Meeting Minutes
Department of Health and Human Services
National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases

I. CALL TO ORDER
Dr. Rodgers

Dr. Griffin P. Rodgers, Director, NIDDK, called to order the 192nd meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m., Wednesday, May 15, 2013, in Building 31, C-Wing, 6th Floor Conference Center, Conference Room 10, NIH Campus, Bethesda, Maryland.

A. ATTENDANCE – COUNCIL MEMBERS PRESENT

Dr. Domenico Accili
Dr. Sharon Anderson
Dr. Gopal Badlani
Dr. Judy Cho
Dr. Gregory Gores
Ms. Jane Holt
Ms. Judy M. Hunt
Dr. Kenneth Kaushansky
Dr. David M. Klurfeld
Ms. Robin Nwankwo
Dr. Jerry P. Palmer
Dr. Thomas Robinson
Dr. Anil K. Rustgi
Dr. Alan R. Shuldiner
Dr. Irving Smokler
Dr. Bruce Spiegelman
Dr. William D. Steers
Dr. Robert A. Vigersky
Mr. John W. Walsh
Dr. Mark L. Zeidel

Also Present:

Dr. Griffin P. Rodgers, Director, NIDDK, and Chairperson, NIDDK Advisory Council
Dr. Gregory Germino, Deputy Director, NIDDK
Dr. Brent Stanfield, Executive Secretary, NIDDK Advisory Council

B. NIDDK STAFF AND GUESTS

Abankwah, Dora – NIDDK
Abraham, Kristin – NIDDK
Andersen, Dana – NIDDK
Appel, Richard – NIDDK
Arreaza-Rubin, Guillermo – NIDDK
Barnard, Michele – NIDDK
Bavendam, Tamara – NIDDK
Begum, Najma – NIDDK
Bishop, Terry – NIDDK
Bleasdale, John – CSR
Blondel, Olivier – NIDDK
Bourque, Sharon – NIDDK
Brown, Sherry – NIDDK
Buchanan, Sarah – The NephCure Found.
Burnett, Arthur – Johns Hopkins Univ.
Calvo, Francisco – NIDDK
Carrington, Jill – NIDDK
Castle, Arthur – NIDDK

Cerio, Rebecca – NIDDK
Cleffi, Kate – RTI International
Connaughton, John – NIDDK
Copeland, Randy – NIDDK
Curtis, Leslie – NIDDK
Davila-Bloom, Maria – NIDDK
Dayal, Sandeep – NIDDK
Densmore, Christine – NIDDK
Dirks, Dale – Natl. Sci. Found.
Donohue, Patrick – NIDDK
Doo, Edward – NIDDK
Drew, Devon – NIDDK
Dugan, Emily – NIDDK
Durrant, Valerie – CSR
Eggerman, Thomas – NIDDK
Evans, Mary – NIDDK
Flessner, Michael – NIDDK
Fonville, Olaf – NIDDK
Fradkin, Judith – NIDDK
Gallivan, Joanne – NIDDK
Gansheroff, Lisa – NIDDK
Garofalo, Robert – CSR
Giambarresi, Leo – Amer. Urology Assoc.
Graves, Reed – CSR
Grey, Michael – NIDDK
Guo, Xiaodu – NIDDK
Haft, Carol – NIDDK
Hamilton, Frank – NIDDK
Hanlon, Mary – NIDDK
Hetkowski, Kimberley – NIDDK
Hoff, Eleanor – NIDDK
Hoofnagle, Jay – NIDDK
Hoover, Camille – NIDDK
Horlick, Mary – NIDDK
Hoshizaki, Deborah – NIDDK
Hunter, Christine – NIDDK
Hyde, James – NIDDK
James, Stephen – NIDDK
Jenkins, Connie – NIDDK
Jerkins, Ann – NIDDK
Jones, Teresa – NIDDK
Karp, Robert – NIDDK
Karimbakas, Joanne – NIDDK
Ketchum, Christian – NIDDK
Kirkali, Ziya – NIDDK
Kuczmarski, Robert – NIDDK
Kusek, John – NIDDK
Laughlin, Maren – NIDDK
Leschek, Ellen – NIDDK
Linder, Barbara – NIDDK
Malik, Karl – NIDDK
Maruvada, Padma – NIDDK
Margolis, Ronald – NIDDK
Martey, Louis – NIDDK
Martinez, Winnie – NIDDK
McKeon, Catherine – NIDDK
Morris, Ryan – CSR
Mowery, Penny – NIDDK
Moxey-Mims, Marva – NIDDK
Mullins, Christopher – NIDDK
Nakamura, Richard – CSR
Narva, Andrew – NIDDK
Newman, Eileen – NIDDK
Nguyen, Van – NIDDK
Nurik, Jody – NIDDK
Patel, D.G. – NIDDK
Pawlyk, Aaron – NIDDK
Pellnitz, Lori – SRI International
Pike, Robert – NIDDK
Podskalny, Judith – NIDDK
Rankin, Tracy – NIDDK
Roberts, Tibor – NIDDK
Rosenberg, Mary Kay – NIDDK
Rosendorf, Marilyn – NIDDK
Rushing, Paul – NIDDK
Rys-Sikora, Krystyna – NIDDK
Salaita, Christine – NIDDK
Salomon, Karen – NIDDK
Sato, Sheryl – NIDDK
Savage, Peter – NIDDK
Scanlon, Elizabeth – NIDDK
Schofield, Geoffrey – CSR
Sechi, Salvatore – NIDDK
Serrano, Jose – NIDDK
Sheard, Nancy – CSR
Shepherd, Aliecia – NIDDK
Sherker, Averell – NIDDK
Silva, Corrine – NIDDK
Smith, Jill – NIDDK
Smith, Philip – NIDDK
Spain, Lisa – NIDDK
Star, Robert – NIDDK
Staten, Myrlene – NIDDK
Swartz, Karyl – CSR
Tatham, Thomas – NIDDK
Torrance, Rebecca – NIDDK
Tuncer, Diane – NIDDK
Van Raaphorst, Rebekah – NIDDK
Vieweg, Johannes – Amer. Urology Assoc.
Wallace, Julie – NIDDK
Wellner, Robert – NIDDK
Williams, Shimere – Lewis-Burke Assoc.
Wilson, Sarisa – NIDDK
Woynarowska, Barbara – NIDDK
Wright, Daniel – NIDDK
Yanovski, Susan – NIDDK

C. ANNOUNCEMENTS

Dr. Rodgers made the following announcements:

Introduction of Dr. Bruce Spiegelman, a New Council Member

Dr. Bruce Spiegelman is a new Council member who was unable to be present at the previous meeting when other new members were welcomed. Dr. Spiegelman is joining the Diabetes, Endocrinology and Metabolic Diseases (DEM) subcommittee of Council. He is the Stanley J. Korsmeyer Professor of Cell Biology and Medicine at Harvard Medical School. He is also Professor of Cancer Biology at the Dana-Farber Cancer Institute. Dr. Spiegelman's research is focused on the regulation of energy homeostasis in mammals, primarily at the level of gene transcription. Among his many accolades, Dr. Spiegelman was elected to the National Academy of Sciences in 2002. Dr. Spiegelman conducted his postdoctoral work at the Massachusetts Institute of Technology subsequent to receiving his Ph.D. from Princeton University.

