

**Department of Health and Human Services  
National Institutes of Health**

**National Center for Advancing Translational Sciences Advisory Council  
and  
Cures Acceleration Network Review Board**

**Minutes of Joint Meeting  
Sept. 15, 2016**

The National Center for Advancing Translational Sciences (NCATS) Advisory Council and the Cures Acceleration Network (CAN) Review Board held a joint meeting in open session on Sept. 15, 2016, convening at 8:30 a.m. ET, in Conference Room 6, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council chair, and Geoffrey S. Ginsburg, M.D., CAN Review Board vice chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Following the joint meeting, the NCATS Advisory Council met in closed session for the review and consideration of grant applications.

**NCATS ADVISORY COUNCIL MEMBERS PRESENT**

***Chair***

Christopher P. Austin, M.D., Director, NCATS

***Executive Secretary***

Anna L. Ramsey-Ewing, Ph.D., Director, Office of Grants Management and Scientific Review, NCATS

***Council Members***

Margaret A. Anderson, M.A.

Jorge L. Contreras, J.D.

Louis J. DeGennaro, Ph.D.

Geoffrey S. Ginsburg, M.D., Ph.D.

Eric D. Kodish, M.D.

Bernard H. Munos, M.B.A.

Harry P. Selker, M.D., M.S.P.H.

Anantha Shekhar, M.D., Ph.D.

Robert I. Tepper, M.D. (by telephone)

Scott J. Weir, Pharm.D., Ph.D.

***Representative Members***

None present

***Ad Hoc Members***

Daniel L. Hartman, M.D., Bill & Melinda Gates Foundation

Richard E. Kuntz, M.D., Medtronic, Inc.

Geoffrey Shiu Fei Ling, M.D., Ph.D., Uniformed Services University

Matthew Might, Ph.D., University of Utah

Megan O'Boyle, Phelan-McDermid Syndrome Data Network

Alan D. Palkowitz, Ph.D., Lilly Research Laboratories

***Ex Officio Members***

Frank F. Weichold, M.D., Ph.D., Food and Drug Administration (representative for Robert M. Califf, M.D.)

## **CAN REVIEW BOARD MEMBERS PRESENT**

### ***Vice Chair***

Geoffrey S. Ginsburg, M.D., Ph.D., Director, Duke Center for Applied Genomics & Precision Medicine; and Professor of Medicine, Pathology, and Biomedical Engineering, Duke University Medical Center

### ***Executive Secretary***

Anna L. Ramsey-Ewing, Ph.D., Director, Office of Grants Management and Scientific Review, NCATS

### ***Board Members***

Margaret A. Anderson, M.A.

Robert J. Beall, Ph.D.

Jorge L. Contreras, J.D.

Louis J. DeGennaro, Ph.D.

Eric D. Kodish, M.D.

Bernard H. Munos, M.B.A.

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Christopher P. Austin, M.D., NCATS

Frank F. Weichold, M.D., Ph.D., Food and Drug Administration (representative for Robert M. Califf, M.D.)

## **OTHERS PRESENT**

NCATS leadership and staff

### **I. CALL TO ORDER**

Christopher P. Austin, M.D., and Geoffrey S. Ginsburg, M.D., Ph.D., called the meeting to order. Dr. Austin welcomed members and guests to the 13th meeting of the NCATS Advisory Council and the 16th meeting of the CAN Review Board. He reminded attendees that the open session was being videocast. Dr. Austin introduced the *ad hoc* members of the Advisory Council and CAN Review Board and guest speaker Tudor I. Oprea, M.D., Ph.D.

### **II. CONSIDERATION OF MINUTES: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board**

The minutes of the joint meeting held on June 13, 2016, were approved as written.

Anna L. Ramsey-Ewing, Ph.D., informed the group that the NCATS Advisory Council and CAN Review Board will have joint meetings in 2017 on Jan. 12, May 4 and Sept. 7. The 2018 meetings will take place on Jan. 11, May 10 and Sept. 27. The CAN Review Board also will meet by teleconference on Dec. 9, 2016; Dec. 15, 2017; and Dec. 14, 2018.

