

Meeting Minutes

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 AND OPENING REMARKS

Dr. Rodgers

The NIDDK Director, Dr. Griffin P. Rodgers, called to order the 197th meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m. on January 28, 2015, in Conference Room 10, Building 31, of the NIH campus in Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Sharon Anderson	Dr. David Klurfeld
Dr. Gopal Badlani	Ms. Ellen Leake
Dr. Joseph Bonventre*	Dr. Jerry Palmer
Dr. David Brenner	Dr. Craig Peters
Dr. Eugene Chang	Dr. Alan Saltiel
Dr. Mark Donowitz	Dr. Jean Schaffer
Dr. Cindy Hahn	Dr. Alan Shuldiner
Dr. Lee Kaplan*	Ms. Pamela Taylor
Dr. Kenneth Kaushansky ⁺	Dr. Robert Vigersky

Also Present:

Dr. Griffin Rodgers, Director, NIDDK, Chairman, NIDDK Advisory Council

Dr. Brent Stanfield, Executive Secretary, NIDDK Advisory Council

* Served as temporary members for this meeting

⁺ Attended via telephone

B. NIDDK STAFF AND GUESTS

Abbott, Kevin - NIDDK	Carrington, Jill - NIDDK
Abraham, Kristin - NIDDK	Castle, Arthur - NIDDK
Andersen, Dana - NIDDK	Cerio, Rebecca - NIDDK
Arreaza-Rubin, Guillermo - NIDDK	Connaughton, John - NIDDK
Barnard, Michele - NIDDK	Copeland, Randy - NIDDK
Bavendam, Tamara - NIDDK	Curtis, Leslie - NIDDK
Begum, Najma - NIDDK	Dayal, Sandeep - NIDDK
Best, Carolyn - Amer. Urol. Assoc.	Densmore, Christine - NIDDK
Bishop, Terry - NIDDK	Dirks, Dale - Hlth. and Med. Counsel of Wash., D.C.
Blondel, Olivier - NIDDK	Doherty, Dee - NIDDK
Bourque, Sharon - NIDDK	Donohue, Patrick - NIDDK
Bremer, Andrew - NIDDK	Doo, Ed - NIDDK
Buchanan, Sarah - Hlth. and Med. Counsel of Wash., D.C.	Drew, Devon - NIDDK
Calvo, Francisco - NIDDK	Evans, Mary - NIDDK
Camp, Dianne - NIDDK	Fang, Raymond - Amer. Urol. Assoc.

Farishian, Richard - NIDDK
Flessner, Michael - NIDDK
Fonville, Olaf - NIDDK
Fradkin, Judith - NIDDK
Garofalo, Robert - CSR
Gallivan, Joanne - NIDDK
Gansheroff, Lisa - NIDDK
Germino, Gregory – NIDDK
Gossett, Ben - NIDDK
Guo, Xiaodu - NIDDK
Haft, Carol - NIDDK
Hamilton, Frank - NIDDK
Hanlon, Mary - NIDDK
Hein, Patrick - Purdue Univ.
Henagan, Tara - Purdue Univ.
Hoffert, Jason - NIDDK
Hoofnagle, Jay - NIDDK
Hoover, Camille - NIDDK
Hoshizaki Deborah - NIDDK
Hyde, James - NIDDK
Iaakso, Joseph - Endocrine Society
James, Stephen - NIDDK
Jerkins, Ann - NIDDK
Karp, Robert - NIDDK
Karimbakas, Joanne - NIDDK
Ketchum, Christian - NIDDK
Kimmel, Paul - NIDDK
Kirkali, Ziya - NIDDK
Kranzfelder, Kathy - NIDDK
Kuaban, Alice - Amer. Soc. Heme.
Kusek, John - NIDDK
Laughlin, Marin - NIDDK
Leschek, Ellen - NIDDK
Li, Yan – NIDDK
Linder, Barbara - NIDDK
Malik, Karl - NIDDK
Malozowski, Saul - NIDDK
Martey, Louis - NIDDK
Martinez, Winne - NIDDK
Maruvada, Padma - NIDDK
McBryde, Kevin - NIDDK
Mende, Andy - Social and Sci. Systems
Miller, David - NIDDK
Mowrer, Karen - Assoc. of Indep. Res. Inst.
Moxey-Mims, Marva - NIDDK
Mullins, Christopher - NIDDK
Mullsteff, Clairisse - NIDDK

Narva, Andrew - NIDDK
Newman, Eileen - NIDDK
Pawlyk, Aaron - NIDDK
Perrin, Peter - NIDDK
Perry-Jones, Aretina - NIDDK
Pike, Robert - NIDDK
Podskalny, Judith - NIDDK
Ramani, Rathna - NIDDK
Rankin, Tracy - NIDDK
Rasooly, Rebekah - NIDDK
Reiter, Amy - NIDDK
Roberts, Tibor - NIDDK
Rosenberg, Mary Kay - NIDDK
Rosendorf, Marilyn - NIDDK
Roy, Cindy - NIDDK
Rushing, Paul - NIDDK
Rys-Sikora, Krystyna - NIDDK
Sahai, Atul - CSR
Sanovich, Elena - NIDDK
Sastry, Chandan - NIDDK
Sato, Sheryl - NIDDK
Savage, Peter - NIDDK
Schwichtenberg, Amy - Purdue Univ.
Serrano, Jose - NIDDK
Shelness, Greg - CSR
Sherker, Averell - NIDDK
Shepherd, Aliecia - NIDDK
Singh, Megan - NIDDK
Smith, Philip - NIDDK
Spain, Lisa - NIDDK
Star, Robert - NIDDK
Stoeckel, Luke - NIDDK
Tatham, Thomas - NIDDK
Teff, Karen - NIDDK
Tilghman, Robert - NIDDK
Torrance, Rebecca - NIDDK
Tuncer, Diane - NIDDK
Unalp-Arida, Aynur - NIDDK
Van Raaphorst, Rebekah - NIDDK
Wallace, Julie - NIDDK
Wellner, Robert - NIDDK
Wells, Ellen - Purdue Univ.
Woynarowska, Barbara - NIDDK
Wright, Elizabeth - NIDDK
Yang, Jian - NIDDK
Yanovski, Susan - NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers

New Council Members

Dr. Rodgers introduced and welcomed six new members to the NIDDK Advisory Council.

- Joining the Subcouncil for the Division of Digestive Diseases and Nutrition (DDN) are Dr. Mark Donowitz and Dr. Lee Kaplan.

