatre Hospital in Bagram, Afghanistan. His area of specialized expertise is acute kidney injury, especially combat-related acute kidney injury. He has an impressive list of honors and awards from the military and strong affiliations including the American Society of Nephology and the American College of Physicians.

NIDDK Staffing Update

Dr. Ashley Xia joined NIDDK's Division of Diabetes, Endocrinology, and Metabolism (DEM) as a program director. Dr. Xia trained in medicine at Beijing University of Chinese Medicine, received her Ph.D. in biology at Wayne State University, and then did postdoctoral research in neuroscience at the University of Kansas. She then joined Celera Genomics in 1998 where she participated in human genome sequencing efforts. Before joining NIDDK, Dr. Xia worked at the National Institute of Allergy and Infectious Diseases (NIAID), where she was responsible for developing NIAID's Immunology Database and Analysis Portal that integrates experimental data and clinical trial data and provides data analysis tools. Within DEM, Dr. Xia will work with Maren Laughlin on the Molecular Transducers of Physical Activity in Humans program, an NIH Common Fund program aimed at understanding the molecular changes induced by physical activity and how physical activity affects health.

Dr. Patricia Greenwel joined the Division of Digestive Diseases and Nutrition (DDN) as program director in July. Dr. Greenwel earned her Ph.D. in experimental pathology from Albert Einstein College of Medicine where she studied the role of acute phase response cytokines in liver fibrogenesis. She received postdoctoral training at Mount Sinai School of Medicine, where she investigated signaling pathways and transcriptional factors responsible for the development of type I collagen genes. As a faculty member of the Department of Developmental and Molecular Biology at Mount Sinai, Dr. Greenwel characterized molecular mechanism involved in alcohol-induced liver cirrhosis, for which she received both NIH and private foundation support. Dr. Greenwel then went on to take a position at NIH's Center for Scientific Review (CSR) where she served as a Scientific Review Officer (SRO) for 15 years within the Digestive, Kidney, and Urological Systems Integrated Review Group. During her tenure at CSR, she was the SRO for the Xenobiotic and Nutrient Disposition and Action (XNDA), and Systemic Injury by Environmental Exposure (SIEE) study sections, as well as various Special Emphasis Panels. Within DDN, Dr. Greenwel will serve as director of the Gastrointestinal Development and Lymphatics programs.

Dr. Voula Osganian has joined DDN as director of the Pediatric Clinical Obesity Program. Dr. Osganian is joining NIDDK from Boston Children's Hospital and Harvard Medical School where she was an Associate Professor of Pediatrics in the Division of General Pediatrics, a program leader for the Hospital's Clinical Research Center, and an associate physician in the Optimal Weight for Life Clinic within the Division of Endocrinology. Dr. Osganian received her medical degree from the University of Massachusetts Medical School and completed her internship in pediatrics at Boston Floating Hospital. She also completed a preventive medicine residency and preventive cardiology fellowship at the University of Massachusetts Medical Center. She received a Doctor of Science in Epidemiology from Harvard School of Public Health with a concentration on cardiovascular and nutritional epidemiology. Dr. Osganian's independent and collaborative research has focused on health promotion and disease prevention in youth. She directed several NIH-funded multi-site studies as Principal Investigator or co-Principal Investigator. She led the Child and Adolescent Trial of Cardiovascular Health (CATCH) study, one of the largest school-based nutrition and physical activity intervention trials designed to promote cardiovascular health in elementary school children. As program leader at Boston's Children's Hospital, Dr. Osganian built a collaborative institutional program with approximately 50 faculty and professional staff who

provided quantitative and qualitative methodological expertise, protocol implementation assistance, as well as education and mentoring to trainees and investigator communities throughout the hospital. She brings to NIDDK a wealth of experience and expertise in the clinical management of obesity in pediatric populations, clinical trials and epidemiologic methods, and program development and leadership.

Dr. John Connaughton was recently appointed Chief of NIDDK's Scientific Review Branch. Dr. Connaughton will be responsible for supervising SROs who oversee and administer scientific review activities for grant applications and contract proposals that are reviewed within NIDDK. John also plans to continue to serve as the SRO for the NIDDK-B subcommittee, which is one of three NIDDK standing committees that evaluate individual mentored career applications (K awards) and institutional T32 training grants. Dr. Connaughton joined NIH in 2001 as an SRO. Since 2007, he has served as Chief of NIDDK's Training and Mentored Research Section. Prior to joining NIDDK, he spent 10 years in private industry at Oncor Inc., then Ventana Medical Systems, Inc., where he led a group that developed and launched commercial assays for cancer detection and disease management.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 201th COUNCIL MEETING

Dr. Rodgers

The Council approved, by voice vote, the Summary Minutes of the 201th Council meeting, which had been sent to them in advance for review.

III. FUTURE COUNCIL DATES

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

2018

January 24-25 (Wednesday and Thursday)
Natcher Conference Center (Building 45)
Conference Rooms E1/E2, D and F1/F2
May 16-17 (Wednesday and Thursday)
Natcher Conference Center (Building 45)
Conference Rooms E1/E2, D and F1/F2
September 12-13 (Wednesday and Thursday)
Building 31, Conference Rooms 10, 6 and 7

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

IV. ANNOUNCEMENTS

Dr. Karl Malik

Confidentiality

Standing in for Dr. Brent Stanfield, who was not present for the first part of the meeting, Dr. Malik reminded the Council Members that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council Members regarding actions on an application must be referred to the Institute. Any attempts by Council Members to handle questions from applicants could create difficult or embarrassing situations for the Members, the Institute, and/or the investigators.

Conflict of Interest

Dr. Malik reminded the Council Members that advisors and consultants serving as Members of public advisory committees, such as the NIDDK Advisory Council, may not participate in situations in which any violation of conflict of interest laws and regulations may occur. Responsible NIDDK staff shall assist Council Members to help ensure that the Member does not participate in, and is not present during, the review of applications or projects in which, to the Member's knowledge, any of the following has a financial interest: the Member, or his or her spouse, minor child, partner (including close professional associates), or an organization with which the Member is connected.