Honors and Awards

Dr. Jeffrey Gordon, a former NIDDK Advisory Council member and long-time NIDDK grantee, will receive the Robert Koch Award in 2013. Dr. Gordon is the Dr. Robert J. Glaser Distinguished University Professor and Director of the Center for Genome Sciences and Systems Biology at Washington University in St. Louis, Missouri. The Robert Koch Award is one of the most prestigious scientific commendations in Germany. Presented annually, the award was created to honor microbiologists who make ground-breaking discoveries or who contribute to global health in a unique way. The award recognizes Dr. Gordon's pioneering work that demonstrated the importance of the human body's trillions of resident microbes--the microbiome--in health and disease.

In addition, Dr. Rodgers noted that two NIDDK extramural grantees and one intramural research scientist have been elected to the National Academy of Sciences.

- ***Dr. Norbert Perriman*** is Professor of Genetics at Harvard Medical School and Investigator with the Howard Hughes Medical Institute. Dr. Perriman has current NIDDK research support to study the structure and organization of the insulin signaling network. His research focuses on understanding mechanisms by which cells and tissues communicate with each other to coordinate the formation of specific structures during development and to maintain homeostasis.
- ***Dr. Ernest M. Wright*** is the Distinguished Professor of Physiology and Mellinkoff Professor of Medicine at the David Geffen School of Medicine at the University of California, Los Angeles. Dr. Wright's work has been supported by the NIDDK for more than 30 years. He is one of the pioneers of expression cloning. His research focuses on understanding sodium-glucose cotransporters from the atomic level to their physiological roles in humans. These transporters are responsible for the active transport of glucose into cells and glucose sensing in the body.

- ***Dr. Wei Yang*** is a Research Scientist in the NIDDK Laboratory of Molecular Biology, which she joined in 1995 after a postdoctoral fellowship with Dr. Tom Steitz at Yale University. In her work, Dr. Yang uses x-ray crystallography to study molecular mechanisms related to DNA replication, repair and recombination. Her structural determinations are coupled with outstanding biochemistry to clarify how enzymatic machinery functions, and how it interacts with nucleic acids.

Finally, Dr. Rodgers noted that ***Dr. Catherine McKeon,*** Senior Advisor for Genetic Research within NIDDK's Division of Diabetes, Endocrinology and Metabolic Diseases, will be presented with the American Society of Gene and Cell Therapy (ASGCT) Distinguished Service Award, along with Dr. Sonia Skarlotos, who is Deputy Director of the Division of Cardiovascular Sciences at the National Heart, Lung and Blood Institute. The award recognizes a person or group for consistently fostering and enhancing the field of genetic and cellular therapy. Drs. McKeon and Skarlatos are receiving the award for their work in catalyzing the evolution of gene therapy from an interesting new science with great potential to a field of clinical medicine.

NIDDK Staff Retirements

Dr. Sandy Garfield retired in May 2013, having served for over 25 years within the Division of Diabetes, Endocrinology and Metabolic Diseases (DEM). The Division's Senior Advisor for Biometry and Behavioral Research, Dr. Garfield guided the landmark Diabetes Prevention Program (DPP) from its inception, as well as the ongoing Diabetes Prevention Program Outcomes Study (DPPOS). His skillful leadership was instrumental in the success of the pivotal DPP clinical trial, which proved that type 2 diabetes can be prevented or delayed. He also led the development of more cost-effective approaches to delivering the DPP lifestyle intervention in communities. That research was a foundation for the National Diabetes Prevention Program of the Centers for Disease Control and Prevention (CDC). Dr. Garfield also contributed to many important efforts to reduce health disparities, and furthered coordination with the Indian Health Service.

Dr. Lakshmanan Sankaran, a Senior Scientific Review Officer in NIDDK Review Branch, retired in January 2013. His initial service was within the Diabetes Branch of the NIDDK Division of Intramural Research. There, he made valuable contributions to scientific areas ranging from the characterization of insulin receptors to the hormonal regulation of mammary gland development and differentiation. In 1991, Dr. Sankaran joined the NIDDK Review Branch within the Division of Extramural Activities, where he has served for over 20 years as a Scientific Review Officer. He oversaw the review of many of the NIDDK's most important and challenging initiatives and was highly respected for his in-depth scientific knowledge and mentoring skills.

NIDDK Staff Appointments

Dr. Robert Tilghman joined the NIDDK Office of Scientific Program and Policy Analysis in February 2013. After receiving his Ph.D. in pathology from Vanderbilt University, Dr.

Tilghman completed post-doctoral work and served as a research scientist at the University of Virginia. He also worked in the biotechnology industry.

Dr. Jian Yang joined the NIDDK Review Branch in the Division of Extramural Activities in March 2013. Dr. Yang's areas of expertise include: lipid disorders, fatty liver, atherosclerosis, obesity, and type 2 diabetes. He was previously a Visiting Scientist in the NIDDK Division of Intramural Research. Prior to joining the NIH, he served as an Assistant Professor in the Department of Physiology, University of South Alabama College of Medicine. Dr. Yang earned a Ph.D. in Biochemistry from the Ohio State University, and conducted post-doctoral work within the Department of Molecular Genetics at the University of Texas Southwestern Medical Center.

II. CONSIDERATION OF SUMMARY MINUTES OF THE 191st COUNCIL MEETING
Dr. Rodgers

The Council approved, by voice vote, the summary minutes of the 191st Council meeting, which had been sent to members for review prior to the meeting.

III. FUTURE COUNCIL DATES
Dr. Rodgers

2013
September 26-27 (Thursday and Friday)

2014
February 5-6 (Wednesday and Thursday)
May 14-15 (Wednesday and Thursday)
September 3-4 (Wednesday and Thursday)

2015
January 28-29 (Wednesday and Thursday)
May 13-14 (Wednesday and Thursday)
September 9-10 (Wednesday and Thursday)

Dr. Rodgers said that most meetings are expected to be a single day; however, the Council is asked to hold two days should a situation arise where a longer meeting is required. Dr. Rodgers pointed out that the September 2013 Council meeting is unusual because it is quite late in September, and it is scheduled for Thursday and Friday, instead of the usual Wednesday and Thursday. Because there will be insufficient time following the September meeting to process grants for payment in the current fiscal year, a special, closed Council session by teleconference will likely be needed in late August or early September to obtain full Council approval for a limited number of grant actions. The NIDDK is working on the logistics of such a special meeting and will advise Council of the date and time for the teleconference.

