

**Meeting Minutes**  
**Department of Health and Human Services**  
**National Institutes of Health**  
**National Institute of Diabetes and Digestive and Kidney Disease**  
**February 13, 2013**

**I. CALL TO ORDER**

*Dr. Rodgers*

Dr. Griffin P. Rodgers, Director, NIDDK, called to order the 191<sup>st</sup> meeting of the National Diabetes and Digestive and Kidney Diseases Advisory Council at 8:30 a.m., Wednesday, February 13, 2013, in Building 31, C-Wing, Conference Room 10, National Institutes of Health.

**A. ATTENDANCE – COUNCIL MEMBERS PRESENT**

Dr. Domenico Accili  
Dr. Sharon Anderson  
Dr. Gopal Badlani  
Dr. Judy Cho  
Ms. Jane Holt  
Ms. Judy M. Hunt  
Dr. Francine R. Kaufman  
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. 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  
Adkins, Ron – CSR  
Agodoa, Lawrence – NIDDK  
Akolkar, Beena – NIDDK  
Andersen, Dana – NIDDK  
Arreaza-Rubin, Guillermo – NIDDK  
Barnard, Michele – NIDDK  
Baruchin, Andrea – FDN for the NIH  
Bavendam, Tamara – NIDDK  
Begum, Najma – NIDDK  
Beverly, Kevin – Soc. & Scien. Sys. Inc.  
Bishop, Terry – NIDDK

Bleasdale, John – CSR  
Blondel, Olivier – NIDDK  
Bourque, Sharon – NIDDK  
Buchanan, Sarah – Health & Med. Counsel of Washington  
Calvo, Francisco – NIDDK  
Carrera, Krysten – NIDDK  
Carrington, Jill – NIDDK  
Castle, Arthur – NIDDK  
Cerio, Rebecca – NIDDK  
Connaughton, John – NIDDK  
Cox, Lisa – American Diabetes Assoc.  
Curtis, Leslie – NIDDK

Dayal, Sandeep – NIDDK  
 Densmore, Christine – NIDDK  
 Dirks, Dale – The NephCure FDN  
 Doherty, Dee – NIDDK  
 Donohue, Patrick – NIDDK  
 Doo, Edward – NIDDK  
 Drew, Devon – NIDDK  
 Dugan, Emily – NIDDK  
 Eggerman, Thomas – NIDDK  
 Evans, Mary – NIDDK  
 Everhart, James – NIDDK  
 Farishian, Richard – NIDDK  
 Feld, Carol – NIDDK  
 Flessner, Michael – NIDDK  
 Fleischhacker, Sheila – NIDDK  
 Fonville, Olaf – NIDDK  
 Fradkin, Judith – NIDDK  
 Froyd, Erica – Lewis-Burke Associates  
 Gallivan, Joanne – NIDDK  
 Gansheroff, Lisa – NIDDK  
 Garfield, Sanford – NIDDK  
 Garofalo, Robert – CSR  
 Giambarresi, Leo – Amer. Urol. Assoc.  
 Goter-Robinson, Carol – NIDDK  
 Graves, Reed – CSR  
 Guo, Xiaodu – NIDDK  
 Haft, Carol – NIDDK  
 Hall, Kathleen – Health & Med. Counsel of  
 Washington  
 Hamilton, Frank – NIDDK  
 Harris, Mary – NIDDK  
 Hetkowski, Kimberley – NIDDK  
 Homes, Melynda – Tech. Resources.  
 International  
 Hoofnagle, Jay – NIDDK  
 Hoover, Camille – NIDDK  
 Hubbard, Van – NIDDK  
 Hunter, Christine – NIDDK  
 Hyde, James – NIDDK  
 James, Stephen – NIDDK  
 Jones, Teresa – NIDDK  
 Karp, Robert – NIDDK  
 Karimbakas, Joanne – NIDDK  
 Ketchum, Christian – NIDDK  
 Kimmel, Paul – NIDDK  
 Kirkali, Ziya – NIDDK  
 Kranzfelder, Kathy – NIDDK  
 Kuczmarski, Robert – NIDDK  
 Kusek, John – NIDDK  
 Lescheck, Ellen – NIDDK  
 Linder, Barbara – NIDDK  
 Malik, Karl – NIDDK  
 Malozowski, Saul – NIDDK  
 Margolis, Ronald – NIDDK  
 Martey, Louis – NIDDK  
 Martinez, Winnie – NIDDK  
 Maruvada, Padma – NIDDK  
 Mascone, Lisa – NIDDK  
 McBryde, Kevin – NIDDK  
 McKeon, Catherine – NIDDK  
 Miller, David – NIDDK  
 Miller, Megan – NIDDK  
 Mowery, Penny – NIDDK  
 Mullins, Christopher – NIDDK  
 Newman, Eileen – NIDDK  
 Nguyen, Van – NIDDK  
 Nurik, Jody – NIDDK  
 Panniers, Richard – CSR  
 Patel, D.G. – NIDDK  
 Pawlyk, Aaron – NIDDK  
 Pellnitz, Lori – SRI International  
 Perry-Jones, Aretina – NIDDK  
 Pike, Robert – NIDDK  
 Podskalny, Judith – NIDDK  
 Rankin, Tracy – NIDDK  
 Rasooly, Rebekah – NIDDK  
 Redmond, Randy – NIDDK  
 Reiter, Amy – NIDDK  
 Rosenberg, Mary Kay – NIDDK  
 Rosendorf, Marilyn – NIDDK  
 Rushing, Paul – NIDDK  
 Salaita, Christine – NIDDK  
 Salomon, Karen – NIDDK  
 Sanovich, Elena – NIDDK  
 Sato, Sheryl – NIDDK  
 Savage, Peter – NIDDK  
 Scanlon, Elizabeth – NIDDK  
 Sechi, Salvatore – NIDDK  
 Sheard, Nancy – CSR  
 Shepherd, Aliencia – NIDDK  
 Sherker, Averell – NIDDK  
 Silva, Corrine – NIDDK  
 Smith, Jill – NIDDK  
 Smith, Philip – NIDDK  
 Spain, Lisa – NIDDK  
 Star, Robert – NIDDK  
 Staten, Myrlene – NIDDK  
 Tatham, Thomas – NIDDK  
 Torrance, Rebecca – NIDDK  
 Van Raaphorst, Rebekah – NIDDK  
 Wallace, Julie – NIDDK  
 Wellner, Robert – NIDDK  
 Wright, Daniel – NIDDK  
 Wright, Elizabeth – NIDDK  
 Yanovski, Susan – NIDDK  
 Zeeshan, Ali – Physicians Committee for  
 Responsible Medicine

## C. ANNOUNCEMENTS

Dr. Rodgers made the following announcements:

### New Council Members

Dr. Rodgers welcomed four new Council members and expressed his appreciation to them for taking time from their busy schedules to advise the NIDDK.