### III. INTRODUCTION OF NEW STAFF

- **Monica R. Shah, M.D., M.H.S., M.S.J.**, is the director of the Clinical and Translational Science Awards (CTSA) Program Trial Innovation Network. She is a board-certified heart failure and transplant cardiologist.
- **Tiina K. Urv, Ph.D.**, is a program director for CTSA Program hubs and the Trial Innovation Network. Her work has centered on developmental disabilities.
- **Patricia L. Jones, Dr.P.H., M.P.H.**, is a program director in the Division of Clinical Innovation, with expertise in behavioral science, clinical trials and dissemination science.
- **Randall J. Redmond** is chief of the Administrative Services Branch of the Office of Administrative Management.
- **Victor M. Henriquez, Ph.D.**, is a scientific review officer in the NCATS Office of Grants Management and Scientific Review.
- **Steven I. Benowitz, M.A.**, is a science writer in the NCATS Office of Communications.

### IV. DIRECTOR'S REPORT: Christopher P. Austin, M.D., Director, NCATS

Christopher P. Austin, M.D., provided a summary of NCATS activities. Each Advisory Council and CAN Review Board member received an electronic version of the entire report, which is summarized below.

#### Selected Translational Innovation Highlights

- **Drug repurposing for Zika virus.** Zika virus infects the brain of the developing fetus of infected mothers, leading to the death of human neural progenitor cells (hNPCs) in the embryonic cortex. Researchers from the NCATS Division of Pre-Clinical Innovation teamed with researchers at Johns Hopkins University and Florida State University to identify approved or investigational drugs to fight the infection or prevent the destruction of hNPCs. The team tested 6,000 compounds, including 2,800 from the NCATS Pharmaceutical Collection. They identified five potential inhibitors of Zika virus infection and brain cell death. This project took only six months from formation of the team to publication, a public health model that can be used in the future. Next steps include validating the results in mouse models and increasing the compounds' oral bioavailability, potency and penetration of the blood-brain barrier.
- **Use of "chaperone" proteins for treatment of diseases stemming from misfolded proteins.** There are a variety of conditions that trace to misfolded proteins, including Parkinson's disease and Gaucher disease. Chaperone proteins reshape misfolded or unfolded proteins into the correct form. NCATS became interested in using chaperone proteins as a therapeutic approach for diseases that trace to misfolded proteins. The researchers found that correcting a glucocerebrosidase defect could reduce pathology and symptoms in both diseases. The team found that a successful chaperone is one that binds to the protein and helps it fold but neither blocks nor activates it. This project illustrates that it is possible to develop treatments for common diseases in the course of investigating rare diseases. The approach may be applicable to the 40 other lysosomal storage disorders, as well as other neurodegenerative diseases characterized by protein misfolding.
- **Gene therapy.** Improvements in vectorology and virology make gene therapy a potential cure for many disorders. NCATS' Therapeutics for Rare and Neglected Diseases Learning Collaborative, in partnership with other organizations, is building a gene therapy toolbox. The project focuses on gene therapy translational issues, including tissue-specific delivery and vehicle cargo design. Dr. Austin gave the example of work with Agilis Biotherapeutics on aromatic L-amino acid decarboxylase deficiency, a rare disorder of the central nervous system

(CNS) that causes severe disability in children. The project's goals are to develop a CNS gene therapy, new devices for gene therapy delivery in infants and a global regulatory approval strategy for ultra-rare diseases.

- **Rare disease patient videos.** NCATS has produced a video series to raise awareness of the challenges faced by patients with rare diseases and to show how collaborative NIH research can help. The 10 videos in the series are very popular on NCATS' social media channels.
- **Medication nonadherence.** NCATS provided Small Business Innovation Research (SBIR) funding to AiCure, which is developing an app to improve medication adherence. Nonadherence can affect clinical trial results and reduce therapeutic benefit to the patient. The app improved adherence in clinical trials in stroke patients and people with schizophrenia. The company is now receiving SBIR funding from NIH's National Institute of Mental Health and the National Heart, Lung, and Blood Institute and has attracted venture capital financing. The mobile app uses facial recognition technology to confirm that a patient is taking the proper pill, that the patient puts the pill in her mouth and that she swallows it. The app records the time of day the patient takes the medication and any doses that are missed.

### ***Discussion***

Robert J. Beall, Ph.D., asked about next steps in the chaperone protein project. Dr. Austin said that the first series of chaperone drugs has been licensed to Lysosomal Therapeutics, Inc., which was involved in the research. NCATS is negotiating the second series with several large pharmaceutical companies.