IV. ANNOUNCEMENTS
Dr. Malik

On Dr. Stanfield's behalf, Dr. Karl Malik, his Deputy, made the following announcements.

Confidentiality

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

Conflict of Interest

Dr. Malik reminded 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 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 noted that each Council member's folder contained a statement regarding the conflict of interest in review of applications. He asked each Council member to read the statement carefully, sign it, and return it to the 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.

With respect to multi-campus institutions of higher education, Dr. Malik stated 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

Dr. Rodgers said that uncertainties have complicated the FY 2013 and FY 2014 budget processes. FY 2013 began with a Continuing Resolution that provided six-months of funding for the NIH and most other federal agencies whose regular appropriations bills had not been completed. Under the Continuing Resolution, these agencies received this short-term funding at their FY 2012 budget levels, plus a 0.612 increase. (For the NIDDK, the FY 2012 funding level was close to $1.8 billion.) For many months, congressional debate continued regarding how to set funding levels for the full fiscal year. In particular, questions and confusion surrounded the implementation of a mandated budget sequestration process, which called for across-the-board reductions in an FY 2013 funding level that had not been determined. These uncertainties delayed completion of the FY 2013 budget cycle, as well as the development of FY 2014 budget proposals.

Final FY 2013 Budget and Impact of Sequestration

The full-year FY 2013 funding level for the NIH became known in March 2013, with enactment of the "Consolidated and Further Continuing Appropriations Act of 2013," which left sequestration in place. For the NIH, the sequester reduced FY 2013 funds by $1.71 billion to produce a final budget of $29.151 billion. For the NIDDK, the sequester of about $102 million resulted in a final budget of $1.693 billion. Sequestration will affect many NIDDK programs. For example, the Institute estimates that it will fund about 63 fewer new and competing research project grants (RPGs) than would have been possible had it received its full FY 2013 budget level and 41 fewer institutional research training grants (T32s). The Special Statutory Funding Program for Type 1 Diabetes Research will also be affected.

President's Budget Request for FY 2014

In April 2013, the President submitted to the Congress his FY 2014 budget request. For the NIH, the request is $31.3 billion, which is 1.5 percent above the FY 2012 budget level. For the NIDDK, the request includes $1.812 billion, plus $150 million for the Special Statutory Funding Program for Type 1 Diabetes Research. The President's budget request is based on a combination of revenue increases, spending reductions, and economic investments, and it is constructed to avoid sequestration. The NIH Director, Dr. Francis Collins, testified regarding the FY 2014 budget at a Senate appropriations subcommittee hearing on May 15, 2013. His written testimony is posted on the NIH website (http://www.nih.gov/about/director/budgetrequest/fy2014testimony.htm).
Dr. Collins also testified before the corresponding House appropriations subcommittee on March 5, 2013, prior to release of the President's budget request.

House and Senate Budget Proposals for FY 2014

The House and Senate passed their budget resolutions for FY 2014 on March 21 and March 23, respectively. These non-binding plans have a ten-year time horizon for funding programs and reducing the deficit. Dr. Rodgers touched briefly on some of the many aspects of the plans, which take very different approaches to deficit reduction.

The Senate plan would reduce the deficit through a combination of steps. Revenue generation would be accomplished through certain tax changes and through economic stimulation via job training and infrastructure projects. Proposed spending reductions would be achieved by targeting specific programs, rather than through the across-the-board approach of the FY 2013 sequestration. Particularly relevant to the NIH is an amendment included by Senator Durbin that would establish a deficit-neutral reserve fund to increase NIH funding.

The House plan centers largely on deficit reduction via reduced spending. The plan would continue sequestration, but redistribute some spending reductions away from military programs and toward discretionary programs. The plan would make significant reductions and changes in entitlement and discretionary programs, but it does not include the tax changes proposed by the Senate. The Affordable Care Act (Obamacare) would be repealed.

Dr. Rodgers noted that these budget proposals are starting points for discussions and negotiations. The significant differences between these plans, as well as their differences with the President's budget request, are likely to result in an extended appropriations process. In the interim, the NIH will continue to manage programs and resources carefully so that investigators can pursue the most promising research avenues to benefit the public health.

VI. COUNCIL FORUM: NIDDK Planning for NIH Common Fund Ideas

NIDDK Deputy Director, Dr. Gregory Germino, introduced the discussion of the NIH Common Fund. Established by the 2006 NIH Reform Act, the Common Fund was intended to support cross-cutting, trans-NIH programs that require participation by at least two NIH Institutes or Centers (ICs) or would otherwise benefit from strategic planning and coordination. The Common Fund is coordinated by the NIH Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI) in the Office of the NIH Director. The Common Fund was initially used to support a series of short-term, exceptionally high-impact, trans-NIH programs collectively known as the NIH Road Map for Medical Research. Dr. Germino pointed out that a number of these projects have been of particular interest and benefit to NIDDK investigators. Each year, the NIH Director asks the Institutes to submit ideas for Common Fund initiatives. The NIDDK is taking a proactive approach to this process by developing concepts well in advance of this request.

A. Overview: NIDDK and the Common Fund

Dr. Philip Smith, Deputy Director, Division of Diabetes, Endocrinology and Metabolic Diseases

Dr. Smith said that the NIH Common Fund provides an opportunity for the NIDDK to propel important research that can benefit the Institute's mission and its investigative community (http://commonfund.nih.gov/). Programs supported by the NIH Common Fund are intended to have the following characteristics, which can be considered criteria for funding:

- ***Transformative:*** Must have a high potential to dramatically affect biomedical and/or behavioral research over the next decade.

- ***Catalytic:*** Must achieve a defined set of high-impact goals within a defined period of time.

- ***Synergistic:*** Outcomes must synergistically promote and advance the individual missions of NIH Institutes and Centers to benefit health.

- ***Cross-cutting:*** Program areas must cut across missions of multiple NIH Institutes and Centers, be relevant to multiple diseases or conditions, and be sufficiently complex to require a coordinated, trans-NIH approach.

- ***Unique:*** Must be something no other entity is likely or able to do. Programs already in place at NIH or elsewhere are not eligible.

Dr. Smith noted that the Common Fund's $550 million annual budget is larger than the budgets of some NIH Institutes and Centers. As Common Fund initiatives are completed, opportunities open up for the support of new ideas. For an initiative to be continued beyond the Common Fund's current 10-year maximum period of support, other funding sources must be used.