Joining the Subcouncil of the Division of Diabetes, Endocrinology and Metabolic Diseases (DEM) is one new member:

***Dr. Bruce Spiegelman*** is the Stanley J. Korsmeyer Professor of Cell Biology and Medicine at Harvard Medical School, and also Professor of Cancer Biology at the Dana-Farber Cancer Institute. Dr. Spiegelman completed his postdoctoral work at the Massachusetts Institute of Technology following receipt of a Ph.D. from Princeton University. Dr. Spiegelman's research is focused on the regulation of energy homeostasis in mammals, primarily at the level of gene transcription. This area includes fat cell development, control of metabolic rates, and pathways of glucose and lipid metabolism. Possible applications for his research include the development of new therapies for diabetes, obesity, muscular diseases, and neurodegenerative diseases. Widely published, Dr. Spiegelman is a long-standing NIDDK grantee. Among his many accomplishments, he a MERIT award recipient and he has been elected to the National Academy of Sciences. Dr. Spiegelman was not able to attend the meeting because of a long-standing prior commitment.

Joining the Subcouncil of the Division of Kidney, Urologic and Hematologic Diseases (KUH) are three new members:

***Dr. Sharon Anderson*** is a member of the Division of Nephrology and Hypertension, and Professor and Vice Chair, Department of Medicine, Oregon Health and Science University (OHSU). She also serves as Chief of Medicine at the Portland Veterans Affairs Medical Center. Dr. Anderson earned her M.D. degree from Louisiana State University Medical Center. Following an internal medicine residency at OHSU, she completed her clinical nephrology training at the Beth Israel Hospital, and her research training at the Brigham and Women's Hospital, Harvard Medical School. Dr. Anderson is an active clinician, educator, and researcher. Her research interests include the progression of chronic kidney disease, with an emphasis on polycystic kidney disease, diabetic nephropathy, and the pathophysiology of the aging kidney. She has received funding not only from NIH, but also other granting agencies, and she has published extensively. As an educator, she is former director of the renal fellowship and Principal Investigator on the nephrology training grant at OHSU, and has won many teaching awards. Dr. Anderson is the first woman elected to the Council of the American Society of Nephrology, and its first woman President. She is past Chair of the Nephrology Board of the American Board of Internal Medicine (ABIM). She has also served as Chair of the NIH General Medicine B and Pathobiology of Kidney Disease Study Sections.

**Dr. Gopal Badlani** is Professor of Urology, Vice Chair of Clinical Affairs, and Director of the Urogynecology Regenerative Medicine Program at the Wake Forest School of Medicine in Winston-Salem, North Carolina. Dr. Badlani earned his M.D. at Bombay University, Topiwala Medical College in India. He then completed his urological training at Long Island Jewish Medical Center in New York, and his fellowship at Baylor University in Texas. Dr. Badlani is an internationally renowned expert in voiding dysfunction. His specialties include urinary incontinence associated with pelvic organ prolapse in women, and prostate surgery and neurological disease in men. His clinical interests more generally include incontinence, urology, and reconstructive urology. He has completed a number of trials for new, minimally invasive treatments for benign prostate obstruction, and is the author and coauthor on many publications. Dr. Badlani currently serves as Secretary of the American Urological Association. He is also the former President of the Endourological Society and the Association of Indian Urologists in North America. In addition, Dr. Badlani has served on the Boards of the International Volunteers in Urology, the National Kidney Foundation, and the Society for Urodynamics and Female Urology, as well as others.

**Dr. Irving Smokler** is the Founder and President of the Nephcure Foundation. The Foundation is committed to the support of research to understand the causes of the kidney diseases Focal Segmental Glomerulosclerosis (FSGS) and Nephrotic Syndrome, to improve the treatment of patients affected by these conditions, and to find a cure. In addition to furthering research, the Foundation is actively engaged in advocacy efforts. Dr. Smokler earned Ph.D. degrees in both Philosophy and Clinical Psychology at the University of Michigan. He also has taught at the University of Michigan, and has served as Dean of Students at the medical school. In addition to his work with Nephcure, Dr. Smokler is Chairman of the Board of the American Jewish Joint Distribution Committee--a Jewish humanitarian assistance organization.

### **NIDDK Research Community**

**Dr. Larry Appel**, a long-standing NIDDK grantee, has been elected to membership in the Institute of Medicine, National Academy of Sciences. Dr. Appel is the Director of the Welch Center for Prevention, Epidemiology and Clinical Research at The Johns Hopkins University. He has led landmark studies that have set national standards for preventing heart disease, stroke and kidney disease. These studies have also provided evidence for current national efforts to reduce racial disparities in cardiovascular health. For example, Dr. Appel chaired the African-American Study of Kidney Disease and Hypertension that documented the benefits of aggressive blood-pressure control in African-Americans with hypertensive kidney disease. Dr. Appel's research team has also tested innovative strategies to accomplish adherence with lifestyle recommendations. The POWER study, published in the *New England Journal of Medicine*, showed the effectiveness of a weight-loss and weight-maintenance program delivered over the phone by health coaches to obese patients.

### **“In Memoriam”**

**Mrs. Suzanne Rosenthal**, who served on the NIDDK Council from 1994-1997, passed away

earlier this month. Mrs. Rosenthal dedicated her life to spreading awareness about two forms of Inflammatory Bowel Disease (IBD): Crohn's disease and ulcerative colitis. Along with her husband, Irwin M. Rosenthal, as well as William D. and Shelby Modell, and Henry D. Janowitz, M.D., she founded the National Foundation of Ileitis and Colitis, now known as the Crohn's and Colitis Foundation of America (CCFA). The CCFA serves as a definitive resource for patient information, funds IBD research grants, organizes an annual scientific meeting, and advocates for legislation to improve the lives of patients. Mrs. Rosenthal also served on the first National Digestive Diseases Advisory Board and on the National Commission on Digestive Disease. She was a major supporter of the NIDDK Digestive Diseases Information Clearinghouse, which was created in response to the Commission report. She was also Founder and past President of the Digestive Diseases National Coalition, an advocacy organization of lay and professional groups.

**Dr. Christa Muller-Sieburg**, an NIDDK grantee, passed away in January 2013. Her research received grant support from the NIDDK since 1989, and she was Principal Investigator on an active grant entitled, "Epigenetic Control of Hematopoietic Stem Cells." Her commitment and dedication made a positive impact on the understanding of the hematopoietic process. For example, under her leadership, her research team demonstrated that hematopoietic stem cells exist in three compartments. The researchers showed that the cells in each compartment are capable of giving rise to all differentiated blood cell types; however, they differ in their capacity for self-renewal.