Geoffrey S. Ginsburg, M.D., Ph.D., asked when a Zika treatment might be available. Dr. Austin said that the project is now with the National Institute of Allergy and Infectious Diseases. The compounds are being tested in animals and also must be tested in humans in a clinical trial.

Megan O'Boyle said that the AiCure medication adherence app is good for people with memory problems who may forget to take their medications, but it may not be effective for those who do not want to take their medications. Anantha Shekhar, M.D., Ph.D., asked whether caregivers could use the app, and there was discussion about how caregivers could help by visually recording patients as they take the medication.

Geoffrey Shiu Fei Ling, M.D., Ph.D., said he was happy to hear the SBIR program is involved. He said that although the program funds relatively small grants, applicants for NCATS SBIR funding have a high success rate, at about 50 percent.

Frank F. Weichold, M.D., Ph.D., said the app could affect significantly the use, distribution and approval of generics. It also could be of interest to insurance companies. Eric D. Kodish, M.D., said that the app has been tested in the context of a clinical trial. It has medical applications, but those are different applications. It is important to separately analyze those uses and not to conflate them. Alan D. Palkowitz, Ph.D., said the app has implications for clinical trials in which complete adherence is required to provide a good dataset. This app could significantly affect translational studies.

Dr. Austin said that NCATS issued a funding opportunity announcement (FOA) that approaches community engagement as a scientific research problem and attempts to integrate community engagement across the spectrum of translational science. One example, the Rockefeller University CTSA Program hub, supports a practice-based research network to form a community-engaged research navigation program. As described in *Academic Medicine*, "Helping Basic Scientists Engage with

Community Partners to Enrich and Accelerate Translational Research,” this model can be used to engage communities, community clinicians, patients and other stakeholders.

### **Policy and Legislative Updates**

- Neither the House nor the Senate has passed a budget yet for fiscal year 2017. Observers expect Congress to pass a continuing resolution that will extend government funding through Dec. 9, 2016. One of the contentious items is the inclusion of Zika funding in the budget.
- The House 21st Century Cures and the Senate Innovations for Healthier Americans acts were expected to be passed, resolved into one bill and sent to the President by the end of September. The House bill included \$8.75 billion over five years for the NIH Innovation Fund. However, the effort may be stalled and may need to be reintroduced in the next Congress.
- Penny W. Burgoon, Ph.D., acting director of NCATS’ Office of Policy, Communications and Strategic Alliances, is the point person on tasks related to the transition to the new presidential administration. She and her staff, along with NCATS’ budget and administrative offices staff, are developing briefing materials for the new administration and the new NIH director.
- The 2015 NCATS Annual Report has been published and can be found on the NCATS website.
- NCATS soon will publish a new Strategic Plan, which reflects the input of the Advisory Council, the CAN Review Board and other stakeholders.
- NCATS has been involved in the effort of the NIH Task Force on Clinical Trial Stewardship Reforms to improve the quality and efficiency of NIH-funded clinical trials. The Center had already implemented many of the reforms, including requiring a single institutional review board (IRB) for multisite studies, having requirements for clinical trial registration and results submission, and requiring that clinical trials be part of a specific FOA and use an FOA-specific template. Dr. Beall asked whether the task force could stop a clinical trial before it began. Dr. Austin said that the idea behind requiring that clinical trials be connected to a specific FOA was to circumvent such a need, by ensuring all trials were evaluated rigorously before they got underway.
- The NIH-FDA Joint Leadership Council is developing a clinical trial protocol template to be used by NIH-funded investigators who plan to submit protocols to the Food and Drug Administration (FDA). The purpose is to ensure that the protocols are consistently organized and contain all of the information FDA needs, making the process more efficient. The Council published a notice in the *NIH Guide* and released a request for information.
- Dr. Austin was elected the chair of the International Rare Diseases Research Consortium (IRDiRC). The next IRDiRC conference will take place in February 2017.
- NCATS was involved in establishing a global pre-clinical collaborative, which is meant to accelerate pre-clinical translational science; a paper describing the formation of the collaborative was published earlier this year. The initial emphasis is on communicating common messages on the importance and identity of translational science, focusing on creating common training platforms, sharing resources and sharing best practices.

### **Discussion**

Dr. Shekhar asked what projects NCATS might be undertaking in the years to come. Dr. Austin referenced the forthcoming Strategic Plan, which will provide a roadmap.