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

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

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

V. REPORT FROM THE NIDDK DIRECTOR
Dr. Rodgers

Budget Update

Dr. Rodgers reported that, despite significant congressional action on the NIH budget since the last Advisory Council in May, the budget for fiscal year 2017 is not settled. The Senate Appropriations Committee approved an allowance for NIH of more than $34 billion, a $2 billion increase over fiscal year 2016. NIDDK's share of this would be an increase of approximately $75 million, or a 4.1 percent increase over fiscal year 2016 levels. The House Appropriations committee passed their version of the budget with an allowance for NIH of $33 billion—still an increase over 2016, but $750 million less than the Senate proposal. NIDDK's share of the House budget would be almost $44 million, an increase of 2.5 percent over 2016 levels. The percentage budget increase for NIDDK in fiscal year 2017 proposed by both the Senate and the House is less than the NIH average, but comparable to the increases proposed by the Senate and House for most other large NIH ICs.

Both the House and the Senate proposed budgets align with the President's proposal, which included major increases for certain research efforts at NIH, including the Precision Medicine Initiative, antimicrobial resistance, the BRAIN initiative, and research focused on Alzheimer's disease. The House budget includes nearly $600 million for these efforts while the Senate includes $650 million for the targeted areas. The largest portion of those targeted funds goes to research into Alzheimer's disease, and those amounts show up in the allowances of the National Institute on Aging (NIA)—amounting to a 24 percent increase for NIA in the Senate budget and 29 percent increase in the House budget. Dr. Rodgers commented that is encouraging to see that the NIH continues to receive strong bipartisan support, adding that the hope is that the NIH budget for 2017 will increase between 3.9 and 6.2 percent.

Dr. Rodgers pointed out that the final budget will probably not be approved by the start of the Federal fiscal year on October 1, and that it was probable that Federal agencies will operate under a continuing resolution for at least several weeks. He added that the outcome of the presidential election, as well as House and Senate elections, will play a major role in determining how quickly the appropriation process is completed. He hoped that the process would be completed favorably by the Advisory Council's next meeting in February 2017.

VI. UPDATE FROM THE DIRECTOR, OFFICE OF BEHAVIORAL AND SOCIAL SCIENCES RESEARCH: Dr. William Riley

Dr. Rodgers introduced Dr. William (Bill) Riley, Director of the National Institutes of Health's Office of Behavioral and Social Sciences Research (OBSSR) and Associate Director of NIH for Behavioral and Social Sciences. Before his appointment to this position in August 2015, Dr. Riley served as health science administrator and deputy director for the Division of AIDS and Health Behavior Research at the National Institute of Mental Health and as a program director at the

National Heart, Lung, and Blood Institute, and as Chief of the Science of Research and Technology Branch in the Division of Cancer Control and Population Sciences in the National Cancer Institute. He also served as a professorial lecturer in the School of Public Health at George Washington University.

Dr. Riley earned his doctorate in clinical psychology at Florida State University and completed his clinical psychology internship at Baylor College of Medicine. He served as an assistant professor in the Department of Psychiatry and Health Behavior at the Medical College of Georgia and as associate professor in the Department of Psychiatry and Psychology at the Virginia Commonwealth University. From there, he became Director of Research at PICS, Inc, a private research and development firm in Reston, VA, working there from 1999 to 2005, when he joined the NIH. Dr. Riley's research interests include behavioral assessment, psychological health risk factors, tobacco use and cessation, and the application of technology to preventive health behaviors and chronic disease management. He has been interested in applying new technologies—such as mobile and wireless—in behavioral measurements and intervention as well as assessment of and intervention in health behaviors. His research has included the use of mobile phones and computer devises to assess and intervene in tobacco use, dietary intake, physical activity, sleep, and medication adherence.

Dr. Riley focused his presentation on the 2017 Strategic Plan for OBSSR, which has been in process since September 2015 and is expected to be released in the coming months. He explained that OBSSR is located within the Office of the Director of the NIH, in the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI). This is the same Division that also houses the Common Fund, the Office of Research in Women's Health, the Office of AIDS Research, and the Office of Disease Prevention. Like most of the components within the Division, OBSSR has a coordination role and works with all the 27 Institutes and Centers within the NIH.

OBSSR was authorized by Congress in 1993 and established in 1995 with two roles: 1) "Coordinate research conducted or supported by the agencies of the NIH;" and 2) "Identify projects of behavioral and social sciences research that should be conducted or supported by the national research institutes, and develop such projects in cooperation with such institutes."

Dr. Riley explained that behavioral and social sciences researchers focus on the factors that change behavior or social systems, from group and family level factors all the way up to geopolitical, economic, and environmental dynamics at the highest level—with other dynamics for example at the work and community and then at the national and state levels in between. The goal is to understand how behavior influences health as well as what drives behavior and how to change it to improve health. Dr. Riley used an example from the National Academies and the American Diabetes Association as a familiar illustration to frame these concepts. Diet and exercise behaviors have direct impacts on energy balance and affect risk for obesity and type 2 diabetes. Layers of influences affect these behaviors starting with individual factors (such as demographics, psychosocial factors, and gene-environment interactions) and expanding out to behavioral settings (home, community, worksites, schools), sectors of influence (health care, government, transportation, education, media, etc.) and social norms and values.

Dr. Riley explained the guiding principles behind the OBSSR Strategic Plan. An important goal is integration of behavioral and social science research into the larger biomedical research enterprise by increasing connections among the different fields. OBSSR will continue to coordinate and collaborate with ICs and identify critical challenges to the advancement of behavioral and social sciences research. Dr. Riley said the job of OBSSR is not to take over the work being done by individual ICs, such as NIDDK, focusing instead on trans-NIH efforts.