### **NIDDK Staff Changes**

**Dr. Jay Everhart** is retiring from his position as Chief of the Epidemiology and Clinical Trials Branch in the Division of Digestive Diseases and Nutrition. Dr. Everhart began his NIDDK career 30 years ago as a Medical Staff Fellow in epidemiology in the intramural Epidemiology and Clinical Research Branch in Phoenix. In 1986, he joined the extramural Digestive Diseases and Nutrition Division in Bethesda as a Medical Officer. Dr. Everhart became a leading expert in the epidemiology of digestive diseases and nutrition in the United States. His far-ranging interests include liver diseases, alimentary diseases, obesity, and nutrition research. He also applied his expertise to the design and conduct of complex clinical research studies, including the hepatitis trial, "HALT-C," and to the Adult-to-Adult Living Donor Liver Transplantation or "A2ALL" consortium. Dr. Everhart also conducted original research using data from the National Health and Nutrition Examination Survey. He authored original research papers, book chapters, and books, including two editions of *Digestive Diseases in the United States*. Dr. Everhart's contributions have been widely recognized by his peers, as reflected in his receipt of the American Gastroenterological Association's Research Service Award.

**Dr. Tamara Bavendam** is joining the NIDDK as the new Senior Scientific Advisor for Women's Urologic Health within the Division of Kidney, Urologic and Hematologic Diseases. Dr. Bavendam received her medical degree from University of Iowa College of Medicine and completed post-graduate training in urology at the University of Iowa. Dr. Bavendam's research interests include urinary incontinence, benign prostatic hyperplasia (BPH), overactive bladder (OAB), and interstitial cystitis (IC). Prior to joining the NIDDK, Dr. Bavendam was Senior

Medical Director in the Global Medical Division at Pfizer. She is widely recognized as an outstanding clinician and research pioneer.

**Dr. Rebecca Cerio** is joining the NIDDK as a new staff member in the Office of Scientific Program and Policy Analysis. She recently completed a postdoctoral fellowship at the National Cancer Institute, during which time she also served as Senior Editor of the NIH Fellows Editorial Board. She received her Ph.D. in microbiology from the University of Wisconsin-Madison.

### **New NIDDK Publication**

The NIDDK is posting on its website the new edition of *Recent Advances and Emerging Opportunities*. The booklet highlights NIDDK-supported research advances published in FY 2012, and presentations by Council members. It also includes stories of discovery and patient profiles. The publication is a collaborative effort among the NIDDK Office of Scientific Program and Policy Analysis, the scientific divisions, and communications staff.

## **II. CONSIDERATION OF SUMMARY MINUTES OF THE 190<sup>th</sup> COUNCIL MEETING AND THE BIENNIAL COUNCIL REPORT ON INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH**

***Dr. Rodgers***

By voice vote, the Council approved the Summary Minutes of the 190<sup>th</sup> Council meeting. Council also approved the 2013 *Biennial Report of the NIDDK Advisory Council on Inclusion of Women and Minorities in Clinical Research*. This later report is required by the NIH Revitalization Act of 1993 (Public Law 103-43). Both documents were sent to the Council for review prior to the meeting.

## **III. FUTURE COUNCIL DATES**

***Dr. Rodgers***

Dr. Rodgers reminded the Council members of future meeting dates.

### **2013**

May 15-16 (Wednesday and Thursday)

September 26-27 (Thursday and Friday)\*

\* The divergence was noted from the familiar Wednesday and Thursday schedule.

### **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)

The meetings will be held in Building 31, Conference Rooms 10, 6 and 7. Although most meetings are expected to be a single day, Council members were asked to reserve two days for each meeting to ensure flexibility should a situation arise where a longer meeting is required.

## **IV. ANNOUNCEMENTS**

*Dr. Stanfield*

### **Confidentiality**

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

### **Conflict of Interest**

Dr. Stanfield 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. Stanfield 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 it carefully, sign it and return it to the NIDDK before leaving the meeting.

Dr. Stanfield pointed out that, at Council meetings when applications are reviewed in groups without discussion, that is, "en bloc" action, all Council members may be present and may

participate. The vote of an individual member in such instances does not apply to applications for which the member might be in conflict.

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

### **Annual Approval of Council Operating Procedures**

By a voice vote, the Council approved the proposed Council Operating Procedures for 2013, which were sent to members for review in advance of the meeting. Dr. Stanfield noted that these procedures are unchanged from those the Council approved last September, at which time the Procedures were updated to accommodate Special Council Review (SCR) of applications from investigators who have existing NIH Research Project Grant support that exceeds \$1 million in direct costs per year.

## **V. REPORT FROM THE NIDDK DIRECTOR**

*Dr. Rodgers*

### **Changes in Congressional Committees**

Dr. Rodgers reported on some changes to the leadership of key congressional committees.

- Representative Nita Lowey of New York is now the senior Democrat on the House Committee on Appropriations.
- Senator Barbara Mikulski of Maryland is the new Chair of the Senate Committee on Appropriations.
- Senator Tom Harkin of Iowa announced that he will not run for re-election in 2014. For many years, Senator Harkin has been Chair of the Senate Labor-HHS-Education Appropriations Subcommittee, which holds annual hearings on the NIH budget. He has also been Chair of the Senate Health, Education, Labor, and Pensions (HELP) Committee, which has jurisdiction for the authorization of NIH programs.

Dr. Rodgers said that the NIH is very grateful for the support shown by these and other Members of the Congress for the Agency's research mission.

### **FY 2013 Appropriations**

The Congress was unable to complete work on any of the 12 regular appropriations bill before the end of FY 2012. Therefore, a Continuing Resolution was signed into law to permit government agencies to continue operating at their FY 2012 funding levels through March 27, 2013. The NIDDK funding level for FY 2012 was about \$1.8 billion.

Legislation will be needed to keep the government operating beyond March 27. As context, Dr. Rodgers reminded the Council that the FY 2013 House bill for the Department of Health and Human Services, including the NIH, never passed the full committee. Under the subcommittee-passed House bill, the NIH funding level would have been \$30.68 billion--an amount equal to both the FY 2012 appropriation and the President's request for FY 2013. Under the corresponding Senate bill, which did pass the full committee, the level would have been \$100 million more than in the House bill. These amounts do not include the \$150 million special statutory funding program for type 1 diabetes research.

Until final FY 2013 funding levels are determined, the NIH will continue to operate cautiously, pursuant to the law, as well as in conformance with general and NIH-specific policies for operating under a Continuing Resolution. The NIDDK will continue to fund non-competing grants in FY 2013 at 90 percent of the approved level, just as the Institute has done under previous Continuing Resolutions.

### **Impending Sequestration**

To achieve U.S. deficit reduction of \$1.2 trillion over 10 years, current law requires that automatic, across-the-board spending cuts to the FY 2013 federal budget must begin on March 1, 2013, with few program exceptions. This process--called sequestration--could be delayed, modified, or averted through alternative deficit reduction legislation; however, public policy makers have not agreed on an approach. The NIH and other federal agencies have made contingency plans for sequestration. Major new initiatives, continuations, and expansions are essentially on hold at NIH. In addition to upcoming deadlines regarding the Continuing Resolution and sequestration, the deadline for raising the U.S. Debt Ceiling is also approaching.