Harry P. Selker, M.D., M.S.P.H., asked whether NCATS has influenced other NIH Institutes and Centers (ICs) to participate in more projects across ICs. Dr. Austin said NCATS must find out what ICs would need to allow them to plug into NCATS programs and what NCATS needs to do to ensure their participation. Advisory Council and CAN Review Board members can help by working with ICs with which they have

relationships and conveying the benefits of translational science. NCATS also will conduct some pilot studies to see what works. Dr. Weichold said coordination among the ICs and executive leadership is critical to success.

Margaret A. Anderson, M.A., said that, within the context of the transition to a new administration, outside communities are asking whether NCATS is allocating its resources wisely and whether it is conducting work in which the pharmaceutical industry should be engaged. Dr. Austin said NCATS has addressed this issue in the past and continues to emphasize that the Center's efforts are complementary.

**V. UPDATE ON THE CTSA PROGRAM AND OFFICE OF RARE DISEASES RESEARCH TOOLKIT  
PROJECT: Petra Kaufmann, M.D., M.Sc., Director, Office of Rare Diseases Research and  
Division of Clinical Innovation, NCATS**

Petra Kaufmann, M.D., M.Sc., provided an update on the CTSA Program, presenting a schematic showing the hubs' five strategic goals and explaining how NCATS encourages collaboration through various networks and task forces. The CTSA Program hubs reach out to ICs, patient groups, the FDA and industry. They form a national network of virtual teams; share information, practices and tools; connect data systems; implement multisite studies; and integrate care and research.

The CTSA Program uses the NCATS Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB Platform to streamline the process for multisite studies. NCATS has established a single authorization agreement to be used across the CTSA Program hubs; the IRB master authorization agreement is now available on the NCATS website. The CTSA Program supports the [Accelerated Research Agreements](#) website, which includes a publicly available accelerated federal subcontracting agreement to enable further streamlining of the paperwork involved in launching a multisite study. This website also provides an [accelerated confidential disclosure agreement](#) and an [accelerated clinical trial agreement](#). The CTSA Program hubs have new practice recommendations for clinical investigators and coordinators, competency-based clinical research professionals' training curricula, and a best practices e-learning course.

NCATS' Trial Innovation Network will help to further streamline multisite studies, which often have difficulty enrolling a sufficient number of patients within the life of the grant. The key components of the network are the Trial Innovation Centers (TICs) and Recruitment Innovation Center. The Network's kickoff meeting is scheduled for Oct. 26, 2016.

NCATS developed the Common Metrics Initiative, a management tool that supports data-driven, results-based decision making, to measure NCATS impact in bringing discoveries to health through the CTSA Program.

NCATS also is developing a rare diseases toolkit in collaboration with patient groups. The toolkit will help patients find resources that currently are dispersed and hard to find, be a repository for online educational research resources and tools, and help identify resource gaps. One goal is to ensure the data that patient groups collect and deposit in a registry will be useful at the FDA. Patient groups are leading the effort. They have ascertained needs and identified useful, accessible and practical tools; they also are organizing the tools and identifying gaps.

## **Discussion**

Geoffrey Shiu Fei Ling, M.D., Ph.D., asked whether NCATS could use its authority to streamline the contracts process. Dr. Kaufmann said NCATS, through its CTSA Program, does this through cooperative agreements with investigators. Christopher P. Austin, M.D., said that NCATS, through CAN, also can use Other Transaction Authority (OTA) to streamline the process. Dr. Ling asked whether NCATS could use OTA for all contracts. Dr. Austin said that NCATS follows NIH policies and authorizations regarding the use of OTA and consults with the NIH Office of Extramural Research on its use.

Harry Selker, M.D., M.S.P.H., said NCATS has taken the right approach in establishing the TICs as a resource for multisite studies funded by other ICs. The ICs can bring their funded studies to the TICs to take advantage of the single IRB and other resources. Dr. Kaufmann said the idea is beginning to catch on within the ICs. She advocated getting more projects launched so that more investigators can see the benefits.

Anantha Shekhar, M.D., Ph.D., said it will be important to publicize the successes of the Trial Innovation Network. He also applauded the use of common metrics. Once it is clear the network and common metrics are successful, more principal investigators will accept it. Dr. Kaufmann said NCATS is implementing change very rapidly, which is challenging. The more NCATS can work collaboratively with investigators, patient groups and others, the better the initiatives will progress. The metrics are being aligned with the CTSA Program's strategic goals so that NCATS can measure the success of its efforts.