Dr. Mark Donowitz is Professor of Medicine, the LeBoff Professor for Research in Digestive Diseases, and Director of Basic Research within the Gastroenterology Division of the Department of Medicine at the Johns Hopkins School of Medicine. In addition, he is Director of the Johns Hopkins Digestive Diseases Basic and Translational Research Core Center and leads an institutional training grant (T32) for basic science research in digestive diseases. Dr. Donowitz is a leader in the field of gastroenterological research, specializing in diarrheal diseases. He is widely respected for a broad cross-section of research, including basic studies in digestive diseases, pre-clinical models using human intestinal organoids to study non-inflammatory diarrhea, and translational approaches to develop drug therapy for diarrhea. He served as President of the American Gastroenterological Association from 2006-2007. He currently serves on the editorial boards of several prominent journals. He has authored nearly 300 publications and holds several patents. Dr. Donowitz earned his M.D. from the Johns Hopkins School of Medicine. After completing residencies in Internal Medicine at Johns Hopkins and the Jacobi Hospital/Albert Einstein University School of Medicine in New York, he went on to a Fellowship in Gastroenterology at Yale University School of Medicine. Dr. Donowitz has several active NIH grants supporting his research.

Dr. Lee Kaplan is Director of the Obesity, Metabolism and Nutrition Institute and founding Director of the Weight Center at the Massachusetts General Hospital and Associate Professor of Medicine at Harvard Medical School. Dr. Kaplan's clinical expertise is in the areas of obesity medicine, gastroenterology and liver disease. The author of more than 150 medical and scientific papers, he has a special interest in the causes and complications of obesity and the development of new and more effective preventive strategies and therapies for this problem. His clinical research is focused on identifying clinically 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. Dr. Kaplan received his M.D. and Ph.D. in molecular biology from the Albert Einstein College of Medicine. He completed an internship and residency in internal medicine and a fellowship in gastroenterology at the Massachusetts General Hospital and Harvard Medical School followed by a fellowship in genetics at the Brigham and Women's Hospital.

- Joining the Subcouncil for Diabetes, Endocrinology and Metabolic Diseases (DEM) are Dr. Alan Saltiel and Ms. Pamela Taylor.

Dr. Alan Saltiel is the Mary Sue Coleman Director of the Life Sciences Institute at the University of Michigan. Dr. Saltiel is also the John Jacob Abel Collegiate Professor in the Life Sciences and Professor of Internal Medicine and Molecular and Integrative Physiology at the Life Sciences Institute. The focus of Dr. Saltiel's research is the hormone insulin and its role in regulating cellular sugar levels, including how cells send and receive signals. Understanding these processes may shed light on dysfunctions in glucose and lipid metabolism, particularly as it relates to type 2 diabetes. Dr. Saltiel hopes to elucidate the precise function of these pathways and their roles in the pathogenesis of diabetes, with the goal of developing new therapeutic approaches to the treatment of diabetes and related disorders. In addition to having published more than 260 research papers, Dr. Saltiel holds 16 patents and has extensive experience with the FDA's testing and approval process for new drugs. Among his many honors Dr. Saltiel is a member of the Institute of Medicine and a fellow of the American Association for the Advancement of Science. He also currently serves on the editorial boards of several high profile journals. Dr. Saltiel earned his Ph.D. in biochemistry at the University of North Carolina and then went on to do post-doctoral work in the Wellcome Research Labs where he first began his investigations of insulin. Dr. Saltiel has spent his research career in both academia and the pharmaceutical industry. Prior to joining the University of Michigan, Dr. Saltiel was Distinguished Research Fellow and Senior Director of the Department of Cell Biology at Parke-Davis Pharmaceutical Research Division (now Pfizer Global Research).

Ms. Pamela Taylor is joining the Council as a public member who has first-hand knowledge of NIDDK clinical research as a participant in one of the Institute's largest and most important trials, the Diabetes Prevention Program (DPP). In the summer of 1997, Ms. Taylor received a postcard inviting her to be tested for possible participation in what was then a new study to determine if lifestyle changes or the drug metformin could delay or prevent type 2 diabetes in people at high risk for the disease. Ms. Taylor was tested and discovered that she had impaired glucose tolerance. As part of the DPP trial she was randomized to receive six months of intensive lifestyle interventions and diabetes education. She achieved all her initial goals and exceeded her weight loss target. Now, more than 17 years later, she remains diabetes free and is free of prediabetes as well. Because of her experience with the DPP, Ms. Taylor has become an advocate for diabetes research and diabetes education. Currently, Ms. Taylor is a communications consultant who has an exceptionally strong professional background in communications, education, policy analysis, and marketing. She has worked with government and both non-profit and for-profit institutions and will bring that important expertise and perspective to the Council.

- Joining the Subcouncil for Kidney, Urologic and Hematologic Diseases (KUH) are Dr. Joseph Bonventre and Dr. Craig Peters.

Dr. Joseph Bonventre is the Samuel A. Levine Professor of Medicine at Harvard Medical School. He is also Chief of the Renal Unit and Director of the Bioengineering Division at Brigham and Women's Hospital. Dr. Bonventre has had a long-standing interest in various aspects of cellular injury and repair mechanisms in the kidney with a special emphasis on the role of inflammation, biomarkers and stem cells. He established the origin of the epithelial cells that repair the kidney after injury as dedifferentiated surviving proximal tubule cells. He was the first to describe the role of proximal tubule cell cycle arrest in the maladaptive fibrosis that can occur after severe injury leading to chronic kidney disease. Dr. Bonventre has a long history of

research support from the Institute. He is highly productive with well over 200 publications to his credit. He has an international reputation as an extraordinary scientist and scholar and serves on the editorial boards of several national and international high profile journals. He has amassed a list of honors and prizes that is extraordinary in terms of number, diversity and profile. He has regularly served as a peer reviewer not only for NIH, including the NIDDK, but also a number of other organizations that support biomedical research. Dr. Bonventre earned his M.D. and Ph.D. degrees from Harvard Medical School. He then completed his internship, residency and fellowships at Massachusetts General Hospital.

Dr. Craig Peters is the chief of the Division of Surgical Innovation, Technology, and Translation in the Joseph E. Robert, Jr., Center for Surgical Care at the Children's National Medical Center in Washington, D.C. Dr. Peters is also a principal investigator at the Sheikh Zayed Institute for Pediatric Surgical Innovation and Professor of Urology and Pediatrics at George Washington University. Dr. Peters has extensive experience with the treatment of pediatric urologic problems, developing minimally invasive surgical techniques, including robot-assisted procedures. He has conducted NIH-funded research in urinary obstruction, vesicoureteral reflux, and bladder dysfunction. Dr. Peters has nearly 200 journal articles to his credit and he has contributed to over 50 book chapters. He earned his M.D. at the Johns Hopkins University. He then went on to complete his internship and residency at Johns Hopkins, and his surgical and surgical research Fellowships at Children's Hospital and Harvard Medical School.