### **FY 2014 Appropriations**

The development of the President's FY 2014 budget is somewhat behind schedule because of uncertainty about the FY 2013 baseline. Dr. Rodgers highlighted the timeline by which major steps usually occur in the NIH budget process. Federal agencies are typically informed in late November of the preliminary decisions made by the Office of Management and Budget (OMB) regarding agency budget proposals submitted the previous summer for the upcoming fiscal year. This process is called the "OMB Passback." After opportunities for appeal, the final OMB-approved funding levels are incorporated into the President's budget request, which is officially released in February. The NIH usually presents its part of the President's budget request at congressional hearings in the Spring. The general expectation is that a final, regular appropriations bill will be passed by both the House and Senate and enacted into law before the start of the new fiscal year, to avoid an interruption in funding from one fiscal year to another. In recent years, however, the NIH has frequently been funded through a series of Continuing Resolutions or by omnibus spending bills that provide funds to several federal agencies.

Dr. Rodgers reminded the Council that, at some points in the calendar year, the NIH is dealing with three different budgets. The agency is executing the budget for the current fiscal year, presenting the budget for the upcoming fiscal year, and formulating a budget for the fiscal year

after that. Right now, the NIH is executing the FY 2013 budget under a Continuing Resolution, while working on the development of the FY 2014 President's budget request. Work is expected to begin in a month on formulating a framework for the FY 2015 budget request.

### **Extension of Special Statutory Funding Program for Type 1 Diabetes Research**

This program has been extended through FY 2014 through a provision contained in the "American Taxpayer Relief Act," which was signed into law in January 2013. This special, targeted program augments funds that the NIH receives for diabetes research through the agency's annual appropriations process. This program has enabled the NIH to create innovative, large-scale research programs that would otherwise not be possible. The NIDDK administers this program on behalf of the Secretary of Health and Human Services. The Institute has been guided by external scientific experts in the program's development, and has produced several program evaluation reports accessible on the NIDDK's website. Dr. Rodgers expressed appreciation for the continuing support for the program.

## **VI. UPDATE FROM THE DIRECTOR, NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS):**

### **"Vision for NCATS and Possible Interactions with NIDDK"**

*Christopher P. Austin, M.D.*

*Dr. Austin was appointed as the Director of the National Center for Advancing Translational Sciences (NCATS) in September 2012. After earning his medical degree from Harvard Medical School, Dr. Austin completed clinical training in internal medicine and neurology at the Massachusetts General Hospital. A developmental neurogeneticist by training, Dr. Austin came to the NIH in 2002 from Merck pharmaceutical company, where his work focused on genome-based discovery of novel targets and drugs. He began his NIH career as Senior Advisor to the Director for Translational Research at the National Human Genome Research Institute, where he initiated the Knockout Mouse Project and the Molecular Libraries Roadmap Initiative. His other NIH roles have included serving as Director of the program on Therapeutics for Rare and Neglected Diseases and the NIH Chemical Genomics Center, and as Scientific Director of the NIH Center for Translational Therapeutics.*

Dr. Austin began his presentation by noting that the NCATS is a new organization, and that he has been the Director for only a few months. The NCATS is therefore a work in progress, with much deliberative strategic planning yet to be done.

The need for the NCATS was recognized by both public and private funders of the biomedical research enterprise who have been concerned that it can take more than 13 years and enormous financial investments before a therapeutically promising molecule is approved for marketing by the FDA. Concerns were expressed about the poor translation of unprecedented advances in fundamental science into interventions that tangibly improve human health; by the crisis in the drug-development system and clinical trial system; and by the poor adoption rate into medical practice of demonstrably useful interventions that can help people lead healthier lives. The Center was therefore established by statute to catalyze the generation of innovative methods and

technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. Dr. Austin said that the NCATS is interested in addressing translational issues such as pre-clinical toxicology, novel efficacy models, clinical trial recruitment, and diagnostic and end-point criteria for clinical trials. The NCATS is also interested in non-scientific issues that impede translation, including those involving the dynamics of collaborative teams, professional incentives, intellectual property, and various policy considerations.

Dr. Austin said that, while the mission given to the NCATS is ambitious and vital, its resources are extremely limited. As a result, it is crucial for the NCATS to catalyze collaborations to which other organizations can contribute needed financial resources and expertise. Importantly, the NCATS does not focus on individual diseases or projects, but rather on efforts that can demonstrate general principles having broad relevance or application. The NCATS does not support or conduct fundamental scientific research. Instead, the Center propels the translation into clinical studies and medical practice of fundamental discoveries achieved by others. In this catalytic process, the NCATS is focused on three “Ds”--to develop, demonstrate, and disseminate. Much work will be empirical and based on a trial-and-error process that includes some failures. Therefore, the Center must do more than develop generally applicable principles, paradigms, tools, and technologies. The NCATS must also demonstrate the usefulness of its work and disseminate it widely. Such a multi-pronged approach can lead to significant improvements in the translational process, which will place the field on a firm footing.

Dr. Austin described how the organizational structure of the NCATS furthers its catalytic mission. Although the NCATS is new, it integrates and synthesizes several NIH components: the Clinical and Translational Science Award program (previously located in the National Center for Research Resources); the National Center for Technology Transfer (previously located in the National Human Genome Research Institute); the Office of Rare Diseases Research (previously located in the Office of the Director, NIH); and the Cures Acceleration Network, which is newly authorized by the Congress. Through the synthesis of these components, the NCATS catalyzes collaborations both within and outside of the NIH. The NCATS works closely with 27 other NIH components, and collaborates with external organizations, such as research foundations, disease-focused not-for-profit groups, and industry. The Center seeks to complement the work of these organizations; revolutionize the process of translation by promoting innovative research; galvanize and support new partnerships; support and augment regulatory science and its application; and expand the pre-competitive drug-development space. The organizational components of NCATS have some activities in common, and all are working toward re-engineering the clinical research enterprise. Dr. Austin elaborated on several NCATS programs and initiatives, with examples of particular relevance to the NIDDK.