Louis J. DeGennaro, Ph.D., said NCATS has made a lot of progress in setting up the Trial Innovation Network within one year. Conducting large multicenter trials within the network, which has some very valuable resources, should now be attractive. The metrics will demonstrate how well the network performs. Dr. Kaufmann agreed, saying the network will greatly reduce the cost of research and will encourage the completion of more studies within the United States rather than abroad. It also will be helpful to patient groups, which could fund useful studies at much lower cost.

Frank F. Weichold, M.D., Ph.D., commented that another strength of NCATS' CTSA Program is that it is a network of investigators with a lot of clinical trial expertise. Dr. Kaufmann agreed, saying that the scientific expertise in the CTSA Program network is broad and deep. She also said a single IRB that other organizations can access is a strong point.

Daniel L. Hartman, M.D., asked how NCATS would solve the problem of the prolonged and over-budget clinical trial and what metric would be used to measure the success of that effort. Would it be based on past performance or some common standards? Dr. Kaufmann said the single contracting agreement, the single IRB, the expertise within the network and the uniform protocol would speed up the process. NCATS uses metrics, such as the time from project start to enrollment of the first patient, to measure success (e.g., whether the project is meeting its timeline and whether it is within budget). NCATS also is conducting a longitudinal study comparing how rapidly investigators complete their studies in comparison to their previous studies.

## **VI. CLEARANCE OF CONCEPTS**

### ***CTSA Data to Health (CD2H) Initiative: Petra Kaufmann, M.D., M.Sc., Director, Office of Rare Diseases Research and Division of Clinical Innovation, NCATS***

Petra Kaufmann, M.D., M.Sc., said NCATS is poised to use advances in bioinformatics to collect and analyze large datasets and to accelerate the translation of discoveries into health. Through the CD2H Initiative, the Center will work to increase the use of data and software standards across the CTSA

Program, the number of collaborative informatics projects, and the biomedical informatics training and skill of clinical and translational science trainees.

CD2H is designed to address obstacles, including the lack of consensus on research data standards, the dearth of business models for academic research software, and the small number of translational researchers and trainees with expertise in informatics and data science.

***NIH-Industry Partnerships Program: Discovering New Therapeutic Uses for Existing Molecules:***  
**Christine M. Colvis, Ph.D., Director of Drug Development Partnership Programs, Office of the Director, NCATS**

Christine M. Colvis, Ph.D., discussed reissuing the FOA under the Discovering New Therapeutic Uses for Existing Molecules (New Therapeutic Uses) program. The goals of testing new assets provided by pharmaceutical companies, demonstrating the utility of template agreements and crowdsourcing, and bringing together the best pharmaceutical assets with the best new ideas from researchers have not changed. The pharmaceutical company involved in the research will have right of first refusal to pursue further clinical development. This program, which has a relatively small budget, is designed to demonstrate the effectiveness of this approach.

The criteria for evaluating success include the efficiency of establishing drug repurposing partnerships through the template agreements, the number of projects that progress to Phase III clinical trials, and the value added by the pharmaceutical company, which may conduct additional studies or provide a drug at no cost.

The program has shown there is interest in repurposing marketed drugs, projects benefit from trial planning support, and there is value in NCATS retaining access to the drugs for further exploration. The first New Therapeutic Uses awards were issued in 2013. Most of the projects awarded then are in Phase II trials now. New awards were issued in July 2015.

***Discussion***

The Advisory Council and CAN Review Board first discussed CD2H:

- Harry Selker, M.D., M.S.P.H., said it would be helpful to have investigators trained to use the same platform and tools. This proposal includes that objective. He said his only concern is that this could be an expensive undertaking.
- Anantha Shekhar, M.D., Ph.D., asked whether this would be a single center or a network of centers. Dr. Kaufmann said it would be a collaborative core that would work with all the CTSA Program hubs.
- Richard E. Kuntz, M.D., said CD2H is focused on informatics, but the real need is for creation of a longitudinal record of meaningful health information from electronic health records (EHRs). This is a big problem that remains unsolved, even though many parties are working on it. He suggested that NCATS hold a workshop for interested parties to identify best practices.
- Alan D. Palkowitz, Ph.D., said it would be helpful to provide some examples that would show how the information could be used.
- Frank F. Weichold, M.D., Ph.D., said the FDA wants health data that is meaningful, accessible and transparent, as do NCATS and other agencies and organizations. Those agencies must coordinate to achieve this goal.
- Geoffrey S. Ginsburg, M.D., Ph.D., said the National Academies are working with EHR vendors to develop common data standards. He suggested that NCATS staff meet with the group that has convened. He asked how CD2H would harmonize with other informatics projects, such as Big