Dr. Riley noted that the working group for the Strategic Plan included representation from several ICs, including Christine Hunter from NIDDK.

The Strategic Plan focuses on three ***Scientific Priorities*** and four ***Foundational Processes*** by which these priorities will be advanced.

The ***Scientific Priorities*** for the OBSSR Strategic Plan are:

- Basic and Applied Research Synergy;
- Methods, Measures, and Data Infrastructures;
- Application and Adoption of Behavioral and Social Science Research.

The ***Foundational Processes*** that OBSSR will use to advance the Scientific Priorities include:

- Communication;
- Program coordination and integration;
- Training;
- Policy and Evaluation.

Some examples of examples of ***Foundational Processes*** include:

- Communicating research findings through lectures and awards;
- Coordinating and integrating with the larger NIH research enterprise by working with a trans-NIH coordinating committee to identify ways OBSSR can strengthen behavioral and social sciences research and by contributing to trans-NIH initiatives (e.g., Precision Medicine Initiative, BRAIN, etc.);
- Training, supported by R25 awards, in advanced approaches to behavioral and social science research, including optimizing designs, mobile health, and community-based participatory research;
- Evaluating the impact of behavioral and social sciences research by developing stronger portfolio analysis capabilities.

Dr. Riley then looked at each scientific priority individually, specifying for each a primary outcome by which to measure impact in that area and pointing to NIDDK examples of research in each area.

Basic and Applied Research Synergy: The two objectives in this area include: 1) identifying and encouraging promising basic behavioral and social sciences research and 2) facilitating bidirectional interaction between basic and applied research to encourage increased translation and uptake of research findings. A primary outcome of this priority would be that grantees in the

behavioral and social sciences will base their interventions not only on theory.

NIDDK examples of research meeting this objective include:

- Eric Stice's work using fMRI technology to test the Dynamic Vulnerability Model of Obesity by investigating if predisposition to elevated responsivity to food cues results in overeating and how that affects striatal dopamine signaling;
- Barry Popkin's analysis of the effect of economic changes on nutritional composition of food, food purchasing, and dietary intake;
- Julie Carlsten Christianson's investigation of comorbid mood and urogenital disorders following neonatal maternal separation in mice;
- Emeran Mayer's study of neurobiological mechanisms of cognitive behavioral therapy in patients with irritable bowel syndrome;
- Million Mulugeta's study of the role of peripheral cortocotropin releasing factor (CRF2) receptors in the colon's response to stress.

Methods, Measures, and Data Infrastructures: The strategic plan also prioritizes the development of improved research processes to encourage cumulative behavioral and social science in which new research builds on the knowledge base of prior research. Objectives in this area include: encouraging data integration and replication in the behavioral and social sciences; facilitating the development and testing of new measurement approaches; and expanding the repertoire of research methods available to social and behavioral researchers. A primary outcome for this scientific priority would be coherent and widely accepted behavioral and social science ontologies that are linked to measures, databases, and common data elements, and that are integrated with biomedical research and clinical ontologies.

As an example of NIDDK research that falls under this priority area Dr. Riley mentioned the work from David Cella's group that is looking at phenotypes of urinary symptoms and their relationships to genotypes, sleep, and obesity. Dr. Riley also discussed the Patient-Reported Outcomes Measurement Information System (PROMIS), a program to develop an efficient state-of-the-art assessment system for self-reported health. PROMIS was an NIH Roadmap program that has now graduated.

Adoption of Behavioral and Social Science Research Finding in Health Research and Practice: Dr. Riley pointed out that a common concern associated with behavioral and social sciences research is that findings are often not adopted into widespread practice. Obstacles include the resource- and labor-intensive nature of the interventions, the lack of an equivalent to the FDA for regulating safe and effective practices, the lack of a profit-driven system to implement interventions, and the broad range of settings where interventions may take place. One way to overcome these obstacles is through more real-world, pragmatic trials that study mechanisms and interventions in the context in which they would be carried out. Another is to enhance the relevance and scalability of social and behavioral interventions, perhaps using mobile technologies and web-based intervention approaches. The third objective under this priority is to foster collaborations with agencies and other entities that utilize and/or deliver social and behavioral research findings, and evaluate systemic and policy changes to facilitate or impede adoption of

effective approaches. A primary outcome of this scientific priority is that behavioral and social intervention research supported by the NIH rapidly and responsibly addresses questions relevant to practitioners and policy makers.

A prominent NIDDK example in this category is the Diabetes Prevention Program, which has been streamlined and adapted so that it could be tested and rolled out in YMCAs as a pilot which has now become part of their obesity management programs. Other examples include the use of technology for better glycemic control in children with Type 1 diabetes, for obesity in adults, and for diabetes education for African Americans with Type 2 diabetes. In addition, Dr. Riley mentioned two studies underway in community-based settings, including a worksite intervention to reduce obesity and diabetes risk in low income individuals and a child care intervention to prevent obesity in infants and toddlers.

Council Questions and Discussion

What period of time does this strategic plan cover?

Dr. Riley explained that the Office of Behavioral and Social Service Research has developed three strategic plans since its establishment; each was conceived as a 5-year plan, yet lasted 10 years. The new plan also covers five years, but the idea is to revisit the scientific priorities in 5 years to make adjustments, rather than undergo a full strategic plan process. Five years ago, he said, the Office could not have imaged some of the technology-based, dynamic modeling and computational modeling approaches now in use, so adjustments may well be necessary in another 5 years.

There seems to be a natural synergy between OBSSR and NIDDK's school outreach programs for measuring outcomes and tracking impact of programs over time.

Dr. Riley agreed with this point.

Is there a way OBSSR could team up with the NPR social science reporter who explains social science in an entertaining and illuminating way?