Dr. Smith said that the Common Fund has supported a number of programs relevant to the NIDDK mission--with outcomes of high utility to the Institute's grantees. These include: the Epigenomics Program, the Human Microbiome Project, the Molecular Libraries Program, the Metabolomics Program, the Mouse Knockout Project, and the High Risk/High Reward Program. The latter program includes Pioneer Awards, Early Innovator Awards, Transformative R01 grants, and Early Independence Awards.

Dr. Smith said that the Epigenomics Program has been particularly pertinent to the NIDDK's research interests in environmental influences on genes and behavior. The Institute led the component of this Program that has discovered 67 novel epigenetic marks. Moreover, the Program has developed 80 comprehensive epigenomes; 4,000 datasets available through the Human Epigenome Atlas; a broad range of primary tissues and stem

cells; and new imaging techniques, such as a method to permit *in vivo* imaging of epigenetic marks. One way the Atlas is being used is to understand the workings of single nucleotide polymorphisms (SNPs) that are in non-coding regulatory regions of DNA. This research has the potential to provide new insights into genetic data collected through previous NIDDK research investments.

The Human Microbiome Project centers on a research area in which the NIDDK has supported pioneering investigators. The Institute has had a major role in this Project. To date, the Project has sequenced the genomes of more than 500 microbial strains; discovered more than 29,000 novel proteins encoded by the human microbiome; analyzed the microbiomes of over 240 healthy individuals; and undertaken projects on Crohn's disease, dermatitis, obesity, abdominal inflammation, acne, and undiagnosed fever. Metabolic disorders will be included in the next phase of the Project.

The Molecular Libraries Program has delivered more than 200 probes to date for various cellular functions or molecules. The third largest set of probes relates to NIDDK research areas. Some probes are moving forward into clinical development, whereas others are clearly designed as biological probes for basic research. The NIDDK has had a major leadership role in this Program.

Dr. Smith said that NIDDK investigators have been heavy users of the Mouse Knockout Project. NIDDK investigators are also benefiting from participation in a new Common Fund Metabolomics Program, which the NIDDK is co-leading with the NCI. The Institute is also pleased that investigators with interest in NIDDK research areas have received awards from the Common Fund's High Risk/High Reward Program, which is designed to foster bold, creative thinking.

Dr. Smith described the planning process for the Common Fund. Extensive external input is obtained from broad-based meetings, requests for information, social media input, and concept clearance by the NIH Council of Councils. Internal input is provided by Institute and Center Directors and their Senior Staff, NIH Office Directors, and the NIH Director. Concepts submitted by the Institutes and Centers as possible candidates for funding undergo a refinement process. This process includes a portfolio analysis to determine what research is already being done in an area, focused meetings, and the development of specific proposals by a Trans-NIH Working Group. Institute and Center Directors engage in additional discussions and priority setting, and the NIH Director makes the final funding decisions. Dr. Smith noted that it can take as long as 18 months between the initial submission of concepts and the launch of initiatives.

To be competitive in this process, the Institute has established a trans-NIDDK Common Fund Working Group, comprising staff from the Divisions, for the early development of scientifically compelling proposals that are consistent with NIDDK research goals and Common Fund criteria. This Working Group will discuss and fine-tune concepts prior to the annual request for proposals from the NIH Director. It is also possible that ideas

generated for the Common Fund could be useful in the NIDDK's own program development. Dr. Smith underscored that the NIDDK is seeking broad input from the Advisory Council and others in the research community as it develops concepts for submission to the Common Fund. Planning is now under way for the use of Common Fund resources in FY 2015, which begins October 1, 2014.

Dr. Smith introduced Dr. Olivier Blondel to present some of the very preliminary ideas currently being discussed by the Trans-NIDDK Common Fund Working Group. He encouraged Council discussion and comments.

B. Initiative Development Report of the Trans-NIDDK Common Fund Working Group

Dr. Olivier Blondel, Director, Endocrine Systems Biology Program, Division of Diabetes, Endocrinology and Metabolic Diseases

On behalf of the Trans-NIDDK Common Fund Working Group, Dr. Blondel provided a brief progress report on the Group's efforts over the prior six months to discuss and refine ideas suggested by NIDDK Program Directors. Dr. Blondel described the following two concepts, which have been discussed most extensively.

- ***Synthetic Biology (SynBio)--Developing Tools and Strategies for the Systematic Engineering of Cells:*** SynBio refers to the construction of biological functions using the combination of genetically-encoded functional parts and cell signaling circuits. An initiative based on SynBio strategies could lead to the safe reprogramming of deficient/diseased pathways; the development of therapeutic cells that respond to a disease or metabolic environment; control of biological functions *in-vivo*--remotely and non-invasively; and tools to study the behavior of signaling circuits *in-vivo* to gain new insights into complex biological or disease pathways. Dr. Blondel provided an example of the generation of therapeutic cells in the cancer field, where researchers are engineering, and implanting into patients, T-cells that can recognize specific tumors. Dr. Blondel also gave examples of the ways that SynBio techniques can be used in laboratory studies to engineer cells to act in ways they don't naturally act, while remaining compatible with life. Researchers have already used these techniques to regulate homeostasis in mouse models of type 2 diabetes and uric acid abnormalities. Dr. Blondel noted that the SynBio concept appears to be well-suited to the Common Fund because it would enable the full potential of cell engineering to be harnessed through the creation of standardized toolkits of molecules and circuits. With such toolkits, investigators could systematically design and manipulate cell function in the laboratory. These efforts could have broad application across the full range of biomedical sciences. (Lead: Dr. Olivier Blondel, NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases)

- ***The Mechanome--Cellular Mechanics and Mechanotransduction in Tissue Development, Maintenance, and Repair:*** An initiative could provide a better understanding of the ways that cellular mechanics and mechanotransduction pathways contribute to tissue development, maintenance, pathophysiology, and tissue repair. Mechanical signals could facilitate the creation of complex organic structures *in vitro* to further laboratory research. The use of mechanical signals in engineered tissue-specific chips--which represent units of human organs such as the liver or kidney--could increase knowledge about cell differentiation and could further efforts to combat organ-damaging diseases. Dr. Blondel said that one example would be the use of these techniques to understand and find ways to interdict the destructive tissue fibrosis that occurs in many disease states. Also, maps could be developed of common pathways and networks that regulate mechanics-induced changes in gene expression across different cell and tissue types. (Lead: Dr. Michael J. Grey, NIDDK Division of Digestive Diseases and Nutrition)

Dr. Blondel also noted the following concepts that were discussed by the Working Group.