Data to Knowledge (BD2K). Dr. Kaufmann said rapid changes in informatics present challenges and opportunities. CD2H is more downstream in translational research than BD2K but will coordinate with BD2K, the FDA and others.

The Advisory Council unanimously approved the concept. The group next discussed the New Therapeutic Uses program:

- Scott J. Weir, Pharm.D., Ph.D., said this program provides an unusual opportunity to investigate abandoned drugs. One of the best aspects of the program is that NCATS maintains rights to investigate the drugs.
- Bernard H. Munos, M.B.A., said pharmaceutical companies are interested in sharing assets, but they do not want liability or to manufacture the drugs. They want to retain the right of first refusal, which the current agreement provides. He suggested structuring the program so there will be some suppliers who will work with academic investigators. He also suggested that NCATS contact as many pharmaceutical companies as possible, obtain the list of all drugs the companies are willing to provide for investigation, and keep that list in one place.
- Margaret A. Anderson, M.A., said this program helps break down the separation of public and private entities. Additional efforts should be implemented to spread the word about the program.
- Dr. Palkowitz said it would be a good idea to go back to the major companies that did not enlist in the first round. Changes in leadership or strategy may result in those organizations being more receptive to participation. He also said the agreements may have to be customized for the various companies, which have different profiles, assets and goals.
- Dr. Weichold said that through this program, NCATS can rescue abandoned drugs that could become treatments. He asked about the process. Dr. Colvis said none of the studies are first-in-human studies. The company has to have already completed a Phase I trial, and many drugs also have gone through a Phase II trial. NCATS would support a pre-clinical study.

The Advisory Council unanimously approved the concept.

## **VII. NIH COMMON FUND UPDATES**

The NIH Common Fund supports incubator projects in new areas of science. Projects are meant to be catalytic, transformative and high risk and to cut across organs and diseases. The projects are meant to move a field forward. Staff presented two of the NCATS programs supported by the Common Fund.

### ***Stimulating Peripheral Activity to Relieve Conditions (SPARC) Program Update: Danilo A. Tagle, Ph.D., M.S., Associate Director for Special Initiatives, NCATS***

Danilo A. Tagle, Ph.D., M.S., said SPARC is exploring electroceuticals, small implantable devices placed near organs to stimulate or calm nerve fibers to make organs function properly. Electroceuticals can control organ function more precisely than drugs are able to. The implantable devices are small and produce highly localized stimulation with fewer side effects than drugs have. One example of an electroceutical is a device for sleep apnea that detects abnormal breathing and provides stimulation to the nerves to restore normal breathing. Other devices to treat heart failure, incontinence, obesity and diabetes are in development.

These therapies have limits and have not performed well in randomized controlled trials. One problem is the incomplete understanding of the peripheral nervous system and end-organ response. There is a

need for a detailed anatomical and function map of the peripheral nervous system. Advancements in miniaturized technology also are needed for more precise control of signaling patterns.

SPARC will receive \$248 million over seven years to identify the mechanisms of neuromodulation therapies and spur development of more advanced therapies. SPARC-supported researchers will develop a map of peripheral circuits controlling major organs, develop new tools and technologies, and create a data management center.

SPARC includes partnerships with private companies to use their approved devices for these new applications. These partnerships make use of template agreements, including a memorandum of understanding, a confidential disclosure agreement and a collaborative research agreement.

SPARC staff also are meeting with leaders of similar projects, such as the NIH Brain Research through Advancing Innovative Neurotechnologies Initiative, which aims to map the anatomy and function of brain cells and circuits. NCATS expects to make its first SPARC awards by early 2017.