Dr. Riley admitted that one of the struggles in the field is that many think they already know about it, even though they may not be applying their knowledge effectively. He said we all develop our own theories for human behavior as our brains try to explain, predict, react to and ultimately regulate the environment around us. But the field also constantly surprises us with new information.

Dr. Rodgers asked about the application of behavioral and social sciences in the areas of justice and education. In justice, there is the emerging field of neurolaw, which uses tools such as MRI scanning to determine whether people are criminally responsible for their behavior. There is also a movement towards competency-based education, in which competency-based behaviors determine whether the student moves on to the next grade or stage of education. Is there much interaction between behavioral science and the fields of education and justice?

Dr. Riley reported that there is an increasing level of integration. For example, there is an increasing interest in the application of neuroscience to a range of behaviors and social phenomena. OBSSR has done some work on the relationship between education and health. Having a high school diploma is one of the biggest predictors of quality of life, premature death and overall health. While tobacco use is rare in groups of highly educated people, it is much higher in groups with lower economic status and lower education. OBSSR has looked at linking educational data bases with health databases for research purposes. However, confidentiality guidelines such as HIPAA (on the health care side) and FERPA (on the education side) differ and have impacted progress in this area.

Does OBSSR work with the NIH Center for Scientific Review? How have the study sections performed?

Dr. Riley replied that many of the applicable study sections fall under CSR's Division of AIDS, Behavior and Population Sciences. One of the challenges for the study sections is that the science changes so quickly, especially in the development of computational models, and sometimes it is difficult to find experts in these new areas. Another challenge in behavioral science is that there is not the same level of agreement about study procedure as there is in research that typically occurs in a laboratory. This can result in differences in opinion among reviewers regarding issues such as the best measures to use for a study.

How does OBSSR plan to translate research findings and communicate them so that they are more widely adopted?

Dr. Riley said he would like the office to highlight major accomplishments and the findings that will be most useful to stakeholders. OBSSR can sift through the data and research available and highlight and communicate the key points. However, Dr. Riley pointed out that OBSSR is a small office with a small budget, and it will probably have to collaborate with other agencies, such as SAMHSA and others, that focus on developing and promoting practice guidelines.

VII. NIH COMMON FUND PROJECT UPDATES:

Stimulating Peripheral Activity to Relieve Conditions (SPARC): Dr. Carrington, Dr. Civillico
Illuminating the Druggable Genome (IDG): Dr. Pawlyk

Dr. Rodgers explained that the Common Fund was enacted into law by Congress through the 2006 NIH Reform Act to support cross-cutting trans-NIH programs that require participation by at least two NIH institutes or centers (ICs) and would benefit from strategic planning coordination. The program encourages collaboration across ICs and provides NIH with flexibility to determine priorities. The Common Fund is coordinated through the Office of Strategic Coordination, one of six offices within DPCPSI, which is part of the Office of the Director. Projects funded by the Common Fund are intended to be transformative (potential to dramatically affect biomedical and behavioral research); catalytic (ability to achieve high impact goals within a defined period); synergistic (outcomes must synergistically promote and advance missions of individual NIH ICs to benefit health); and cross-cutting (relevance to multiple diseases or conditions and requiring a coordinated trans-NIH approach). Projects supported by the Common Fund must also be unique--

something no other entity is likely to take on. More information about the Common Fund is available at commonfund.nih.gov. Dr. Rodgers explained that the presentation will focus on two Common Fund projects—SPARC and IDG—that are especially relevant to NIDDK because of their scientific focus and because NIDDK staff hold key leadership positions.

Dr. Rodgers first introduced Dr. Jill Carrington, an NIDDK program director and program lead for the biology initiative under SPARC. He explained that Dr. Carrington would give an overview of the SPARC initiative and its relevance to NIDDK. She would then introduce Dr. Gene Civillico, SPARC program manager who would give an update on the program and its progress.

Dr. Carrington

Dr. Carrington explained that SPARC is a new Common Fund program aimed at understanding the science and technology necessary to stimulate peripheral nerves specifically, safely, and effectively to affect organs and the conditions and diseases of organs. She explained that neuromodulation in the peripheral nervous system is an emerging area of research. Several different devices are in various stages of development; a few have been approved for use in the United States. But, despite these successes, failures are still common with these therapies and procedures, and there are several open questions about how to effectively modulate peripheral nerves. She attributed these issues to a lack of understanding about the peripheral nervous system as it affects end organ response. She commented that there is a need for new devices for both research and therapy to affect components of the peripheral nervous system effectively and specifically.

SPARC is being designed to fill these gaps and to capitalize on recent advances in technology to deliver detailed, integrated, functional, and anatomical neural circuit maps for organs and to provide the scientific foundation necessary to pilot new and improved neuromodulation devices and stimulation protocols to treat diseases and conditions.

Dr. Carrington noted that neuromodulation therapy has potential application in multiple organ systems and multiple conditions affecting these organs, including organ systems and conditions of interest to NIDDK. SPARC projects will focus on the peripheral nervous system and understanding organ response to peripheral nerve innervation. The program will emphasize understanding human anatomy and function and areas of need that have previously been under-studied.

SPARC has been in the planning and early implementation stages. A working group has been established with four co-chairs at the director and deputy director level within NIH (including Dr. Germino from NIDDK). The working group membership includes representatives from across NIH, including four NIDDK staff members: Daniel Gossett, Karen Teff, Deborah Hoshizaki, and Dr. Carrington. Within the working group, subgroups focus on the four major components of SPARC: 1) Anatomical and Functional Mapping of the Innervation of Organs, 2) Next Generation Tools and Technologies, 3) Use of Existing Market-approved Technology for New Market Indications, and 4) SPRAC Data Synthesis Center.

Dr. Carrington mentioned that SPARC is using a comparatively new method of making awards, called “Other Transactions,” which allows more flexibility both for investigators and program

management. The policy and implementation associated with "Other Transaction" awards have been a major effort associated with the SPARC program. SPARC also has its own project manager and staff assigned to the program.