- ***Targeted Therapy in Humans:*** An initiative could develop delivery technologies such as targeted microbubbles, magnetic nanoparticles, or programmable nanomaterials for monitoring, diagnosis and treatment of diseases. (Lead: Dr. Michael Flessner, NIDDK Division of Kidney, Urologic and Hematologic Diseases)

- ***Mapping the Human Vasculature:*** Creating an atlas of the human vasculature could enable researchers to look at the molecular signature of different tissues in both health and disease in order to facilitate the development of tissue-targeted therapeutic strategies. (Lead: Dr. Olivier Blondel, NIDDK Division of Diabetes, Endocrinology and Metabolic Diseases)

- ***3D Nucleome:*** the goal would be a systematic integration of the three-dimensional architecture of the interphase nucleus, the transcriptional landscape, and the consequent phenotypic variation in cellular differentiation and disease, in order to understand how changes in the genome/epigenome regulate the architecture of the nucleus and the transcription equilibrium. The program would help develop maps of the interphase nucleus (using chromosome conformation capture technology and super-resolution imaging) across different cell types and physiological states. This would include developing experimental tools, bioinformatics resources, and reference database. (Lead: Staff at the National Cancer Institute developed this proposal and NIDDK agreed to serve as a co-sponsor, but would likely recommend some sculpting of the focus and scope if given the opportunity to do so in the context of a co-leadership role)

Dr. Blondel said that the NIDDK plan is to submit the SynBio concept for possible support under the Common Fund, and also, to support the concept of the 3D Nucleome proposed by the National Cancer Institute, which originated that idea.

Council Questions and Discussion

Usefulness of Common Fund Initiatives: *Are there any long-term analyses regarding the impacts of Common Fund investments on the NIDDK mission and other research? Databases are not useful if there is no support for regular research grants (R01 grants) to use them for generating discoveries or new therapies. It would be advisable to conduct such analyses, as well as to reserve some funds for more detailed proof-of-concept of the ideas developed.* Dr. Smith responded that Common Fund programs undergo an internal and external peer-review analysis as to whether they have accomplished their goals. He also gave some examples of the value of Common Fund projects. The Molecular Libraries initiative has evolved to include drug development. The pharmaceutical industry is requesting that assays be screened on the Molecular Libraries collections because they are more diverse than their own libraries. A number of compounds already being used in human beings are directly related to that program, and are germane to the NIDDK mission. The Epigenomics Program is gaining important insights into autoimmunity and new targets for therapeutics relevant to the NIDDK's mission. The Program shows promise of revealing parts of the genetic landscape that are undiscoverable with standard techniques. It may help to decipher some extremely complex diseases such as type 2 diabetes. NIDDK grantees are taking advantage of tools available through the Common Fund to conduct highly promising research in terms of histone-modifying enzymes and their roles in diabetes and fatty liver disease. NIDDK grantees are likewise benefiting from the Metabolomics Program and the Human Microbiome Project. Dr. Smith emphasized that the Common Fund has been established by the Congress, which provides funds to be used specifically for that Program, and not for other purposes. Hence, the NIDDK and other Institutes have an opportunity to take advantage of the availability of these funds through a highly consultative and competitive process that culminates in decisions by the NIH Director.

Regenerative Medicine: *With regard to the cellular engineering concept, does the scope include tissue engineering in regenerative medicine? If so, is it possible that cellular engineering could move in the direction of replacing whole organs?* Dr. Blondel responded that there are two steps that need to be taken--engineering and reprogramming. The proposed concept is focused on the first step, which is to build libraries of functional circuits that are compatible with the cell types of tissues into which they would be placed so that they would not disrupt regular biological processes. Extensive additional work would then need to be done before researchers could proceed to thinking about the second step of actually using those tools to accomplish cell reprogramming for purposes of regenerative medicine.

Imaging: *In addition to the proposed concepts, which are excellent, have the NIH Institutes begun to look at new imaging tools as a possible trans-disciplinary initiative?* Dr. Smith responded that imaging is within the mission of the National Institute of Biomedical Imaging and Bioengineering, so it is not possible to propose it as a stand-alone concept that would meet the eligibility criteria of the Common Fund. Occasionally, it has been possible to include imaging as a component of a Common Fund initiative, such as in

the Epigenomics Program. It would also likely be a part of the proposed concept on the 3D nucleon.

Mechanical Forces Concept: *This is an excellent concept to submit for the Common Fund. The ability of mechanical forces to promote the differentiation of human cells or stem cells in the laboratory provides a new model system that could be applied across all organs and tissues addressed by NIDDK research. Work on mechanical forces could enhance or replace the use of mouse models, whose complexity can make it difficult to interpret basic phenomena. One can imagine the ability to simulate in the laboratory different parts of the intestinal and renal systems, which would permit easier experiments than with the mouse as a whole. The study of mechanical forces that are physiologic to cells is also an area that has been under-explored at the basic level.* Dr. Smith commented that input along these lines is very helpful because the initial concepts undergo considerable development and improvement based on comments received. Undoubtedly, for example, the 3D nucleon concept would be refined and tightened to determine the most important components for investments. To that end, input from Council members would be very valuable. In terms of the Mechanome concept, the NIH is already partnering with the Defense Advanced Research Projects Agency (DARPA); therefore, the NIH Director is clearly interested in this topic.

Dr. Germino closed the discussion by noting that the newly established Trans-NIDDK Common Fund Working Group started its concept-development process in December. The NIDDK hopes that this process will become a full-year endeavor in the future. Dr. Germino emphasized the importance of submitting concepts that meet the Common Fund criteria. The ideas must go beyond what the NIDDK could do on its own, and they need to be catalytic and transformative. There is a great deal of strategy that goes into this process. Moreover, there is a reasonably high likelihood that unaccepted concepts will be greatly discounted if resubmitted. For that reason, initial submissions must be robust. The NIDDK welcomes ideas as it considers and refines concepts, and negotiates with other Institutes regarding joint submissions.

VII. UPDATE FROM THE NIH CENTER FOR SCIENTIFIC REVIEW (CSR)
Dr. Richard Nakamura, Director

Dr. Rodgers introduced Dr. Richard Nakamura, who was named Director of the NIH Center for Scientific Review (CSR) in December 2012, following his service as Acting Director since September of 2011. In his new position, Dr. Nakamura is leading the CSR in organizing and managing the work of the first-level, external NIH Scientific Review Groups, known as Study Sections, which perform the initial peer review for over 70 percent of the research grant applications submitted to the NIH. The scores the Study Sections give to these applications are then considered in second-level peer review performed by the external experts of the relevant National Advisory Councils. Funding decisions are made by the Institutes and Centers at the end of this two-level peer review process. Dr. Rodgers commented that Dr. Nakamura accepted the CSR top leadership

position at a particularly challenging time. Currently, the research community is extremely concerned that only about 10 percent of grants reviewed through the Center can be funded at any given Council round, due largely to the disparity between the number of grant applications received and the funds available to support them. Dr. Rodgers said that, prior to becoming Director of CSR, Dr. Nakamura served for 32 years in the National Institute of Mental Health, in the positions including Scientific Director, Deputy Director, and Acting Director. A recipient of the prestigious Presidential Rank Award, Dr. Nakamura earned his Ph.D. in psychology from the State University of New York at Stony Brook. His areas of expertise include cognitive and comparative neurosciences, science policy, and resource-allocation issues.