"In Memoriam" - Dr. Donald F. Steiner

Donald F. Steiner, M.D., the A.N. Pritzker Distinguished Service Professor Emeritus in Medicine and Biochemistry and Molecular Biology at the University of Chicago, passed away in November 2014. Dr. Steiner revolutionized thinking in the research and medical communities about how the body produces insulin. In 1967, he showed that insulin, previously thought to be made from two separate protein chains, began instead as a longer single chain, which he named proinsulin. This fundamental discovery paved the way to understanding how other hormones, as well as neuropeptides in the brain and endocrine system, are made and processed, and it was the foundation for establishing the field of protein-precursor processing. Dr. Steiner's discovery also enabled the pharmaceutical industry to improve the purity of insulin preparations, leading to insulins that are less likely to provoke an immune response and paving the way for biosynthetic human insulin production. Dr. Steiner published more than 400 peer-reviewed papers, and his work has been cited by other researchers more than 10,000 times. He won dozens of prestigious national and international honors and awards, often several per year. Among Dr. Steiner's many honors was his election to the American Academy of Arts and Sciences in 1972, the National Academy of Sciences in 1973, and the American Philosophical Society--the United States' oldest learned society--in 2004.

NIDDK Staff Changes

Dr. Mary Horlick retired at the end of 2014 after nine years at NIH. Dr. Horlick came to the NIDDK in 2005 as the first Program Director for the newly-established Pediatric Clinical Obesity Program. A hands-on Program Director with great skill and enthusiasm, she developed a very vibrant and exciting research portfolio. She served as Project Scientist for both the Longitudinal Assessment of Bariatric Surgery Study (LABS), as well as the Adolescent Bariatric

Surgical Study (Teen LABS), in addition to other important multi-site studies and cooperative agreements.

Dr. Michael Grey is leaving the NIDDK to become an Instructor at Harvard Medical School and Children's Hospital, Boston. In 2009, Dr. Grey joined the Institute as a Health Science Policy Analyst in the Office of Scientific Program and Policy Analysis. The following year, he became a Program Director in the Digestive Diseases and Nutrition Division, where he revitalized and developed new programs in epithelial transport, host-microbial interactions, and pre-clinical translational biology. He has been a key collaborator in a number of working groups within NIDDK.

Dr. Aynur Unalp-Arida joined the NIDDK Division of Digestive Diseases and Nutrition as a Health Scientist Administrator in June 2014. She will manage research grants in epidemiology and also some of the Division's clinical trials. Her areas of expertise and interest include public health, epidemiology, clinical trials, translational research, regulatory science and off-label use of approved drugs, and epigenomics. She holds an M.D. and a Ph.D. in epidemiology. Previously, she was an Associate Scientist in epidemiology at the Johns Hopkins Bloomberg School of Public Health.

Dr. Cindy Roy has joined the Division of Kidney, Urologic and Hematologic Diseases as a Program Director. Previously, she was Assistant Professor of Geriatric Medicine and Gerontology and Adjunct Assistant Professor of Hematology at the Johns Hopkins University School of Medicine, where she ran a hematology research program with NIH grant support. Dr. Roy earned her Ph.D. from the Oregon Health Sciences University, and she completed her research fellowship with former Council member, Dr. Nancy Andrews, at Children's Hospital in Boston.

Ms. Jenna Norton has joined the Division of Kidney, Urologic and Hematologic Diseases as a Program Manager for the Kidney and Urologic Science Translation Program. She will support this Program with strategic program planning and content development for the translation of kidney and urologic research to clinical and community settings. Prior to joining the NIDDK, she worked in the private sector as an account director, and before that she was a Health Communications Fellow at the National Cancer Institute. She earned her M.P.H. at the George Washington University.

NIDDK Recent Advances and Emerging Opportunities

Dr. Rodgers announced that the 2015 edition of the NIDDK publication, *Recent Advances and Emerging Opportunities*, is now posted in the "Strategic Plans and Reports" section of the NIDDK website. The report includes examples of NIDDK-supported research advances published in Fiscal Year 2014, stories of discovery, patient profiles, and scientific presentations made by three Council members--Doctors Spiegelman, Chang, and Anderson. At the end of the report, there are data on funding trends and support of NIDDK's core values that were first presented at the May 2012 Council meeting by Dr. Germino, and are now updated through Fiscal Year 2014. Dr. Rodgers thanked the Office and of Scientific Program and Policy Analysis and the various Divisions for their work on the report.

In Remembrance of Alaina Hahn

Dr. Rodgers expressed collective condolences on behalf of the NIDDK and the NIH to Council Member Cindy Hahn, whose daughter, Alaina, passed away on January 15, 2015 from complications of Alagille Syndrome. Alaina inspired Cindy to start the Alagille Syndrome Alliance 21 years ago.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 196th COUNCIL MEETING AND THE REPORT ON INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

The Council approved by voice vote the Summary Minutes of the 196th Council meeting. The Council also approved by voice vote the NIDDK's 2015 Biennial Advisory Council Report on the Inclusion of Minorities and Women in Research, consistent with the requirements of the NIH Revitalization Act of 1993, P.L. 103-43. Both documents had been sent to the Council for review in advance of the January 2015 meeting.

III. FUTURE COUNCIL DATES

The Council was reminded of upcoming meeting dates.

2015

May 13-14 (Wednesday and Thursday)
September 9-10 (Wednesday and Thursday)

2016

January 27-28 (Wednesday and Thursday)
May 18-19 (Wednesday and Thursday)
September 7-8 (Wednesday and Thursday)

All meetings will be held in Building 31 in Conference Rooms 10, 6 or 7. It is expected that most meetings will be a single day. However, Council members were asked to reserve both days to ensure flexibility should a situation arise where a longer meeting is required.

IV. ANNOUNCEMENTS

Dr. Stanfield

Confidentiality

Council members were reminded that material furnished for review purposes and discussion during the closed portion of the meeting is considered confidential. The content of discussions taking place during the closed session may be disclosed only by the staff and only under appropriate circumstances. Any communication from investigators to Council members regarding actions on an application must be referred to the Institute. Any attempts by Council members to handle questions from applicants could create difficult or embarrassing situations for the members, the Institute, and/or the investigators.

Conflict of Interest

Dr. Stanfield reminded the Council that advisors and consultants serving as members of public advisory committees, such as the NIDDK National 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 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 for which he/she is in conflict, a written certification is required. Dr. Stanfield said that a statement is provided for the signature of the member, and this statement becomes a part of the meeting file. Dr. Stanfield said that each Council member's folder contained a statement regarding the conflict of interest in his or her review of applications. He asked each Council member to read it carefully, sign it, and return it to the NIDDK before leaving.

Dr. Stanfield said 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.