Steps in SPARC's early development included gathering input from the scientific community through Requests for Information issued in fall 2014 and a strategic planning workshop that was co-organized by NIH staff and experts in the field held in February 2015. Information from these activities was synthesized and used to develop multiple Requests for Applications that have been issued and, in some cases, awards have already been made.

In spring 2016, Dr. Gene Civillico became the SPARC program/project manager. Dr. Carrington introduced Dr. Civillico, explaining that he was previously at the US. Food and Drug Administration in the Center of Devices and Radiological Health. He obtained his bachelor's degree at Harvard University and studied neuroscience for his doctorate from University of Pennsylvania Medical School. For his postdoctoral research at Princeton University, he studied the cerebellar cortex. At the FDA, he was group leader in the Human-Device Interaction Laboratory and also a research fellow in experimental neurophysiology.

Dr. Civillico

Dr. Civillico described in more detail the justification of the SPARC program, the program structure, as well as some of the science underway in this area.

Dr. Civillico began his presentation using the vagus nerve as an illustration of the rational underpinning the SPARC program. The vagus nerve has 100,000 fibers and acts as part of the "Internet of the body," connecting the brain and spinal cord to several organs. Even through the vagus nerve is more accessible than the brain and offers great therapeutic potential through its many end targets, he explained that there is a disconnect between the therapeutic relevance and the amount of study and detailed mapping that the nerve has received.

Current Status of Research and Justification for SPARC

Dr. Civillico outlined the status of neuromodulation research and practice. Several devices have received FDA approval, including some of interest to NIDDK. However, there have also been several devices that showed efficacy in open-label studies (in which the caregiver or the participant knows whether who is getting real versus sham treatment) but were not successful in double-blind studies, suggesting a large placebo effect. Nonetheless, after controlling for placebo effect, some patients still had a remarkable response compared with available conventional therapies. Unfortunately, we cannot predict who will respond and who will not.

Dr. Civillico explained that a better understanding of the mechanisms behind these therapies is needed to determine where they may be most effective. Often the engineering of the devices for therapies outpaces the knowledge regarding cellular/biological underpinnings associated with effective treatment. Examples of areas in which more information is needed to make treatment response more consistent include identifying desired cellular targets; determining the amount of activation volume and temporal pattern of stimulation needed to create an effect; and establishing

how variances in anatomy, pathology, and drug interactions as well as long-term systemic or neural interface adaption affect response to therapy. He also said there were many questions about how animal models translate to humans. He pointed out that, for example, the vagus nerve differs substantially between small animals and larger animals and humans, especially in terms of spatial scale, orientation of fibers, and myelination.

Dr. Civillico explained that one way to begin to answer these questions might be to develop functional maps of peripheral nerves. In some cases, this could be achieved using existing stimulation technology and end organ readout. These maps could be used to generate hypotheses, which can then be combined with anatomical studies and cellular subtype analyses to explore systems in more detail. However, Dr. Civillico explained that there remain important gaps in available technology, for example associated with end organ read-out for many organs of interest, to apply this approach broadly. Overall there remains a large set of multidisciplinary set of problems needed to advance the field, which makes SPARC ideal for the Common Fund.

SPARC Structure and Approach

According to Dr. Civillico, the SPARC Program takes a multidisciplinary approach with a biology component, a technology component, a translation component, and a data synthesis component, all working together. The idea is that each of the components has something to offer all the others. ***Biology*** reveals the resolution and timing needed for precise modulation of the system of interest; ***Technology*** provides the tools to make better maps and to perturb circuits for function studies. The ***Translation*** component brings in knowledge of health needs, experience with benefit/risk ratios, and insight into established strategies. The ***Data Synthesis Center*** serves as a public resource that collects and disseminates data sets and tools to researchers in the field to speed the rate of discovery, while still preserving the intellectual property of the Principal Investigators. The role of the Program Manager and staff is to coordinate among the individual initiatives and ensure that the program is harmonized in a way that makes it more than just the sum of its parts.

Dr. Civillico explained that there are three major ways that SPARC is unique. First, SPARC is a Common Fund program. Its funding is through the Office of Strategic Coordination within the NIH Office of the Director. As a Common Fund program, SPARC is intended to be catalytic, lasting fewer than 10 years, and addressing a recognized need for targeted investment with trans-NIH impact. Second, the program uses an active management strategy, with the program vision coming from the Office of the Director (where the program manager is based) with a high level of NIH involvement in ongoing activities. Third, to give the program maximum flexibility to combine disparate expertise in pursuit of defined goals, SPARC can use "Other Transaction" awards, which are not grants, contracts, or cooperative agreements. This allows use of an innovative review mechanism and allows the staff quickly to add or subtract from the program based on performance and changing scientific needs. It also allows for awards to people who may not have gotten an NIH grant before or who may not have thought about working with the government on research and development.

SPARC is budgeted through 2021 and Funding Opportunity Announcements (FOAs) have been developed to advance the four areas outlined above (e.g., biology, technology, translation, and data coordination). In the area of ***biology***, at the time of the presentation the receipt date for the

NIDDK-led "Foundational Functional Mapping of Neuroanatomy and Neurobiology of Organs" FOA had past, but applications to the "Comprehensive Functional Mapping of Neurobiology of Organs" FOA would continue on a rolling basis at least through the next year. In the area of ***technology***, awards had already been made under the "The Exploratory Technologies to Understand the Control of Organ Function by the Peripheral Nervous System" FOA (led by National Institute of Biomedical Imaging and Bioengineering, NIBIB). Larger awards to applications received under the "Technologies to Understand the Control of Organ Function by the Peripheral Nervous System" FOA had not yet been made. The technology awards are focused on tools to create better biological maps. In the area of ***translation***, The National Center for Advancing Translational Sciences (NCATS) is leading an initiative through the "Pre-Clinical Development of Existing Market-approved Devices to Support New Market Indications" FOA that will encourage academic researchers to partner with medical device companies to test their devices in new animal models with the hope that this could eventually lead to new indications for existing approves devices. In the area of ***data coordination***, SPARC has the "Data Coordination, Modeling, and Mapping Center" FOA for a data synthesis center that will be responsible for coordination and hosting computational models, posting synthesized maps that will be created across the different initiatives, and making the data sets available first within the consortium and then as quickly as possible to the public.