Dr. Nakamura described the responsibilities of the CSR as the portal for grant applications from the extramural research world. The CSR mission is to ensure that grant applications receive fair, independent, expert, and timely peer reviews--free from inappropriate influences--so that the NIH as a whole can fund the most promising research. Dr. Nakamura noted that he enjoys working with the leadership of the NIDDK--an Institute that strives to fund the very best science to combat the many burdensome diseases within its broad research mission.

The CSR receives all grant applications to the NIH, whether they are submitted on the sole initiative of applicants or in response to an NIH solicitation of grants for a specific research initiative. The CSR refers these applications for review to either CSR-organized initial review groups, called Study Sections, or to the review components of the relevant NIH Institutes or Centers.

Applications reviewed by a CSR Study Section typically receive a score, called a priority score, and a written critique called a "Summary Statement." The priority scores are also translated into percentiles to normalize the output of all Study Sections, and to standardize the distance between scores. The numeric ratings and critiques given to applications inform investigators of the results of the review process, and enable the Institutes and Centers to make comparisons among applications. The Institutes and Centers share this information with their respective National Advisory Councils, which perform a second-level peer review before the Institutes and Centers make funding decisions. Dr. Nakamura noted that, in light of reduced resources, the strategic goals of the Institutes and Centers are increasingly guiding these decisions. The Institutes, Centers, and the CSR follow the progress and results of funded research, including publications and citations.

The CSR provides administrative management for the reviews of about 58,000 of the 85,000 applications it receives annually. In FY 2011, this review process involved 16,000 reviewers, 230 Scientific Review Officers, and 1,465 review meetings. As of last year, the CSR provided reviews for 68.8 percent of grant applications assigned to the NIDDK for potential funding; other external peer reviews of NIDDK-relevant applications were organized and conducted under the auspices of the NIDDK Review Branch.

Dr. Nakamura said that the likelihood that any grant application to the NIH will be funded in Fiscal Year 2013 is about 10 percent. Dr. Nakamura noted that the CSR is constantly

assessing the quality of peer review and striving to make improvements in the process. He commented on the following issues that are being addressed in FY 2013.

Compression of Scores

The CSR has recognized that, over time, peer review scores have become compressed, which makes it difficult to reach funding decisions among grant applications that differ by only a few points. To help decompress scores, NIH adopted an expanded 1-9 scoring system in 2009, and CSR in conjunction with the NIH Office of Extramural Research provided additional guidance to reviewers about the meaning of the scores. One unintended consequence of providing this guidance regarding the meaning of scores was that reviewers erroneously perceived an inverse relationship between the underlying strength or significance of an application and its number of weaknesses—they often wanted to quantify weaknesses and then use this information to assign a score. The CSR consulted on this issue with the Review Policy Committee, the Extramural Program Management Committee, the Extramural Activities Working Group, and incoming Study Section Chairs. As a result, the CSR took steps to emphasize the importance of the "overall impact" of an application, and to make clear that both strengths and weaknesses could be found in applications with high, medium or low impact scores. "Overall impact" is defined as the likelihood for a project to exert a sustained, powerful influence on the research field(s) involved. The CSR advised reviewers that, for example, an application with good medium impact could reasonably be given a score of 5. This guidance helped Study Section members to better anchor their scores, and the CSR has noted greater score decompression following these changes. Nonetheless, there is not a smooth, normal distribution of final scores--a fact that makes the Summary Statement narrative extremely important. The CSR will continue to address issues surrounding the scoring process.

Diversity and Fairness

Dr. Nakamura said that the CSR is built on a foundation of diversity and fairness in peer review. The entire NIH was therefore very concerned about the findings of Ginther, *et al*. in the article "Race, Ethnicity, and NIH Research Awards," which was published in *Science* in 2011 (http://www.sciencemag.org/content/333/6045/1015.full).

This study showed that applications with strong priority scores were equally likely to be funded regardless of race. However, it also showed that African Americans were less likely to receive NIH research funding compared to Whites (after the authors controlled for "the applicant's educational background, country of origin, training, previous research awards, publication record, and employer characteristics"). Dr. Nakamura noted that the Ginther article offered different possibilities to explain the data on award probability, but two that stood out were the possibility of bias in peer review and the possibility of cumulative disadvantage experienced by African American scientists.

Dr. Nakamura said that the NIH Director, Dr. Francis Collins, and his Principal Deputy Director, Dr. Lawrence Tabak, brought the issues raised by the Ginther article to the Advisory Committee to the Director, NIH (ACD), which made a number of

recommendations. Dr. Nakamura reported that progress is being made on implementing these recommendations. For example, external experts are serving on a newly formed Subcommittee on Peer Review within the ACD's Workgroup on Diversity. Dr. Nakamura is a co-chair of the new Subcommittee. The CSR is encouraging peer review committees to discuss applications for which there is a high discrepancy in scoring among reviewers. Efforts are under way to develop and test hypotheses regarding scoring, and to conduct an analysis of the scoring of applications without compromising confidentiality. In addition, NIH is enhancing diversity awareness training and will perform an analysis to determine the effects of the training.

The CSR is also working with Dr. Tabak to increase the representation of minorities--particularly of African American and Hispanic scientists--on the Scientific Review Groups it organizes. Since December 2011, the percentage of minority reviewers has increased from 8.1 percent to 10.1 percent. Since that time, the numbers of African American and Hispanic reviewers have increased, respectively, by approximately 42 percent and 22 percent. Dr. Nakamura pointed out that the latter percentages represent the reversal of a recent trend in declining numbers of reviewers in these two groups.