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

Annual Approval of the Council Operating Procedures

The Council approved, by voice vote and without any questions or discussion, the Council Operating Procedures for 2015. The Procedures had been sent to them in advance of the January 2015 meeting and included in their meeting folders. Dr. Stanfield noted that the 2015 Procedures are essentially identical to the procedures approved for 2014.

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

Budget and Appropriations Update

Dr. Rodgers said that uncertainties regarding FY 2015 funding for the NIH were resolved when an omnibus spending bill was signed into law on December 17. The legislation funds all agencies except the Department of Homeland Security through September 30, 2015. The NIH enacted funding level is slightly over \$30 billion, which reflects an increase of almost \$150 million or 0.5 percent over the FY 2014 level. The NIDDK enacted funding level is almost \$1.8 billion, which reflects an increase of \$5 million or 0.31 percent over the FY 2014 level.

As in past years, the overall NIH increase was distributed proportionately among most Institutes and Centers, with a few NIH components receiving a larger amount for particular research areas. These components were: NCI for precision medicine and other priorities; NINDS and NIMH for the BRAIN Initiative; NIA for Alzheimer's research; and the NIH Common Fund to implement the Gabriella Miller Kids First Act for pediatric research. Funding was also provided to the NIH outside of the regular appropriation for emergency Ebola research; programs related to the clean-up of hazardous waste under the Superfund law; and mandated type 1 diabetes research.

Special Statutory Funding Program for Type 1 Diabetes Research

This Program will receive a full \$150 million in FY 2015 through the continuation of a separate mandatory appropriation. The Program did not receive the full \$150 million amount in either 2013 or 2014 because mandatory programs were subject to sequestration. However, it escaped sequestration reductions for FY 2015 because the OMB locked in government-wide sequestration amounts before the Program was extended.

Prospects for FY 2016

Federal agencies have completed spending proposals for 2016, and the President is scheduled to transmit his FY 2016 budget request to the Congress shortly. Until the President's Budget is officially released, details cannot be discussed publicly by Executive Branch agencies. Regarding the overall funding process for FY 2016, it can be noted that the Congress has not yet passed a Budget Resolution to provide a framework for discussions. With or without a Budget Resolution, it is likely that discretionary spending across the government will again be capped. To exceed a discretionary funding cap, it is likely that the Congress would also have to pass a bill to temporarily or permanently end sequestration.

Precision Medicine

Dr. Rodgers noted that the President's State of the Union address called for an expansion of medical research, including combating antibiotic resistance, and studies into "precision medicine" based on a person's genetic makeup, to "bring us closer to curing diseases like cancer and diabetes." Drs. Collins and Varmus elaborated on "A New Initiative on Precision Medicine," in the *New England Journal of Medicine*.

< <http://www.nejm.org/doi/full/10.1056/NEJMp1500523> >

Dr. Rodgers noted that the NIDDK is already involved in these kinds of studies. One example is the Accelerating Medicines Partnership (AMP), which the NIH started last year. At the September 2014 Council meeting, presenters described a prototype for the AMP type 2 diabetes partnership, including a "Knowledge Portal." The NIDDK issued a Funding Opportunity Announcement to fully develop such a web portal and to deposit, aggregate, and process the tremendous amount of population-specific genetic data on type 2 diabetes that have accumulated through NIDDK-supported research. In addition, the NIDDK issued another Funding Opportunity Announcement to support a consortium of investigators with expertise in human genetics, genomics, and type 2 diabetes, who will augment and refine the data available through the "Knowledge Portal." Applications received in response to both of these announcements have been reviewed and funding decisions will be announced shortly.

In addition, the Foundation for NIH has released AMP T2D-GENES companion funding announcements. It is expected that the first public data release under AMP T2D will be in late spring, with the public launch of the “Knowledge Portal.”

VI. UPDATE FROM THE DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS) AND NATIONAL TOXICOLOGY PROGRAM (NTP)

Dr. Linda S. Birnbaum

Dr. Rodgers introduced Dr. Birnbaum, who leads NIH efforts to discover how the environment influences human health and disease. A board certified toxicologist, Dr. Birnbaum has served as a federal scientist for nearly 35 years. Prior to her appointment as NIEHS and NTP Director in 2009, she spent 19 years at the U.S. Environmental Protection Agency (EPA), where she directed the largest division focusing on environmental health research. Dr. Birnbaum also spent 10 years with the NIEHS--first as a senior staff fellow in the National Toxicology Program, then as a principal investigator and research microbiologist, and later as a group leader for the Institute's Chemical Disposition Group. Dr. Birnbaum received her M.S. and Ph.D. in microbiology from the University of Illinois at Urbana-Champaign and is a Diplomate of the American Board of Toxicology. Among her many honors, Dr. Birnbaum was elected to the Institute of Medicine in 2010.

Dr. Birnbaum began her presentation by conveying a few key points about NIEHS. Unlike the NIH components focused on categorical diseases, the NIEHS funds very broad research to discover how the environment affects people so that the knowledge gained can promote healthier lives. The NIEHS supports a considerable amount of population-based research that can inform public health action. The Institute leads the National Toxicology Program (NTP) in coordination with the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA). The NTP is a problem-solving effort dedicated to testing chemicals that may have adverse effects, and to developing and evaluating new testing methods. The NIEHS is the only Institute located off the NIH campus--in Research Triangle Park, North Carolina. The Institute has a large, vibrant intramural laboratory program, and a small clinical research program with a day clinic. Research patients needing overnight stays are seen at the NIH Clinical Center or at a collaborative research institution near the NIEHS.

In addition to its regular appropriations, the NIEHS receives funds annually under the legislatively mandated Superfund Program. The NIEHS uses about two-thirds of those funds for research related to hazardous chemicals and their clean-up in the environment, and the rest for support of a worker training program related to hazardous waste clean-up and emergency response. Whenever there is a disaster, natural or man-made, NIEHS-trained workers are in the forefront of assistance efforts. In 2014, the NIEHS also received funds from the CDC for worker training related to dealing with the Ebola virus.

Conceptual Shift in Environmental Health Sciences

Dr. Birnbaum described the important conceptual shift that has occurred regarding the environmental health sciences. The long-held, traditional view of the environment focused on high-dose exposure to chemicals in occupational settings or in the developing world. Now, there is a greater realization that, throughout the many stages of life, a person faces ubiquitous exposure to chemicals that are widely dispersed in the environment, and that encompass much more than industrial and agricultural chemicals and air/water pollutants. For example, there is a greater realization that the environment includes foods and medications, and that more attention needs to be paid to lifestyle choices and to the issues of substance abuse, psycho-social stress, and socioeconomic factors. The environment can also affect the human microbiome, which in turn can alter a person's response to medications. There is a new appreciation that the environment can interact with infectious agents. For example, exposure to a range of different environmental chemicals in early life can suppress the ability of the body to mount a response to vaccines. Similarly, a person with an infection can have an altered response to environmental chemicals.