Sampling of Current SPARC Projects

Dr. Civillico explained that only one of the award sets, the "Exploratory Technologies to Understand the Control of Organ Function by the Peripheral Nervous System" awards, had been made and were at a point where they could be discussed at the time of the presentation. He gave a synopsis of the teams and the technologies they will address:

University of Pittsburgh (Horn/Jenkins): This team is working on the physiologic control of gastric function. They are using several different techniques to understand the circuit that connects the vagus nerve to gastric motility. They are also working on infrared, non-electrode technologies for modulating nerve activity (and thereby, for example, gastric motility). The group is committed to the idea of shareable workflow and completely reproducible experiments. They design and 3-D print their own recording chambers and other gear and share the designs on the NIH 3-D print exchange. They are also making available their lab notebooks electronically using a system called Jupyter; this includes the code the groups uses to run their electrophysiology analysis. All of this will enable other researchers to reproduce everything the group is doing and take advantage of equipment design, analysis code, etc. to advance the field.

UCLA (Ardell/Shivkumar/Kipke): This joint industry/academic effort between UCLA and NeuroNexus (a company that is a pioneer in multi-site electrophysiology) is focused on the nervous system of the heart. The team is creating new electrode arrays that adhere to the wall of the heart while it is beating to create detailed electrical activation maps. This will help us begin to understand the intrinsic cardiac nervous system, which has its own modulatory loops that function on a very short timescale. The group is also beginning to record from cardiac neurons and capture information about the resulting cardiac muscle activity at an unprecedented level of scale. They are starting by studying animal models, such as pig and mouse hearts and have the potential, because of the neurocardiology center at UCLA, to expand the work into humans so there can be

matching data from animals and humans.

Cincinnati Children's Hospital (Wells/Helmrath): This group has recently demonstrated the ability to make human intestinal organoids and can establish an enteric nervous system of sorts by introducing neural crest stem cells into the organoids. Now they are working to transfer that technology to other kinds of organoids, such as gastric and colonic organoids to further their understanding of the development of the enteric nervous system and how different cell types separate and contribute different functions.

University of Minnesota (Vulchanova): This group is working on a new mouse model that has Cre-dependent combinatorial vector system to target an inhibitory neuromodulatory gene controlling selective inhibition of particular sensory neurons for colon function. This will allow the investigators to begin to investigate the importance of those sensory neurons for colonic function.

Case Western (Durand/Lewis): This group is developing an extremely fine wire (nanowire) that records nerve activity from inside the nerve. The wires are so fine that recordings can be targeted to specific zones of a nerve fascicle. Because the groups can record from specific neurons inside nerves they are finding previously unknown functional correlations through this method.

New York Institute of Technology (Farajidavar): This team is working on surgical insertion of a small chip into a pig's stomach to act as a gastric stimulator to study gastric neurophysiology.

New Market Indications

Dr. Civillico reiterated that the ***translation*** initiative under SPARC is focused on encouraging the use of market-approved technology for new market indications through the creation of partnership between academic and industry scientists. As part of the strategy to accomplish this, SPARC is putting together a list of industry partners (see https://commonfund.nih.gov/sparc/newmarkets) who have made available data about technology that they own or control. Academic investigators can then consult this list to find potential collaborators with whom they may wish to contact and develop/propose a collaborative-agreement mechanism SPARC project application to investigate possible new uses for that existing technology. Dr. Civillico noted that the first round of these awards would be made public within the next few weeks.

SPARC Data Center

Dr. Civillico reported that at the time of his presentation an FOA was under development for the SPARC Data Center, which constitutes the ***data coordination*** initiative under SPARC. The Data Center is inspired by other data efforts that have come out of the Common Fund, including the exRNA Research Portal, the Metabolomics Workbench, and the Undiagnosed Diseases Network, and other resources not associated with the Common Fund including the Allen Institute's Allen Brain Atlas, which, offers interactive visualizations, physiological parameters, and circuit information. The expectation is that the center will follow FAIR data principles--that data should be Findable, Accessible, Interoperable, and Reusable. The center is envisioned to serve as clearinghouse for all the anatomical and physiologic information that is going to be coming in through the program.

Moving Forward
Dr. Civillico explained that the SPARC program launched with the Exploratory Tool Development initiative in 2015 and the program will be making awards totaling $22 million before the end of FY 2016. In FY 2017, the number of awards will expand.

As SPARC matures the goal will be to establish a culture of sharing and encourage collaboration through horizontal and vertical cross-project links facilitated through frequent communication, meetings, data sharing, and other collaborative activities.

The program will also work to recruit nontraditional applicants, such as non-medical school laboratories, startup companies, and individuals through the "Other Transactions" mechanism. He pointed out that this mechanism allows dynamism and innovation at every stage of an award: there is no template for the funding announcement, the review process can be customized to allow new reviewer voices and interactive discussion with program staff. In addition, the mechanism makes it possible to accept some parts of a proposal and not others. In the awards management stage, using the "Other Transaction" mechanism, SPARC can rapidly expand, modify, partner or discontinue award activities based on program needs and emerging methods, technologies or approaches.

Dr. Civillico articulated what he considers to be the mission of the project, which is to empower rational target development for peripheral neuromodulation indications of scientific and clinical importance. He said that the project will accomplish this by 1) producing go-to resources for developers of research strategies in therapeutic nerve modulation, 2) acting as a successful example of a multidisciplinary consortium pursuing open science, and 3) recruiting physiologists, anatomists, and engineering to this area where their skills and ideas can make a difference for patients.