Ensuring High-Quality Reviews through Training and Mentorship

Dr. Nakamura said that the CSR works very hard to ensure high quality in the reviews rendered by individuals who serve on peer review groups. Reviewers are oriented to the peer review system before they perform their reviews. The CSR has developed an Early Career Reviewer Program to train and mentor qualified scientists who lack significant review experience; to help emerging researchers advance their careers by exposing them to review experience; and to enrich the existing pool of reviewers. To be eligible for this program, a scientist must not have reviewed for the NIH beyond a mail review and must demonstrate scientific qualifications such as a faculty appointment or active independent research program. Prior NIH funding is not a requirement for the program. Thus far, over 2,100 individuals have been accepted into this program. Nearly 700 of these Early Career Reviewers have served on a Study Section; 223 Study Sections have included these reviewers on their rosters; and 32 percent of these reviewers have been under-represented minority scientists. Dr. Nakamura said that a survey of individuals who have participated in the program found that most considered the experience useful, would recommend the program to a colleague, and reported being in a better position to write their own grant applications. He said that individuals interested in participating in this program should send their current *curriculum vitae* and a list of terms that describe their scientific expertise to the CSR (CSRearlycareerreviewer@mail.nih.gov). If the CSR determines that they are eligible, their names will be placed into the Program's database and they will be invited to serve when their expertise is needed.

Justification for Changes in Peer Review System

Dr. Nakamura expressed his belief that there should be a good justification for changes in the peer review system, advance notice of changes and, where possible, experiments that can inform change. The CSR is interested in answering several questions, for example: Is it

possible to measure differences in the quality of applications across Study Sections? Is there a random distribution of high-quality applications and reviewers across Study Sections? What can the CSR do to make the critiques of the peer reviewers contained in the Summary Statements more informative, coherent, and useful? Can the CSR create more useful tools for applicants and reviewers? What additional steps can the CSR take to maintain diversity and reduce disparities in awards for applicants from minority groups? How can the CSR develop the science of peer review so that the quality of the process and the assessments are continually improved? Dr. Nakamura said that the CSR is working to find ways that Principal Investigators can have more input into the peer review process, such as by indicating the Study Sections they consider most relevant for review of their applications. The CSR is also working to provide applicants and the Institutes with better advice and service, including the identification of score-driving issues from the perspective of reviewers.

In closing, Dr. Nakamura said that the CSR can aid the deliberations of program staff, Council members and Institute leaders with respect to funding issues by improving the way that the views of peer review committees are reflected. He expressed his appreciation for the support of the Institutes and Centers, their Council members, the scientists who serve on peer review panels, and the NIH Scientific Review Officers.

Dr. Rodgers thanked Dr. Nakamura for his excellent presentation.

Council Questions and Discussion

Outreach: *Does the CSR engage in outreach efforts to attract reviewers?* Dr. Nakamura replied that the CSR reaches out to many organizations, particularly under-represented minority institutions, and also reminds NIH program staff to engage in outreach when they attend meetings and conferences. The CSR can also offer a lighter review schedule to attract reviewers. Moreover, the CSR is working to advance additional review platforms, such as electronic review, as well as meetings that are assisted by telephone, video and Internet communications. Review formats modeled on editorial boards have also been piloted.

Amendments/Resubmissions: *Does it really help an investigator when he or she is advised by a Study Section to modify aspects of an application and reapply--especially if a new set of reviewers may identify new issues in the amended application? There is no assurance that scores will be better, and the process is very time-consuming and frustrating for investigators. Do the current review criteria encourage reviewers to merely count mistakes or flaws?* Dr. Nakamura commented on the process for revising and resubmitting applications. He said that the NIH had observed an alarming trend in 2008 whereby initial applications--A0 applications--had become the least common form of award relative to applications that underwent a first-round and second-round amendment/resubmission process--A1 and A2 applications, respectively. The data suggested the unintended formation of a queue-like process in which review committees were expecting individuals to wait for their turn to obtain a good score. Importantly, the NIH determined that the resubmission process did not significantly affect outcomes in

terms of the funding of new *vs.* established investigators, or the relative funding probability of highly meritorious applications, whose investigators were simply waiting a longer "time to award" before they could begin their research projects. After considerable deliberation, the NIH decided to sunset the A2 amendment/resubmission process in the hope that applicants would not have to "wait in line" to be funded. After this change, the A0 awards rebounded. Dr. Nakamura said that he has not yet received the most recent analysis on this issue, but there still seems to be some tendency among reviewers to give a little more credit to an applicant at the A1 level than at the A0 level. Regarding the review criteria, Dr. Nakamura said that the most recent modifications were intended to promote more meaningful reviews by emphasizing the importance of overall impact; however, if reviewers want to focus on identifying "weaknesses," that can encourage more A1 resubmissions, which will give applicants another chance at possible funding. Although the research community generally favors the amendment/resubmission process, Dr. Nakamura said that the CSR National Advisory Council has suggested that he broach with the NIH leadership the possible consideration of completely eliminating amended applications, along with taking a more liberal view about what constitutes a new application. If amended applications were no longer accepted, applicants would have an early, definite answer about their ability to compete successfully for funding. They would all be on a level playing field, and that would eliminate frustrations about the review of amended applications by new sets of reviewers. These ideas about the process will likely be broadly discussed before any consensus would be reached about possible changes to the present system.

Sharing Peer Review Results with Other Funding Sources: *Has the CSR or the NIH considered expanding the Center's mission and scope? Specifically, given the high regard in which the NIH peer review system is generally held, would it be possible for the CSR to share peer review results with foundations, industry, and others to attract potential funding sources for these applications beyond the NIH? To this end, is it possible to re-engage the National Health Council, which previously tried to facilitate this type of arrangement?* Dr. Nakamura agreed that it would be helpful if--at the active request of a Principal Investigator--one or more external organizations could serve as a depository for unfunded, NIH peer-reviewed applications so that other organizations beyond the NIH might come forward to fund them. The Foundation for the NIH has identified some organizations who are interested in benefiting from the NIH peer review process in this way; however, other foundations are reluctant to say that they would rely on the Government for assessments that would guide their funding decisions. Although the NIH is not permitted to provide peer review information directly to external organizations, the Foundation is asking Principal Investigators if they want to share information about their own applications, which they are free to do. Another issue is that a number of countries would like to co-fund applications with the NIH, particularly when an investigator from another country is collaborating with one from the U.S. However, the NIH has been advised that such an arrangement would require a legislative change.

Realistic Critiques: *Can reviewers be encouraged to be more explicit regarding an applicant's realistic chances of being funded if he or she makes the changes suggested in a*

peer review critique? Dr. Nakamura responded that CSR has found that reviewers are very reluctant to discourage applicants from amending and resubmitting applications, even if their chances of eventual funding are perceived to be very low. Moreover, the CSR has been advised that reviewers should not try to mentor Principal Investigators.