As part of this conceptual shift, there is an appreciation that, even at very low doses and exposures, elements of the environment can act like hormones and drugs to disrupt the control of development and function, and to confer disease susceptibility that persists long after initial exposure--as the field of epigenetics is revealing. Windows of susceptibility to environmental impacts include key points in human development, such as formation of the immune system, as well as stages in the lifespan. The *in utero* period and the early years of life are particularly vulnerable windows of time because they are marked by rapid growth, widespread active cell division/differentiation, and increased metabolism. Recognizing that environmental exposures are not isolated, self-contained events, researchers are now looking at the totality of a person's lifelong environmental exposures, which is referred to as the "exposome." The NIEHS works very closely with the CDC on biomonitoring approaches to identify associations between environmental exposures and health status that persist beyond one generation.

Research Findings of Concern

Health conditions with a known or suspected environmental component, include cancers; birth defects (cleft palate, cardiac malformations); reproductive dysfunction (infertility); lung dysfunction (asthma, asbestosis); neurodegenerative diseases (Parkinson's); neurodevelopmental disorders (autism); cardiovascular disease; and endocrine disorders (diabetes). Dr. Birnbaum described the importance of understanding the role the environment in the reported increases in type 1 diabetes, attention deficit hyperactivity disorder (ADHD), asthma, and autism. For example, 50 to 60 percent of the increase in autism spectrum is likely related to environmental causes.

Dr. Birnbaum described several other findings of concern.

- Prenatal pesticide exposure has been found to lower a child's IQ by several points, which can have significant negative impacts on school performance. Importantly, it is now known that pesticides don't stay where they are sprayed; they migrate. Therefore, legal restrictions on the use of certain pesticides in the home may not reduce their levels in adults or children who are exposed to the same chemicals outdoors, for example, on farms.

- Air pollution is a complex mix of different compounds that contribute to a wide range of health problems, including obesity, diabetes, developmental disabilities, and asthma. For example, research has shown that exposure to air pollution from living near a roadway is associated with an increased risk of asthma, especially in children, and that the exposure of women to heavy air pollution during pregnancy is associated with cognitive defects in their offspring. Research partnerships are coalescing to combat not only outdoor air pollution, but also indoor exposure to pollution, such as from the use of certain cooking stoves.
- Arsenic in drinking water and elsewhere has been associated with respiratory effects; vascular and cardiovascular disease; reproductive and developmental problems; neurological problems and reduced cognitive function in children; and type 2 diabetes. Arsenic is also an endocrine disrupter and may affect the synthesis of biological receptors, such as the estrogen receptor, and the PPAR gamma receptor, which plays a role in diabetes.

NIEHS-NIDDK Connections

With regard to the NIDDK, Dr. Birnbaum mentioned several metabolic diseases and findings of interest to the NIEHS. Research studies have shown a clear association between a mother's smoking and the development of overweight, obesity, and type 2 diabetes in her offspring. Nicotine likely acts as a developmental obesogen in humans. Bisphenol A affects insulin release and cellular signaling in pancreatic beta cells. A positive association exists between diabetes and certain organochlorine pesticides environmental pollutants. Exposure to multiple classes of pesticides may affect risk factors for diabetes and obesity, although gaps still remain in the knowledge base.

Dr. Birnbaum noted that Dr. Rodgers has visited the NIEHS campus and met with the leadership and members of the scientific community there. She said that the NIH Metabolomics Initiative, which is led by the NIDDK and the NCI, is closely related to NIEHS work on exposomics. The NIEHS has also worked with the NIDDK as part of the Epigenetics Program of the NIH Roadmap for Medical Research. Scientists supported by both Institutes have forged research collaborations, for example, on muscarinic receptors in mice. The NIDDK epidemiology program in Phoenix, Arizona, has provided valuable data regarding the relationship between arsenic exposure and type 2 diabetes. Future areas of possible collaboration include the TEDDY Study, obesity/diet, developmental origins of health and disease, the metabolic syndrome, and the microbiome.

Examples of NIEHS Studies and Programs

Dr. Birnbaum highlighted several NIEHS research activities. The Institute funds 14 Children's Health Centers with the Environmental Protection Agency, and a large joint research program with the National Cancer Institute on breast cancer and the environment, with an emphasis on puberty. The NIEHS "Sister Study" is examining environmental risk factors for breast cancer in a diverse group of 51,000 sisters of women who have had the disease in order to assess the interplay of genes and the environment in disease risk. Early findings indicate disease associations with obesity and perceived stress, but multivitamin use appears to confer benefits.

In the “Two Sister Study” of more than 1,600 women, early findings show an association between fertility drugs and reduced risk of young-onset breast cancer.

The Gulf Long-term Follow-up Study (GuLF Study) is a large, prospective epidemiology study begun about two months after the Deepwater Horizon oil spill in the Gulf. For over 10 years, the study is following 32,608 adults who were involved in oil spill clean-up or support. Working with partners in a consortium, the Institute’s preliminary findings include indications of respiratory symptoms, depression, and post-traumatic stress in the study population. The NIEHS is also working with the Assistant Secretary for Preparedness and Response and other agencies to help develop protocols for responding to public health emergencies and disasters.

Dr. Birnbaum said that climate change is an important research area for the Institute. The NIEHS previously led a work group across federal agencies to consolidate existing scientific information about the health effects of climate change, and is currently providing leadership within the Department of Health and Human Services related to the President’s Executive Order on this issue. Dr. Birnbaum brought to the Council’s attention a report by the Environmental Protection Agency: *A Human Health Perspective on Climate Change: A Report Outlining the Research Needs on the Human Health Effects of Climate Change*. Among the areas identified as needing research attention are asthma, respiratory allergies, and airway diseases; foodborne diseases and nutrition; and human developmental defects.

The NIEHS is working closely with the National Center for Chemical Genomics to further the rapid screening of chemicals with a wide variety of end points. Biomonitoring programs will be crucial to determine which chemicals are present in human tissue. Although the CDC produces annual updates to its National Report on Human Exposure to Environmental Chemicals, there are little or no hazard and exposure data on 80,000 chemicals currently in commercial use, of which about 15,000 are of environmental concern. Traditional methods of toxicity testing cannot meet this daunting challenge. New approaches and tools need to expand the use of alternative animal models, such as zebrafish models to study chemical mixtures; increase the use of mechanistic approaches to assess toxicity pathways; and harness computational tools to move toxicology into a predictive science.