Dr. Civillico ended by acknowledging the individuals and teams working together on SPARC, including the project management team in the Office of the Director, the IC Project Team Leaders (including Dr. Carrington of NIDDK), and the officers in the Office of Grants Management at the NCATS who oversee the Other Transaction awards.

IDG
Dr. Rodgers introduced Dr. Aaron Pawlyk, program director in the Division of Diabetes, Endocrinology, and Metabolism, who is involved in another Common Fund Program, IDG. Dr. Pawlyk's portfolio at NIDDK includes research on key regulators of intermediary metabolism, drug discovery, pharmacogenetics, and precision medicine. In addition to his regular duties, Dr. Pawlyk serves as program coordinator for IDG.

Dr. Pawlyk explained that, as is the case for most Common Fund projects, the working group for the IDG initiative includes representatives from different NIH ICs, including NIDDK. Work started in 2012 and first awards were given out in Fiscal Year 2014 for the pilot phase of the program. Early this year, the program received approval for full implementation. Dr. Pawlyk thanked Director Rodgers for his support at multiple levels that allowed the program to go forward.

Dr. Pawlyk explained that the human genome contains 20,000-25,000 genes, depending on how

one analyzes it. Of these, about 3,000 genes produce proteins that are considered "druggable," meaning that they interact with a biologic neutralizing antibody, or small molecule (i.e., drug). Only 10 percent of these druggable proteins are targeted by currently approved drugs.

Dr. Pawlyk explained that part of this low percentage may be attributed to the tendency to study what is already known. He explored this point by first reviewing a chart of citations associated with human protein kinases. A few kinases have many thousands of citations while some have only a small fraction of that number. Overall, most kinases are understudied. Dr. Pawlyk noted that depending on the metrics, that about half of the human proteome is understudied. Part of the problem is that we don't know what many of these proteins do, that is their biological relevance. As he explained, it is difficult, for example, to apply for an R01 grant to study a protein if there is little information regarding what it does as a starting point. Approximately one quarter of kinases, G-protein-coupled receptors (GPCR), ion channels, and nuclear receptors remain understudied even though we have known for decades that these proteins have human utility. We also know these proteins can be modified. However, until certain information is "cracked open" it is likely that they will continue to be understudied.

In response to this issue, the goal of IDG is to illuminate or tackle understudied proteins that have high potential to impact human health, focusing on areas where the targets can be druggable. The program will approach this in three ways: 1) identifying biochemical, cellular, or animal model phenotypes for understudied proteins; 2) enabling further investigation of those proteins by providing reagents and tools; and 3) generating and maintaining a minable knowledge base. The idea, to a certain extent, is that a resource could be developed for previously understudied proteins that would serve as a starting point for a preliminary data section for a grant.

IDG is currently in a "Pilot Phase" that has two components. The first component is the Knowledge Management Center, whose purpose is to 1) integrate existing data about understudied proteins and make it searchable through a single portal; 2) define the current state of knowledge/ignorance on each; and 3) prioritize proteins for study. The second component involves Scalable Technology Development to develop tools and approaches for efficiently investigating the function of protein families, rather than looking at proteins one by one. The pilot phase is focusing on kinases, G-protein-coupled receptors, ion channels, and nuclear receptors.

In the Pilot Phase IDG has funded two projects towards the development of a Knowledge Management Center and nine projects adapting scalable technologies (under the Scalable Technology Development component) to illuminate the druggable genome.

Dr. Pawlyk pointed out that the Knowledge Management Center is aggregating data from more than 100 different databases. The data pulled together spans a variety of different data types including interactome, pharmacology, gene knockout, gene-drug interaction, etc. The Knowledge Management Center aggregates and sorts this complex information in several different ways to make the information more digestible. Dr. Pawlyk played a video about PHAROS (https://pharos.nih.gov/idg/index), the user interface/portal for the IDG Knowledge Management Center.

Dr. Pawlyk highlighted two of the technology pilot awards. First, he explained scalable GPCR tools developed by Bryan Roth and Brian Shoichet. They have developed a license-free beta-arrestin-based platform to study GPCR action. The system has been made commercially available, which fits with the spirit of IDG. Drs. Roth and Shoichet are using this platform in the pilot to screen orphan GPCRs against a library of compounds, that include FDA-approved compounds. Using this methodology, they have identified Ogerin as a GPR68 ligand. GPR68 is a proton sensing GPCR that is broadly expressed, including in specific areas of the brain. Further work has shown that Ogerin affects GPR68 to selectively decrease hippocampal-dependent fear conditioning. This research was published in the journal Nature in 2015 (Nature, 527:477-483, Nov. 2015).

The second pilot project that Dr. Pawlyk highlighted focuses on zebrafish behavioral phenotyping. This work, by David Kokel at University of California, San Francisco, and Joanna Yeh, Massachusetts General Hospital, involves an automated system to look at zebrafish larvae. Larvae are phenotyped both morphologically and behaviorally in the system. Using a CRISPR-based system to knockout an understudied protein, larvae with and without the knockout can be tested in the system. For the behavior component, the larvae are run through a battery of acoustic stimuli. Habituation to the stimuli between larvae with and without the understudied protein knockout can be compared to determine if the behavior of larvae with the knockout differs. Follow-up work can determine the nature of differences and may shed light on the function of the protein about which virtually nothing is known.

Dr. Pawlyk explained that the IDG initiative is moving now from the pilot phase to the implementation phase. There has been substantial consultation and input from experts during the planning for this phase. This consists of site visits and external scientific advisor input, discussions with experts in the four pilot classes (kinases, GPCRs, ion channels, and nuclear receptors) as well as meetings with more than a dozen representatives from seven pharmaceutical companies. Dr. Pawlyk reported that the consistent message from these experts is that understudied proteins become studied when there are tools to study the protein (especially tools to modulate protein activity) and when there is biochemical, cellular, or animal model evidence of disease or physiological relevance.