### **Clinical Innovation: Clinical and Translational Science Activities**

The Clinical and Translational Science Award (CTSA) program is a national consortium of 60 centers located at academic medical research institutions. The centers work together to improve the way clinical and translational research is conducted nationwide; to accelerate the research translation process; and to provide robust training for researchers in this area. In Dr. Austin’s

view, the CTSA program has positively changed the landscape of translational and clinical sciences at the participating academic institutions, but the program has not yet realized its full transformative potential. Nation-wide, systemic problems are still impeding the acceleration of translation, including the need to enhance career-development paths for scientists working in this field. Suggestions Dr. Austin has received from CTSA Directors and Principal Investigators are leading to an evolving vision. Dr. Austin sees the program as providing new national leadership in enhanced quality, safety, and efficiency in translational research, as well as innovation in methods, resources, and services that catalyze the spectrum of translational research. As the program evolves, it will facilitate the training and career development of a robust translational workforce for interdisciplinary team researchers, and encourage institutions to build on their strengths. It will be informed by an increased emphasis on transparency and fiscal oversight. It will also feature flexible academic, community, and industry collaboration, as well as partnership models built on a shared commitment to translation.

Dr. Austin gave some examples of CTSA activities involving the NIDDK. He noted that 14 of the CTSA's are co-located with sites of the NIDDK's Childhood Liver Disease Research and Education Network (ChiLDREN). These CTSA's provide clinical research support in the form of nursing and laboratory resources, as well as assistance with research coordination. In another example, the NIDDK has received CTSA support for the study of neurological factors that might underlie associations between fructose consumption and weight gain. The NCATS supported functional brain imaging studies, statistical analysis, hospital research unit/nursing support, and core laboratory analysis of blood samples.

### **Pre-Clinical Innovation**

When researchers are stymied in the development of a novel target or discovery, a partnership with the NCATS can help them bridge gaps and produce deliverables--such as data, compounds, and probes--that will move the research forward and also provide generalizable insights about the translational process. About 90 percent of the projects involve extramural investigators. Dr. Austin noted that efficiencies in drug development can be achieved by capitalizing on previous research. For various scientific and business reasons, chemical entities may not have met their initial intended purposes or been fully exploited. However, with additional work, they could have value for advancing the research and treatment of diseases, particularly rare and neglected diseases. It is possible to "rescue" small molecules and biologics whose development was abandoned prior to FDA approval, and also to "re-purpose" FDA-approved drugs for the treatment of additional diseases. Dr. Austin highlighted some of the innovative pre-clinical efforts the NCATS is pursuing.

- ***National Chemical Genomics Center (NCGC):*** This Center was founded in 2004 and is now a part of the NCATS. The NCGC is engaged in collaborations with hundreds of investigators worldwide in such important drug-development steps as assay development, high-throughput screening of compounds, chemical informatics, and medicinal chemistry. The focus is on unprecedented targets and on rare/neglected diseases. The NCGC's mission includes advancing chemical probes and leads; using new technologies and paradigms to improve the efficiency and success of drug development; and enhancing chemical genomics

based on general principles about the interactions of small molecules and targets. To foster and enable comprehensive drug re-purposing, the NCGC has created a definitive, complete, and non-redundant list of all approved molecular entities as a freely available electronic resource, as well as a physical collection of small molecules amenable to high-throughput screening. Dr. Austin provided an NIDDK-relevant example spearheaded by the NCGC in conjunction with a biochemist and a diabetes researcher. This collaborative effort led to the identification of a selective inhibitor of the enzyme 12-lipoxygenase (12hLO), which was discovered decades ago. This new-found inhibitor, ML 127, gave researchers the missing tool needed to demonstrate the enzyme's long-suspected involvement in inflammatory processes in diseases such as diabetes, and thus showed its usefulness as a therapeutic target. ML 127 is a valuable pharmacologic tool for research on diabetes, and it may prove useful in protecting insulin-producing islets from destructive inflammatory processes.

- ***Therapeutics for Rare and Neglected Diseases (TRND) Program:*** This program fosters collaborative projects in which the pre-clinical drug expertise of NIH intramural scientists is paired with the disease-focused expertise of extramural researchers in academia and elsewhere. Participating investigators become members of project teams that set up milestones and deliverables. Work includes drug discovery, drug optimization, and the clinical testing of therapies, with the goal of generating sufficient quality data to support an Investigational New Drug Application to the FDA.
- ***Bridging Interventional Development Gaps (BrIDGs) Program:*** This program provides in-kind, government contract-based services to a range of eligible applicants. It is geared to helping researchers meet discrete needs--such as performing specific tests--in order to overcome obstacles in later-stage preclinical development. Projects may address any disease or disorder, and might be missing only one or two key developmental steps. Products and information return to the originating investigator in support of additional studies, or the filing with the FDA for an Investigational New Drug. Investigators retain intellectual property rights. This program grew out of the former Rapid Access to Intervention Development (RAID) Program.

### **Office of Rare Diseases Research**

This Office supports the Rare Diseases Clinical Research Network, a Scientific Conferences Program, the NIH Clinical Center Bedside-to-Bench Program, and the Genetic and Rare Disease Information Center (GARD).

### **CURES Acceleration Network**

Recently established by the Congress, this is a small program that seeks to speed high-need cures. A high-need cure is defined as a drug, biological product or device that, in the determination of the NCATS Director, is a priority to diagnose, mitigate, prevent or treat harm from any disease or condition; and for which the incentives of the commercial market are unlikely to result in its adequate or timely development. The Network promotes innovation in technologies, accelerates cure development, and assists award recipients in navigating the

process of establishing protocols that comply with FDA standards through all the stages of a medical product's development.

- ***Tissue Chip Program:*** The goal of this program is to develop an *in vitro* drug-screening platform using human tissues. Such a platform could be predictive of the efficacy, pharmacokinetics, safety and toxicity of promising therapies in a way that is suitable for regulatory science use. A Microsystems Initiative will screen for safe, effective drugs using the best ideas in engineering, biology and toxicology. Joint funding is being provided by the NIH and the Defense Advanced Research Projects Agency (DARPA), while the FDA is providing regulatory and toxicology expertise.
- ***Pilot Program for Discovering New Therapeutic Uses for Existing Molecules:*** This program is propelling translation by enabling NIH researchers to study compounds de-prioritized by the pharmaceutical industry for efficacy and/or business reasons. The NCATS is creating template agreements intended to streamline negotiations between researchers and industry with a view toward re-purposing nearly 60 drugs from various pharmaceutical companies, which are contributing the drugs and the associated data. The NIH is providing project management and funding. This program will be evaluated in terms of whether the template agreements speed negotiation time, and whether the pilot program helps to advance disease understanding and results in promising therapeutics.

### **Examples of Collaborative Projects**

Dr. Austin gave examples of several projects where NCATS serves as a collaborative partner by performing various tasks (such as medicinal chemistry, synthesis of materials, formulation development, pharmacokinetics, or toxicity studies) or providing support for regulatory affairs. One project supported by BrIDGS, TRND, the National Institute of Arthritis and Musculoskeletal Diseases and the NIDDK is focused on a therapeutic agent for fibrodysplasia ossificans progressive (FOP) and the anemia of inflammation. A second example is a BrIDGS project to develop a long-acting parathyroid hormone analogue for subcutaneous administration in the treatment of one form of thyroid disease. A third example involves collaboration among TRND, a private company, and the NIH Clinical Center for the testing of a compound to treat sickle cell disease.