Strategic Plan and Vision

Dr. Birnbaum commented that the NIEHS has engaged its stakeholders in a very broad-based strategic planning process to identify exciting and compelling research ideas in the environmental health sciences. The Institute’s 2012-2017 Strategic Plan has 10 overarching goals and is available on the Internet. < <http://www.niehs.nih.gov/about/strategicplan/index.cfm> >

In closing, Dr. Birnbaum said the vision of the NIEHS, moving forward, is to provide global leadership for innovative research that improves public health by preventing disease and disability. To that end, the Institute will seek increased partnerships with sister institutes and other federal agencies; the best individual and team science to address complex diseases, gene-environment interactions, windows of susceptibility, and complex environmental impacts; improved integration across research disciplines and partnerships; and improved translation and communication of basic findings into human health protection. Dr. Birnbaum emphasized that environmental factors are more readily identified and modifiable than genetic factors, and that the opportunities to prevent non-communicable diseases are compelling.

Council Questions and Discussion

Measurements: *What is being done on the measurement of environmental exposures, both acute and chronic, with biological sensors and similar tools?* Dr. Birnbaum said that the NIEHS Strategic Plan for 2012-2017 addresses that research area. Many sensors have been developed, both of environmental exposure and early markers of the body's response. Other sensors are undergoing validation. The NIEHS led the Exposure Biology Program under the NIH Roadmap Initiative on Genes and the Environment that went on for several years. A major goal was to develop new technologies for accurate measurement of environmental exposure to chemicals, and to lifestyle factors such as psychosocial stress and diet. The NIEHS also works with the National Institute of Biomedical Imaging and Bioengineering (NIBIB) on developing different kinds of exposure monitors. The NIH small business grant programs (SBIR/STTR) have been quite successful in developing new approaches. The advent of smart phones and GPS tracking are helpful tools.

Engaging Industry: *How does the NIEHS engage industry in furthering its mission when industry representatives often criticize or oppose the Institute's efforts?* Dr. Birnbaum replied that the NIEHS recognizes the need to have an open, broad, and balanced approach for seeking and gaining input from stakeholders, including researchers, industry, and non-governmental organizations. She said that excellent scientists from industry have served on the National Toxicology Board of Scientific Counselors and provided important information and insights. Whenever the Institute drafts documents, it provides multiple opportunities for comment at meetings, and through the Internet, webinars, and video conferencing. As part of that process, the NIEHS uses "systematic reviews" whenever clinical trial data are available. However, the challenge is to find ways to meld and assess in a highly transparent and repeatable process the quite different streams of data from observational, clinical, laboratory, and mechanistic studies.

VII. COUNCIL FORUM: Big Data and Informatics Barriers to and Career Paths for Integrating Big Data into Traditional Science, and Traditional Science into Big Data

Dr. Rodgers introduced the Forum, which was intended to explore the challenges of harvesting and exploiting the wealth of biomedical data being generated at an enormous speed. One of the hurdles is to improve the integration of Big Data with biomedical research efforts. Council Members Dr. David Brenner and Dr. Kenneth Kaushansky were asked to describe the efforts of their respective institutions toward that end, and to identify steps that could be taken to enhance bi-directional knowledge sharing between biomedical scientists and data scientists. Dr. Rodgers said that some of the key questions are: What are the barriers? What are the career paths? What are the opportunities, and how can NIDDK take advantage of them?

A. Perspective from the University of California, San Diego

Dr. David A. Brenner, Vice Chancellor, Health Sciences, and Dean of the School of Medicine

Dr. Brenner began his presentation by referencing the 2012 report of an NIH Health Data and Informatics Working Group. The Working Group noted that NIH funding for computational-related methodology has not kept pace with the Big Data environment, and that the interpretation of data will prove to be more costly than its acquisition. The Working Group recommended that the NIH provide serious, substantial, and sustained increases in funding for computational efforts, resources, and infrastructure.

With that backdrop, Dr. Brenner focused on the question: “What are the new career paths and support mechanisms needed, and how can a shared computational infrastructure be built to help NIDDK investigators?” He described the need to foster the bi-directional sharing of knowledge and skills between experimentalists and computational biologists. The experimentalists are laboratory and clinical scientists who perform studies to develop new biomedical and behavioral knowledge. They are well versed in the biomedical and behavioral sciences, but usually not in bioinformatics. In contrast, the computational biologists usually analyze and interpret large sets of data, and are well versed in mathematics, but untrained in understanding and addressing important biological questions. Bringing these two fields together can improve the capture and analysis of large amounts of different types of data to produce more robust results, which can then be used to predict disease outcomes and develop more precise therapies.

Dr. Brenner suggested that one way to combine both types of expertise for the benefit of science and human health is the cross-training of experimentalists and computational biologists so that multi-disciplinary teams can work effectively together. The overriding goal is to analyze patients using multi-“omics” approaches in order to gain greater insights into diagnosis and therapy. To that end, the University of California, San Diego, has established a Center for Bioinformatics Analysis to provide the platform technology to enable experimentalists to apply Big Data approaches to their research. The Center fosters collaborations and services just like any research core, integrates bioinformatics software platforms, provides educational training programs at different levels, and offers advisors/consultants to help in the design of experiments. The Center also provides for the writing of software, as needed, and consultations on analyses with respect to the genome, metagenome, epigenome, transcriptome, and proteome.

The Center is largely supported by the Vice Chancellor’s Office, including the initial investment. The first level of funding is for pilot projects. The second level is from existing centers and programs, such as the Diabetes-Endocrinology Research Center in Southern California. The third level is through re-charges (user charges). The hope is that the Center will also garner funds from new grants and contracts and intellectual property. The Center has become a national resource used on-line by thousands of people every month in a user-friendly, no-cost manner.

Dr. Brenner also described U.C. San Diego’s efforts to make medical informatics more user-friendly in a HIPPA-compliant way, and to populate research data with clinical data. All five of the university’s health systems can store de-identified clinical data that can be interrogated at the same time. Thus, researchers interested in doing a clinical trial can see how many patients would meet the protocol for a study before proceeding further. Dr. Brenner noted that his institution has

made decisions about how best to support these efforts effectively and efficiently. For example, the university decided that it was unwise to invest in hardware that could quickly become obsolete. It is therefore outsourcing genomic sequencing, but conducting clinical sequencing in-house in its pathology department. The university is exploring the benefits of using a super computer relative to cloud computing.

Dr. Brenner conveyed several thoughts that have emerged from discussions at U.C. San Diego about ways to bolster medical informatics, including the engagement of undergraduates in the field. Ensuring appropriate computational expertise on NIH Study Sections is considered one way to further development of the medical informatics field. It is also crucial to provide informatics experts with financial recompense that is competitive with salaries offered to them by industry. New paths also need to be forged in academia for their recognition, promotion, and tenure based on achievements different from traditional scientific publication.