In summary, Dr. Pawlyk explained that IDG has received approval to expand informatics tools, data sources, and user base; to continue work to elucidate understudied protein function from key druggable protein families; and broadly disseminate IDG-generated resources and data. Information about funding opportunities will be available soon from the website: https://commonfund.nih.gov/idg/index. The program seeks input from the scientific community on the distribution of Funding Opportunity Announcements to interested applicants as well as improving the reach and usability of the Knowledge Management Center database and portal.

Council Questions and Discussion

It seems that the success of the program depends on sharing new data through the portal as it becomes available. Have you thought about incentivizing that by time-stamping submissions and

attributing them to contributors in a way that they can use as an entry on their Curriculum Vitae?

Dr. Pawlyk replied that they are looking into incentives, but hadn't thought of that one specifically. He agreed that making the data accessible to the community is key for the program's success.

Should part of the goal of IDG be to change what we view as "druggable"? Will there be some RFAs that might encourage people to look into this?

Dr. Pawlyk said that the team has discussed that part of illuminating the druggable genome may be to expand our concept of it. Current approaches tie us to the biologic and small molecule approach.

Dr. Civillico talked about the failure of some of the technologies once they got into randomized controlled trials, with extremes of response as a driving force of those failures. Could there be biology that determines different thresholds for stimulation or different paradigms for stimulation? Could this be a Precision Medicine issue?

Dr. Civillico agreed that this is an area that SPARC will address. He explained that the vision for the project is to enhance the resolution at which this biology is studied and to reveal the sources of variation and the extremes of response. Those are likely explained by variation in human biology, and better modeling systems may increase understanding of that.

Will the SPARC program consider non-neuronal biologic stimulators? That is, not just devices but biologics?

Dr. Civillico explained that the scope of the program is targeted at devices. The way the program is conceived, it is focused on improving the biological knowledge base that could be used to target device therapies.

There are a lot of biological phenomena attributed to stretch pressure, tension, and other physical interventions that would seem to be in line with SPARC. Is there any work being done in that area?

Dr. Civillico answered that the team is very interested in nonelectrical perturbations of nerves, but this area is not yet ready for biological experiments. For example, ultrasound can drive neurons, but there are different theories about how this happens. We don't know if ultrasound could be driving neurons in a way that may also be killing them.

What kind of care is being taken to ensure that these devices help more than they harm?

Dr. Civillico answered all devices investigated or developed by the SPARC program have to go through the same processes for investigational device exemption and meet the same Institutional Review Board requirements as for any other clinical trial. The key language regarding medical devices is that the benefit should outweigh the risk.

Is acupuncture part of the discourse?

Dr. Civillico answered that it was, pointing out that there was some discussion at the start of the program about whether the skin qualified as an organ for this program, and it was decided that investigators with a focus on skin are welcome to apply for SPARC funding.

In his presentation, Dr. Pawlyk showed an inverted pyramid of the total number of genes narrowed down to the 10 percent that are targeted by approved drugs. But there is more going on beyond coding proteins. It would be exciting to include non-coding RNAs because these elements control regulation over gene expression and could be an exciting area for therapeutics.

Dr. Pawlyk said that one of the points considered in the implementation phase is how to bring in other appropriate protein classes or what else is appropriate to include. One of the purposes of IDG is to show that this approach has value. One of the aspects of the Common Fund is that it is limited but has transformative potential by showing that a project can do something at a class level which can then lead others to try a similar approach for another class.

In closing the discussion, Dr. Germino (who as noted above is one of the four co-chairs of the SPARC working group) noted that one of the challenges with drug development is off-target effects, especially if you give a systemic drug—you may be aiming for a receptor in the kidney, but that receptor may be elsewhere in the body as well. The idea behind SPARC is that by understanding what the nerves do and what they control, you might be able access them in controlled and safe ways to turn them on or off and to send your therapy exactly to the point where you want it and nowhere else.

VIII. SCIENTIFIC PRESENTATION: GI Regulation of Metabolic Homeostatis
Dr. Kaplan

Dr. Rodgers introduced the Scientific Presentation "GI Regulation of Metabolic Homeostatis" by Dr. Lee Kaplan, director of the Obesity, Metabolism, and Nutrition Institute and founding director of the Weight Center at the Massachusetts General Hospital. Dr. Kaplan is also an associate professor of medicine at Harvard Medical School.

Dr. Kaplan received his medical degree and Ph.D. in molecular biology from Albert Einstein College of Medicine. He completed an internship and residency in internal medicine and a fellowship in gastroenterology at Massachusetts General Hospital and Harvard Medical School. He then did a fellowship in genetics at Brigham and Women's Hospital.

Dr. Kaplan's clinical expertise focuses on obesity medicine, gastroenterology, and liver diseases. He has authored more than 150 medical and scientific papers and has a special interest in the causes and complications of obesity and the development of more effective preventive strategies and therapies for this problem. His clinical research is focused on identifying clinical relevant subtypes of obesity, identifying predictors of outcome of obesity therapies, and exploring novel combination therapies for obesity and its complications. His basic research is focused on the physiological and molecular mechanisms of gastrointestinal regulation of body weight and metabolic function, and his group has pioneered the development and use of rodent models of

weight loss surgery and gastrointestinal devices to explore these mechanisms.

IX. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1261 grant applications (336 primary and 925 dual), requesting support of $683,045,931 were reviewed for consideration at the September 7, 2016, meeting. An additional 266 Common Fund applications requesting $98,842,266 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1275 applications requesting $365,430,342 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 7, 2016, meeting.

X. ADJOURNMENT

Dr. Rodgers

Dr. Rodgers expressed appreciation on behalf of the NIDDK to the Council members, presenters, and other participants. He thanked the Council members for their valuable input. There being no other business, the 202th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m. on September 7, 2016.

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

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