In closing, Dr. Austin emphasized that the NCATS is centered on collaborations that pursue novel processes to accelerate translation and to establish generally useful paradigms. He encouraged Council members to learn more about NCATS on its website ([www.ncats.nih.gov](http://www.ncats.nih.gov)), on the NCATS Facebook page ([facebook.com/ncats.nih.gov](https://facebook.com/ncats.nih.gov)), via Twitter ([twitter.com/ncats\\_nih\\_gov](https://twitter.com/ncats_nih_gov)), and by using the NCATS website to join the organization's listserv and subscribe to its e-newsletter ([www.ncats.nih.gov/news-and-events/e-news/e-news.html](http://www.ncats.nih.gov/news-and-events/e-news/e-news.html)).

## **Council Questions and Discussion**

***Evaluation Metrics:*** *What are the evaluation metrics for the NCATS and the timeline for applying them?* Dr. Austin responded that he takes seriously the need to assess new organizations. However, because it has taken decades for bottlenecks in translation to develop, it is unlikely that they can be eradicated or ameliorated immediately. There will probably be a portfolio of evaluation metrics for the NCATS--both short-term and long-term. Areas that may be amenable to short-term metrics include the Tissue Chip Program, TRND, and drug re-purposing efforts. The CTSA Program is also making progress in terms of improving the processes of Institutional Review Boards, and developing common informatics platforms that permit identification and qualification of patients for clinical trials. Dr. Austin said that other NCATS efforts will take time to come to fruition, and it would be a mistake to take short-cuts around the science in order to demonstrate immediate results.

***Trends in FDA-approved Drugs:*** *What is responsible for the upward trend reported in the number of FDA-approved drugs over the last few years? Are they highly targeted agents? What are the implications for the NCATS?* Dr. Austin said that, according to the available data, most of these recent FDA-approved drugs are for rarer diseases that involve a simpler biochemistry than complex diseases such as type 2 diabetes. Dr. Austin expressed concern, however, that the trend may be driven by an unrealistic and unsustainable business model in the private sector. For example, if the U.S. pharmaceutical industry were successful in developing and marketing drugs for every rare disease, the costs of treating patients would be economically prohibitive. Therefore, Dr. Austin hopes that the insights gained from research on rare diseases may be generalizable to common diseases.

***Dissemination of Research Results:*** *What will be the role of NCATS in dissemination?* Dr. Austin commented that he sees two roles for the NCATS in this area. First, the NCATS is developing and will make available a whole series of technologies, databases and other tools to aid translation. Second, the NCATS works with the Institutes and Centers, which have disease-specific knowledge, to further the dissemination of new findings about translation. If a program or activity proves valuable, an Institute or Center may accept responsibility for the later steps in the dissemination process. The NCATS is carefully exploring its role in dissemination given that its resources are extremely limited. One approach under discussion is the possibility that the NCATS could do research on the process by which scientific findings are actually disseminated and adopted by other researchers. This process needs to be understood in order to effect changes in populations.

***Interfacing with the FDA:*** *How will the NCATS facilitate a timely, productive interface between NIH-funded researchers and the FDA's regulatory framework and requirements for clinical science?* Dr. Austin noted that there are many talented FDA scientists who want to advance clinical research and can identify problems in the system that need resolution. However, the FDA does not have the resources to resolve the problems. The NCATS is engaged in discussions with FDA officials to address this issue. For example, the NIH may be able to provide researchers with easily accessible, general information about regulatory processes at an early stage in their efforts. The NCATS is also working with the FDA to incorporate that

agency's knowledge, experience and perspectives regarding regulatory processes into some evolving NIH projects, such as the Tissue Chip Program.

***Collaboration with Industry:*** *In addition to collaborating with industry on the sharing of compounds, has the NCATS considered whether core facilities could be established in industry that would be available to both intramural and extramural scientists? Such a concept could be tethered to a financial model in which there is not only cost-sharing, but also profit-sharing. Is there an opportunity to think innovatively about such possible arrangements?* Dr. Austin said that, along the lines of the model described, the NCATS has put in place several collaborations through the TRND program. In many cases, intramural scientists are primarily or exclusively serving in the role of project managers who interface with extramural investigators and companies. The vast majority of ideas and programs originate with extramural investigators. However, Dr. Austin noted that, when companies are under financial pressures, they are likely to reduce funding for early-stage research, such as chemistry studies. The drug re-purposing efforts of the NCATS may help by building confidence within the pharmaceutical industry that collaborations involving shared data and resources can work well and can benefit all participants.

***Institutional Review Boards (IRBs):*** *Can the NCATS assist in the development of a single, standardized form that would be used by all IRBs and thus save time on the part of investigators? Could the NIH convene a group of experts to develop such a form and then tie it into the NIH funding system for clinical research?* Dr. Austin responded that he has received suggestions regarding such a standardized form from many Principal Investigators and that addressing this issue is important to NCATS.

## **VII. UPDATE FROM THE DIRECTOR, NATIONAL HEART, LUNG AND BLOOD INSTITUTE (NHLBI):**

### ***“Vision for NHLBI and Possible Interactions with NIDDK”***

***Dr. Gary Gibbons***

*Dr. Gary Gibbons was appointed as the Director of the National Heart, Lung and Blood Institute (NHLBI) in the summer of 2012. Dr. Gibbons received his M.D. degree at Harvard Medical School and then completed his residency and cardiology fellowship at the Brigham and Women's Hospital in Boston. Before joining the NHLBI, Dr. Gibbons served as the founding Director of the Cardiovascular Research Institute, Chairperson of the Department of Physiology, and Professor of Physiology and Medicine at the Morehouse School of Medicine in Atlanta. During his leadership of the Cardiovascular Research Institute, Dr. Gibbons directed NIH-funded research in the fields of vascular biology, genomic medicine, and the pathogenesis of vascular diseases. Under his leadership, the Institute emerged as a center of excellence, with important discoveries related to the cardiovascular health of minority populations. Prior to joining the Morehouse School of Medicine in 1999, Dr. Gibbons was a member of the faculty at Stanford University, and at Harvard Medical School.*

Dr. Gibbons said that he is privileged to serve as the new NHLBI Director, and that he will vigorously pursue the Institute's mission to provide global leadership for research, training and

education programs to promote the prevention and treatment of heart, lung and blood diseases. He believes that diversity, collaboration, synergy, and the networked leveraging of resources are particularly important in meeting today's scientific and fiscal challenges. He therefore looks forward to working collaboratively with the NIDDK to combat the chronic diseases and health inequities that are within the research missions of both Institutes.