Discussions at U.C. San Diego have also touched on ways that NIH Institutes, such as the NIDDK, could incorporate medical informatics more fully into biomedical research and training programs. For example, a required quantitative component could be included in NIDDK training and fellowship awards. Supplemental training slots could be added to current training grants. Dr. Brenner said it would be important to define a curriculum in advance that would include biostatistics, bioinformatics, and clinical trial design, in addition to mathematics, so that the training conveys knowledge of biological processes important for designing rational experiments. The NIDDK might also consider funding one or more large centralized computing centers that could be used efficiently by its investigators, similar to the National Science Foundation model.

B. Perspective from Stony Brook Medicine

Dr. Kenneth Kaushansky, Senior Vice President for Health Sciences; Dean School of Medicine; Distinguished Professor, State University of New York

Dr. Kaushansky described the field of medical bioinformatics and the new educational programs Stony Brook is developing at several levels to provide needed expertise in this area.

The World of Biomedical Informatics

The American Medical Informatics Association defines biomedical informatics as: "The interdisciplinary field that studies and pursues the effective use of biomedical data, information, and knowledge for scientific inquiry, problem solving and decision making, motivated by efforts to improve human health." The discipline is at the intersection of information science, computer science, basic biology and medical sciences, and health care.

Dr. Kaushansky said that there are essentially five different areas of application: the actual bioinformatics, which is focused on looking at big databases, such as genomics and proteomics; clinical research informatics; clinical informatics, which is a much more applied field; consumer health informatics; and public health informatics. The discipline develops and applies novel approaches for optimizing the acquisition, storage, retrieval, synthesis, and analysis of the large amounts of data involved in modern advances in biomedical sciences. Informatics experts develop theories, methods, and processes, which build on computing, communication, and

information sciences. Skills are needed in reasoning, modeling, simulation, experimentation, and translation. The field recognizes that people are the ultimate users of information, and that it is therefore important to draw upon social and behavioral sciences to further the design and communication of solutions to the individual. In essence, biomedical informatics seeks to turn Big Data into knowledge that will benefit human health. That process brings together the fields of engineering, data and computer science, biomedical science, and clinical medicine and population health.

Biomedical informatics involves the synthesis and mining of information from several sources including “omics” studies, electronic health records, computerized physician order entries, laboratory values, imaging, and decision support. Instrumentation, surveillance and analytic tools are key as to bringing data into a storehouse where simulation, visualization, and algorithms can be applied. The biomedical informatics establishment integrates, manages, and analyzes the data, and disseminates conclusions derived from analyses. According to the American Medical Informatics Association, 70 U.S. universities have biomedical informatics programs involving all types of degrees. However, only 21 of them grant Ph.D.s in biomedical informatics.

New Biomedical Informatics Programs at Stony Brook

Dr. Kaushansky described new programs being initiated or envisioned in biomedical informatics at Stony Brook.

Ph.D. Level: A new Ph.D. program will focus on research in clinical informatics, public health informatics, computational biology, computational imaging, artificial intelligence, and database networking. New interdisciplinary collaborations will take advantage of neighboring efforts at Cold Spring Harbor Laboratory and Brookhaven National Laboratory. Within Stony Brook, there are strong resources to leverage, including the Institute for Advanced Computational Sciences and the Laufer Center for Physical and Quantitative Biology. Stony Brook intends to create an interdisciplinary educational experience by bridging traditional boundaries in scientific, engineering, and medical education. A priority is to train a new generation of medical informatics practitioners--stressing the interdisciplinary nature of this emerging scientific discipline--reinforced with multiple rotational experiences.

Students are expected to have diverse educational backgrounds. Rarely will individuals have a bachelor's degree in biomedical informatics. They will typically enter with post-baccalaureate training, most likely in the physical sciences, computer sciences, or other engineering disciplines. Alternatively, they may come from biology, biochemistry, pharmacology or the social sciences. Occasionally, a student will come from the humanities, or with a medical degree. Once enrolled, the computer scientists will need more biological science training, and the biologists will need more computer science training. The founding chair of biomedical informatics at Stony Brook, Dr. Joel Saltz, set up the curriculum. There are a certain number of core biomedical informatics courses, for example: introduction to biomedical informatics; introduction to clinical environments; introduction to clinical and translational informatics; high performance computing; and imaging informatics. In addition, there are computer science courses, biological science courses, and interdisciplinary courses. The program focuses on the top three of the

classical five areas of biomedical informatics: clinical informatics, translational informatics, and imaging informatics.

The first major track is clinical informatics, which essentially is the application of informatics and information technology to deliver health care services. It is concerned with information used in health care by clinicians. Clinical informatics includes clinical decision support, clinical documentation, the human-computer interface, usability, sensor data, mobile health, and informatics methods to improve health care quality and efficiency. Big Data will enable predictive modeling, sensor data analysis, large-scale data visualization, sonification, and immersion in clinical environments.

The second major track is translational bioinformatics. It is concerned with analytic, and interpretive methods to optimize the transformation of increasingly voluminous biomedical, genomic and proteomic data into proactive, predictive, preventive, and participatory health care. Research in this realm focuses on the development of novel techniques for the integration of biological and clinical data into precision medicine. Translational bioinformatics involves the application of integrative bioinformatics to medicine. The use of Big Data will involve computational models, statistical algorithms to integrate multiple complementary data types; machine learning to correlate heterogeneous data inputs with outcomes; and algorithmic treatment-response prediction.

The third track is imaging informatics, which has a strong foundation at Stony Brook. Imaging techniques range from microscopic, submicroscopic, and molecular approaches to whole body visualization. Many areas in clinical medicine are encompassed, including radiology, pathology, dermatology, and ophthalmology. There is great potential to diagnose disease, particularly earlier; to tailor optimal treatment; to track disease response to interventions; and to predict outcomes. The use of Big Data will involve quality checks on human reads, calculation of probabilities, and predictive power to determine when and how to do imaging.

Joint Programs: Dr. Kaushansky said that Stony Brook is also developing joint programs in biomedical informatics, such as a combined Ph.D./M.D. and fellowship program. Graduates are expected to focus on precision medicine from a diagnostic and therapeutic perspective, and on health care quality, effectiveness, and efficiency. Population health management will incorporate sensor data and mobile health data into big databases. Graduates will create a new generation of principal investigators to lead integrative research efforts, and to create, test and deploy tools. They will integrate and extract meaning from clinical, “omics,” and imaging data, and leverage electronic health record data for hypothesis-generating biomedical research. Graduates will find many career opportunities with competitive salaries in academia, the private health sector, the pharmaceutical industry, and technology industries.