Drawing Investigators To Service on Peer Review Panels: *How can the NIH foster a culture within the scientific community in which individuals want to serve on peer review panels because such service is an honor and a duty, as well as a needed model for younger scientists? What makes a good reviewer? Are the best scientists turning down the opportunity to serve on NIH Study Sections, and if so, how can that trend be reversed? Should the NIH provide incentives or make it mandatory for established investigators to serve on Study Sections? Could the NIH follow the incentivizing model of some journal editors who publish the names of the top peer reviewers of manuscripts and honor them with awards? Could the Presidents of research institutions and societies receive information on peer review service so that they could provide recognition to those within their organizations who do serve, as well as additional encouragement to those who have not yet served? Is there a bias against potential reviewers based on their academic rank? Is it important to bring to a review panel individuals who not only have a broad perspective, but also those skilled in analyzing details—so that a combination of thought processes and intellectual talents creates a group dynamic that is likely to culminate in a high quality review?* Dr. Nakamura said that a problem impeding the peer review service of individuals who are considered the best and most experienced scientists is that they are very busy. They have heavy demands on their services and, at any time, they also tend to be working on more than one research application of their own. Usually, the scientists who decline because of time constraints will agree to serve at some point in the future. However, about a third of Principal Investigators who receive NIH awards never agree to serve on Study Sections. Serving on peer review panels when invited to do so is entirely voluntary, and there is no consequence for those who decline. Dr. Nakamura said that, whenever he meets with scientific organizations and societies, he encourages them to underscore the importance of the peer review infrastructure with their members. With respect to the issue of academic rank of reviewers, Dr. Nakamura said that the CSR strives to keep the academic rank of reviewers high, but recognizes that there is a cohort of faculty members who are not yet at a senior level, but who are phenomenally talented. On a selective basis, these individuals can contribute to the peer review process. Scientific Review Officers are constantly looking for assistant professors with awards and other positive indicators who can be brought in as *ad hoc* reviewers. As to the attributes of a good reviewer, Dr. Nakamura commented that the best scientists are not necessarily the best reviewers, although these characteristics can overlap. The more that the CSR can learn about constructing quality reviews, the better off the research community will be. Right now, the CSR is mainly trying to address this issue by recruiting and developing very high quality and experienced Study Section Chairs and Scientific Review Officers. The CSR has been fortunate in identifying and enlisting the services of such individuals.

Effects of Changes in Application Length: *Are there any data that show the effect of shortened grant applications on the funding success of new vs. established scientists?* Dr.

Nakamura responded that the CSR is not collecting data along those lines. However, the NIH has created a process to help ensure that new investigators receive a certain proportion of awards.

Evaluation Measures: *Regarding the science of peer review, what are the measures of quality in this process—reliability, consistency, distal outcomes, impact of research funded?* Dr. Nakamura said that there is a huge debate on this subject. The CSR is looking at different ways to conduct scientific evaluations, not only within peer review panels, but also across Study Sections. Some questions the CSR would like to answer include: What factors affect the outcomes of review? How rapidly do ideas turn over, and is high turnover a good thing? How can one measure connectivity among scientists, including so-called "old-boy" or pedigree networks, and does this connectivity link to review outcomes? How can the CSR identify review panels or processes that are not working well, so that corrective action can be taken? Dr. Nakamura pointed out that long-term results alone, such as those obtained through bibliometrics, do not enable needed short-term adjustments in the peer review process. He said that the primary standard the CSR will use in weighing the results of various evaluations will be the expert assessments of scientists, not just numeric data.

Unduly Influential Reviewers: *Is there a way to determine the degree to which the scoring of an application is influenced by just a few reviewers who carefully read it in detail, who have strong opinions, and who try to sway the judgment of other reviewers who are less familiar with an application?* Dr. Nakamura said that the CSR selects and trains Study Section Chairs and Scientific Review Officers in the hope that they will be broad thinkers who are well aware that one or two reviewers should not impose their views on other panel members. The CSR is fortunate to have many excellent individuals in these positions. The Center also sends representatives to a significant number of review meetings to observe the way that situations, such as the one described, are handled. Problematic reviewers are no longer invited to serve.

Issues of Best Science, Relevance and Public Perceptions: *How does the CSR determine that the NIH is funding the best science and then make that known to the Congress and to others who make research funding decisions for the agency? Also, does the NIH sufficiently emphasize the importance of "relevance," that is, the ability of a scientific project to transform biomedical research or the well-being of patients?* Dr. Nakamura said most observers would agree that, overall, the NIH is funding excellent science that advances knowledge and improves human health. The issue is really whether some research proposals would contribute more in this regard than some others, and the NIH does its best to identify and fund the most promising research. Dr. Nakamura said other countries--such as China, Japan, and Sweden--are very impressed with the scientific return from the NIH process for funding research since the end of the Second World War. They are seeking to increase their long-term funding investments in science through similar review and funding processes in their own countries. They believe that the future of the next generation is dependent on their ability to build and sustain top-notch scientific and technologic capabilities. However, several of these countries are not following the U.S.

model of fostering independent thinking in peer review, which has been an underpinning of U.S. scientific accomplishments. The failure or near-failure of some corporate entities in the U.S. should also teach the worldwide scientific establishment that both quality control and receptivity to change are vital to sustaining robust endeavors. Regarding the issue of relevance, Dr. Nakamura agreed that it is extremely important for the NIH to cite examples of research studies that are relevant to or have already led to progress in advancing further scientific endeavors or to combating diseases. This is particularly the case for fundamental research that may appear esoteric without explanation. Elaborating on the relevance of research is a major way to foster the positive perception of science by the general public and by policy makers.

VIII. SCIENTIFIC PRESENTATION: Genetics of Type 2 Diabetes and Metabolic Syndrome--Lessons from a Founder Population
Dr. Shuldiner

Council Member Dr. Alan Shuldiner is the John Whitehurst Professor of Medicine; Associate Dean for Personalized Medicine; Director of the Program in Personalized Medicine; and Head of the Division of Endocrinology, Diabetes and Nutrition at the University of Maryland School of Medicine. After receiving an M.D. from Harvard Medical School, Dr. Shuldiner completed his residency in Medicine at Columbia-Presbyterian Hospital in New York and a Fellowship in Endocrinology within the Diabetes Branch at the NIDDK, which has supported his research since 1996. His major research interests are the molecular basis and genetics of type 2 diabetes, obesity, and insulin resistance. He has published over 200 peer-reviewed articles, and his research is supported by NIH, the American Diabetes Association, and the Juvenile Diabetes Foundation.

IX. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1403 grant applications, requesting support of $ 422,995,257 were reviewed for consideration at the May 15, 2013 meeting. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1020 applications requesting $ 286,007,233 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 May 15, 2013 meeting.

X. ADJOURNMENT
Dr. Rodgers

Dr. Rodgers expressed appreciation to all the presenters and discussants. He thanked the Council members for their attendance and valuable input. There being no other business the 192nd meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m., May 15, 2013.

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