Based on his experiences as a physician, scientist, educator and community servant, Dr. Gibbons thinks that science and scientists can be considered "public goods" for which NIH leaders must be accountable stewards. He outlined five enduring principles he believes are essential for successful stewardship of the NHLBI. They are to:

- Value and support investigator-initiated fundamental discovery science;
- Maintain a balanced, cross-disciplinary portfolio that includes basic, clinical and population sciences;
- Support implementation science that empowers patients and enables partners to improve the health of the nation;
- Train and nurture a diverse new generation of leaders in science; and
- Value the health of all communities; and elucidate and eliminate health inequities in the U.S. and around the globe.

He will be guided by these principles as he leads the NHLBI in forging new efforts that will extend its legacy of accomplishments.

### **Imagining the Future: Toward a More Diverse, Networked Scientific Community**

Dr. Gibbons said that diversity has been a source of American excellence on many fronts, and that a biomedical workforce needs to reflect a diverse nation. Yet, data show a striking lack of diversity in the scientific enterprise. For example, the percentage of Black and Hispanic individuals who serve as Principal Investigators on NIH grants is astonishingly low relative to their representation in the U.S. population. A similar disconnect in representation is seen in the tenure track of the NIH intramural program. This lack of diversity is particularly problematic when one considers the enormous inequities that exist along ethnic and racial lines with respect to major public health problems such as cardiovascular disease, stroke, diabetes, obesity, and kidney disease.

Dr. Gibbons commented that minorities who have the talent, passion and creativity to consider a research career often take a leap of faith in pursuing a path that may be unfamiliar to them and to their families, networks, and communities. As stewards of the public trust, the leaders of the NIH have a collective responsibility to present research training and career-development opportunities to those who have the courage to seize them. Dr. Gibbons noted that the NIH Director, Dr. Francis Collins, is taking steps to address the lack of diversity in the biomedical research workforce. For example, plans are underway to develop a national mentor network that will leverage digital and social networking capabilities to provide career guidance to minority scientists. Another initiative will target the crucial transitional period between undergraduate education and Ph.D. training.

Dr. Gibbons said that it is an appropriate time to reflect on the NHLBI's past achievements and to exploit unprecedented research opportunities. The NHLBI has a legacy of excellence and strong stewardship. For example, the Institute contributed substantially to the remarkable decline in U.S. deaths from coronary heart disease (CHD) from 1970 to 2010. This story of discovery involved the identification of CHD risk factors through the Framingham Study; elucidation of the roles of high-density and low-density lipoprotein by intramural and extramural scientists; collaboration with industry to develop and demonstrate the clinical effectiveness of cholesterol-lowering drugs; and the implementation science that has empowered patients to use these scientific advances to reduce their disease risk. The interweaving of fundamental research, translational research, clinical research, and national public education programs made this progress possible. The lessons learned can serve as a paradigm for building the next generation of scientists, and for sustaining a balanced, multi-level, collaborative research portfolio through which discovery science can lead to public health impacts for all Americans.

Looking to the future, Dr. Gibbons asked the Council to envision achievements the NHLBI might highlight at its 75<sup>th</sup> anniversary. In the coming years, great progress could emerge from the exploitation of many avenues, such as applying systems biology/medicine and reparative biology/medicine; undertaking predictive health and disease pre-emption trials; and combating health inequities--both local and global. The tools, platforms, and mechanisms to propel research achievements include biomarkers, imaging techniques, informatics/computational modeling, stem cell biology, nanotechnology, bioengineering, "omics" fields, and collaborative networks for intervention trials. Because of the nature of these technologies and tools, the research enterprise will need to become increasingly collaborative, cross-disciplinary, and networked.

The ability of the research community to transform its traditional models in response to innovative thinking, new methods, and emerging trends will help to sustain its strength and productivity. The private sector is replete with examples of companies, such as Kodak, that failed to heed signs of change. One way the research enterprise can avoid that mistake is to rethink approaches to clinical science--to "disrupt" traditional models in a good way. The clinical trial model can be re-engineered to integrate randomized, controlled, patient-centered trials into existing clinical-practice centers in low-cost, high-impact ways. A larger number of trials could be undertaken in community settings with the view of patients as research partners, not subjects.

The research community could capitalize more fully on extensive existing data and resources by applying the new tools of genetics, gene expression and microRNA profiling, as well as discovery-oriented proteomics and metabolomics. The NHLBI plans to take a systems approach to its portfolio by tapping into the collective intelligence of the "Scientific Commons." For example, the NHLBI will take advantage of various health system networks, diverse cohort-study datasets, clinical research registries, biobanks, biorepositories, bioinformatics tools, and computer models. The digital exploitation of "big data" may help to streamline the recruitment of patients for clinical trials, increase sample sizes, and achieve other efficiencies. It may also uncover new knowledge that is predictive and actionable in clinical settings.

With concerted efforts, it may be possible to put some costly, debilitating chronic diseases into remission, or even to pre-empt them, and to turn downward the current statistical curves for health inequities.

### **Factors Contributing to Health Inequities**

Dr. Gibbons elaborated on the complex, multi-level, global system problems that contribute to health inequities. Many factors play a role, including the genetics and behavior of individuals, the culture of families, and aspects of the community, including access to quality medical services. Some factors in the larger environment are the risk of infections, the formulation and execution of health policy, socio-cultural context, and the economy.

The “Bio-Social Interface” is a term that underscores the interaction of environmental forces--known collectively as the “exposome”--with biological characteristics. The exposome includes racism, social deprivation, inactivity, diet, psychosocial stress, and the social network. Biological characteristics include the microbiome, immune system, and epigenome, as well as genetic variation and population history.

Ecosystems of health inequities can lead to conditions such as obesity, diabetes, and hypertension, which, in turn, are drivers of stroke, heart disease and kidney failure and their attendant health care costs. To address the complexities of these health problems, Dr. Gibbons said that transformational change will be needed. Such change will integrate the classical approach of reductionist research with a holistic, systems-medicine approach. Transformational change will also require a circle of partners within the research community to build the next generation of diverse, talented scientific investigators and leaders.

Dr. Gibbons gave several examples of health inequities.

- ***Risk Factors for Cardiovascular Disease (CVD):*** Opportunities now exist to explore the important interplay between social/environmental and biological systems in the manifestation of cardiovascular disease (CVD). For example, studies have shown that social and community forces, such as lack of access to healthful foods in minority communities, can contribute to CVD risk in populations that have biological risks. New research could seek ways to reduce the high CVD risk profile observed in studies of African Americans.
- ***Sickle Cell Disease:*** Race-ancestry, population history, immune defense systems and genomic variation are key elements in this disease of African Americans. A major research finding that could be exploited is the identification of a Sickle Cell antigen. The research community could also build on the discovery that blood transfusions can reduce the probability of stroke recurrence in children who have Sickle Cell Disease. It may be also possible to prevent recurrent stroke in these children through studies of modifier genes, immune system targets, and vasculopathy targets. The research community could establish and attain the ambitious goal of having a stroke-free generation of children who have this disease.