Envisioned Master's or Certificate Program: Stony Brook is envisioning the establishment of a master's degree and/or a certificate program involving 30 credits of coursework. A Ph.D. is not required in the field of medical informatics, but training at an advanced level is being increasingly recognized as a valuable asset. Stony Brook expects that most applicants for this program would have already achieved or be working on a graduate degree or post-graduate degree, and that many would be M.D.s. This program would focus on data science methods that are becoming an integral component of virtually all biomedical research, especially the interpretation and analysis of data from “omics” platforms. Students would work on many areas

such as capture analysis and interpretation of biomedical imaging data; the appropriate extraction and interpretation of electronic health care data; and workflow and data systems for clinical research.

In closing, Dr. Kaushansky presented an example of a grant that the National Cancer Institute has awarded to Stony Brook for research in computational pathology. The grant involves anatomic/functional characterization of cancer tissue at the fine and gross levels, and the integration of imaging tools with “omics” data to monitor the treatment and outcomes of patients. It is this type of biomedical informatics research that will help to generate hypotheses about the origins of disease; contribute to the development and testing of new prevention and treatment modalities; and further health care quality, effectiveness, and efficiency.

Council Questions and Discussion

Data Integration Issues: *What is being done to meet the challenge of integrating sets of data that involve different sources, software and thinking about health problems?* Dr. Brenner agreed that this is an important issue. He said that the Holy Grail for “omics” is to take disparate data sets for the same patient, or the same experimental system, and make them more robust by comparing them. For example, if protein data can be used to confirm predictions based on genetic data, then a more robust data set will result. The development of new software will help to resolve data integration issues. U.C. San Diego has set up a type of central advisory board for biomedical informatics, which approves all software purchases as a means of promoting compatible systems, productive consultations, and the avoidance of silos.

Data Validation Issues: *What is being done about the need for validating, at the experimental level, the interpretations and conclusions that are being made based on data analyses, particularly with respect to data on the human microbiome or mammalian microbiome? What is being done to further an iterative process between computational processing and validation?* Dr. Brenner agreed with the importance of validating informatics-based data interpretations with further experimental testing. This will be a long-term process. Dr. Kaushansky said that almost all biomedical informatics outputs can be viewed as hypotheses that need to be proven or refuted by experimentalists.

Training Time: *What effect will these programs have on the length of time for training? As a practical matter, will institutions only be able to recruit students who have the time and resources to engage in these training pathways?* Dr. Kaushansky said that the Ph.D. program at Stony Brook will be long and rigorous, particularly if people enter with backgrounds that are exclusively computationally or biologically oriented. However, the vast majority of students will probably apply for certificates or for master's degrees that will take about two years to achieve. Ideally, a person who is already well trained, such as a physician, could easily acquire the biomedical informatics tools needed to work with a software engineer to interpret data. The foundation of a stellar mathematics department at Stony Brook should enable the training of highly qualified people within a reasonable time period.

Patient Data Beyond Academic Research Centers: *Programs are being developed to enhance the integration of informatics at academic research centers. However, patient-related information resides largely outside academia. Can the NIH develop a glue for patient-related informatics?* Dr. Kaushansky agreed to the need. It will be imperative to overcome the challenges of bringing together large numbers of different types of patient care organizations,

and in integrating data from different kinds of electronic medical records. This must be done to realize the power of Big Data. Dr. Brenner commented that at his institution, all five health systems are using a common clinical data warehouse. Certain non-academic centers are also making progress in interrogating data from different hospitals.

Quality Control: *What is being done to address quality control issues?* Dr. Kaushansky agreed that data analyses and interpretations rely on the quality of data input. One way to improve quality control further is to enter primary data such as actual digital images and pathological slides. Laboratory values are more problematic, but most reasonable hospitals will have quality laboratories. Dr. Brenner said that computational biologists recognize the existence of bad data and know when quality control was absent in the initial data collection and entry. That's why experimentalists need to work with informatics experts who can assess whether data are sufficiently robust for the application of informatics tools. There are fairly well-accepted ways of deciding whether or not the data has reached a level of quality for analysis. These include re-sequencing to see if the same result is obtainable, having internal standards to avoid contamination, and assessing the quality of mathematical curves.

Proprietary Algorithms: *How can biomedical research find a HIPAA-compliant way to access and take advantage of proprietary algorithms, which have been tested in the military, as well as in a variety of other places by companies such as Google and Amazon?* Dr. Kaushansky said that Stoney Brook is seeking non-traditional ways of using non-academic software that successfully integrates disparate data sources. Partnerships with the private sector may be possible.

In concluding the Council Forum, Dr. Rodgers said that the NIDDK will continue to explore the enhanced integration of bioinformatics with its biomedical research programs. There will be further discussions about how the Institute can best position itself in the bioinformatics arena.

VIII. SCIENTIFIC PRESENTATION: Metabolism: SNO in the Forecast

Dr. Jean Schaffer, the Virginia Minnich Distinguished Professor of Medicine at Washington University School of Medicine, St. Louis

Dr. Rodgers introduced Dr. Schaffer, whose research is focused on lipotoxicity, which occurs when fatty acids accumulate in excess amounts in non-adipose tissues, leading to cell dysfunction and cell death. Lipotoxicity plays an important role in the pathogenesis of heart failure and other complications of diabetes. Some of the goals of Dr. Schaffer's research include characterization of the fundamental cellular mechanisms of metabolic stress from substrate excess, and understanding how this process contributes to diabetes complications. Through basic studies involving genetic screens in cultured cells, Dr. Schaffer's laboratory has identified critical molecular players in the lipotoxic response. This work uncovered a role for small nucleolar RNAs in the response to metabolic and oxidative stress. Dr. Schaffer earned her M.D. from the Harvard Medical School and the Harvard-Massachusetts Institute of Technology, Division of Health Sciences and Technology. She then completed an internship and residency at Brigham and Women's Hospital and a fellowship within the Cardiovascular Division at Beth Israel Hospital. She completed a post-doctoral fellowship at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts.

IX. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1,614 grant applications (452 primary and 1162 dual), requesting support of \$450,131,101 were reviewed for consideration at the January 28, 2015 meeting. An additional 18 Common Fund applications requesting \$5,826,915 were presented to Council. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, 1328 applications requesting \$ 388,299,152 received second-level review through expedited concurrence. All of the expedited concurrence applications were recommended for funding at the Scientific Review Group recommended level. The expedited concurrence actions were reported to the full Advisory Council at the January 28, 2015 meeting.

X. ADJOURNMENT

Dr. Rodgers

In adjourning the meeting, Rodgers expressed appreciation on behalf of the NIDDK to the presenters and other participants. He thanked the Council members for their attendance and valuable input. There being no other business, the 197th meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m. on January 28, 2015.

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

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