- ***Chronic Kidney Disease and Kidney Failure:*** A major research advance toward combating health inequities in African Americans would be the ability to precisely predict and pre-empt chronic kidney disease, which can progress to irreversible kidney failure. New studies could build on the knowledge that two variants of the *APOLI* gene confer increased risk in African Americans for kidney failure. One possible research avenue is the development of an *APOLI*-based predictive, therapeutic, and preventive strategy using genomic medicine approaches. For example, it may be possible to identify high-risk individuals and give them early, aggressive treatment with hypertensive medication. At the same time, researchers could strive to develop new drugs to target mediators downstream of *APOLI* to prevent the progression of chronic kidney disease. The public health and economic imperative for developing new strategies becomes clear given the disproportionate burden of kidney disease in African Americans, and the escalating Medicare costs of treating kidney failure.

### **NHLBI-NIDDK Collaborative Opportunities**

Dr. Gibbons said that the NHLBI and NIDDK have important areas of mutual research interest and responsibility with respect to chronic diseases, many of which are also areas of health inequities. Topics of ongoing or potential collaboration include:

- ***Obesity:*** Conducting research on bariatric surgery and undertaking early-life-stage family studies.
- ***Hematology:*** Offering investigator training opportunities through the NIDDK Centers of Excellence.
- ***Diabetes:*** Pursuing a comparative cost-effectiveness study in early type 2 diabetes--the Glycemic Reduction Approaches in Diabetes (GRADE) study.
- ***Kidney Disease:*** Harnessing the health system network platform to conduct low-cost, simple, embedded trials; using large-scale clinical cohorts with clinical follow-up based on electronic medical records (EMRs); conducting genomic medicine trials.
- ***Public Health Promotion:*** Engaging in health education for at-risk target audiences common to both the NIDDK and the NHLBI.

In closing, Dr. Gibbons re-emphasized that a transformative and transcendent scientific community is needed to achieve the goal of predicting and pre-empting chronic diseases and reducing health inequities. A diverse, global, networked approach could advance discovery and implementation science to positively change clinical practice. Enhanced health promotion and treatment initiatives could be instrumental in effecting improvements in public health. Collectively, these steps could start to “bend the curves” downward with respect to the chronic diseases and health inequities within the missions of the NHLBI and NIDDK.

### **Council Questions and Discussion**

***Collaborations Regarding Clinical Trial Endpoints:*** *Given the strong intersection between heart and kidney disease, clinical trials should be designed to include patients with both conditions. The NIH SPRINT study should be commended for addressing not only hypertension, which is a huge risk factor for all organ systems, but also for specifically including patients with kidney disease, as well as older patients who also have a disproportionate burden of heart*

*failure and kidney disease. At a minimum, the NIDDK and the NHLBI should be encouraged to work together to include kidney patients and kidney endpoints in cardiac trials. Dr. Gibbons said that he is encouraged by the direction the SPRINT study has taken. Protein in the urine has long been an important and predictive disease marker, and it generally aligns with blood-vessel disease. Dr. Gibbons said that he would like to see a dialogue about enhancing collaborative research to understand the earliest stages of kidney and heart disease.*

***Birth Weight:*** *Given the importance of birth weight relative to the biological basis of disease, should this information be included in research studies and in the presentation of clinical cases in academic settings? Dr. Gibbons agreed with the importance of birth-weight data. He said that opportunities may exist to explore its role more fully in the earliest stages of disease.*

***Role of Medical Associations:*** *With respect to the catalytic role the NIH plays in exploiting “big data,” the medical associations could be important neutral sites for encouraging collaboration among multiple institutions and community-based, large data banks. The medical associations should be considered along with research institutions and individual investigators in furthering these catalytic efforts. Dr. Gibbons agreed. He also noted that a patient-centered and patient-empowered approach involves data collection not only by investigators within academic health centers, but also the leveraging of patient-driven registries and interfaces in a more networked, interconnected way. Patient interest groups are already organizing along those lines, and the NIH can think about ways to frame partnerships with them to further new advances in biomedical research.*

***Endothelial Cell as a Research Platform:*** *The influence of APOL1 in hemoglobin diseases calls to mind the importance of the endothelial cell, which is known to be critical in coagulation, sickle cell disease, kidney disease, and liver disease. Perhaps there are opportunities that might be explored for a collaborative “cellomics” effort using the endothelial cell as a research platform. Dr. Gibbons agreed.*

***NIH Organization in Era of Research Commonalities:*** *With the advent of new technologies and scientific areas such as proteomics, researchers appear to be focusing more on the commonalities among different diseases and less on the discrete organ systems around which research studies and medical treatments have traditionally centered. Will the organization of the NIH evolve in similar new directions? Dr. Gibbons responded that, within its statutory framework, the NIH can be nimble in responding to the new emphasis on disease commonalities. For example, the NIH can view and manage patient cohorts as a collective resource. It can also explore opportunities for co-investments in shared research platforms that can answer questions relevant to several diseases.*

***Patient Advocacy Organizations:*** *The Alpha 1 advocacy community values the important research insights arising from the leadership and collaborative efforts of the NHLBI and the NIDDK. For example, important knowledge is being gained from the Alpha1 patient registry regarding the interconnections between liver and lung damage in this disease. Dr. Gibbons expressed his appreciation for the many contributions of patient advocacy organizations to advancing the NIH mission.*

## VIII. SCIENTIFIC PRESENTATION:

### **“The LIN28b-Let-7 Axis in Intestinal Epithelial Biology”**

**Anil Rustgi, M.D., Chief of Gastroenterology in the Department of Medicine and the T. Grier Miller Professor of Medicine and Genetics at the University of Pennsylvania School of Medicine**

*Council Member Dr. Anil Rustgi earned his M.D. at Duke University and completed his internship, residency, and fellowship work at Harvard Medical School. Dr. Rustgi’s research explores the molecular genetics of gastrointestinal cancers, including those originating from the esophagus/head and neck, pancreas and colon. A widely published investigator, Dr. Rustgi is supported by both the NIDDK and NCI. He is Editor-in-Chief of Gastroenterology, Editor of the textbook Gastrointestinal Cancers, and Associate Editor for Cecil’s Medicine. In addition, Dr. Rustgi is fully engaged in the teaching and mentorship of students and research fellows.*

## IX. CONSIDERATION OF REVIEW OF GRANT APPLICATIONS

A total of 1136 grant applications, requesting support of \$330,131,921 were reviewed for consideration at the February 13, 2013 meeting. Funding for these applications was recommended at the Scientific Review Group recommended level. Prior to the Advisory Council meeting, an additional 1064 applications requesting \$284,649,450 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 February 13, 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 191st meeting of the NIDDK Advisory Council was adjourned at 4:30 p.m., February 13, 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***