Richard E. Kuntz, M.D., suggested that Dr. Tagle contact the Feinstein Institute for Medical Research, which conducts research in bioelectronics medicine. Dr. Tagle said he is indeed considering contacting the Institute to determine whether it would be interested in being involved in SPARC. He said that some companies may want to become partners, whereas others may be interested in funding opportunities. NCATS is planning to hold a meeting with potential partners. Dr. Kuntz also recommended contacting companies such as Boston Scientific, which has been spending about \$75 million annually on neuromodulation, adding that there is talent and interest there.

Bernard H. Munos, M.B.A., said this project resembles acupuncture. Dr. Tagle agreed but said the project is more precise because the electrical potential pattern is recorded to identify normal function. This approach also removes the guesswork of where to place the needle.

Anantha Shekhar, M.D., Ph.D., asked whether the purpose of the current work is to map the peripheral nervous system or to treat disease. Dr. Tagle said the work will help create a functional map of the peripheral nervous system, which will help scientists understand the mechanisms of disease. This effort can lead to the development of better treatment devices and clinical outcomes.

Geoffrey S. Ginsburg, M.D., Ph.D., asked what will happen when the funding ends after seven years. Dr. Tagle said NCATS will see whether the work could lead to a discrete project or two. If so, NCATS could ask for an additional three years of funding. If the work has produced enough foundational knowledge, NCATS also could end the project and allow private companies to take over.

Daniel L. Hartman, M.D., asked whether NCATS would be developing a data-sharing component. Dr. Tagle said NCATS, through SPARC, has not moved forward on data management because this is such a complex dataset with electrophysiological maps involving amplitude, frequency, clinical transplantation, imaging and other facets. The investigators working on this project will share data and use a central data coordination center. NCATS is crafting a data-sharing agreement.

Christopher P. Austin, M.D., said because so little is known about the peripheral nervous system, this project to map it is an exciting opportunity. SPARC could lead researchers to the key for puzzling disorders such as irritable bowel syndrome.

***Illuminating the Druggable Genome (IDG): Program Overview: Christine M. Colvis, Ph.D., Director of Drug Development Partnership Programs, Office of the Director, NCATS***

Christine M. Colvis, Ph.D., said there are 3,000 genes in the druggable genome that can be modulated by small molecules. Only 10 percent have been drugged, and even those have not been studied sufficiently. NCATS wants to stimulate study in this area.

IDG began as a pilot program in 2014. The program includes two objectives. The first is to create a knowledge management center to integrate and make existing data searchable through a single portal. The center would prioritize proteins for exploration (illumination). The second objective is to adapt scalable technology, including assays, to explore the function of protein families and develop tools to facilitate experiments at scale. Pharmaceutical companies have expressed interest in the program. Implementation-phase FOAs are coming in the fall.

***IDG: Recent Advances: Tudor I. Oprea, M.D., Ph.D., Professor and Chief, Division of Translational Informatics, University of New Mexico School of Medicine***

Tudor I. Oprea, M.D., Ph.D., said his team is finding and integrating large datasets to help prioritize the study of understudied human proteins that could be drug targets. This project also includes a technology development center to devise new tools to shed light on these targets. The integrated dataset is accessible through [Pharos](#), the NCATS online portal.

Dr. Oprea's work focuses on two levels of drug target development. The first level includes proteins that appear in clinical research (Tclin proteins) and those that have bioactivities in [DrugCentral](#) and human curation for some targets (Tchem proteins). The second level includes proteins that basic scientists have studied (Tbio proteins) and those that have been studied very little (Tdark proteins).

His research shows a significant knowledge deficit with Tdark proteins — few large-scale tissue expression data, no genome-wide association studies and no literature. More than 37 percent of proteins are poorly described and would be considered Tdark. Only about 10 percent of the proteome (Tclin and Tchem) is specifically targeted by small molecules.

Dr. Oprea described the database, DrugCentral, which catalogues drugs and the diseases they treat. The catalogue shows there are at least 331 off-label diseases in treatment that are not subject to primary (on-label) indications from approved drugs.

Dr. Oprea detailed some other findings from his collection and analysis of available datasets, including:

- The number of drugs targeting protein kinases showed the most dramatic increase between 2011 and 2015. Kinases are drug targets in the oncology category.
- The most progress has been made in the oncology, antiviral, immunosuppressant and diabetes drug categories.
- There are therapeutic agents for only 15 percent of human diseases, so there are many new therapeutic opportunities. However, research tends to focus on the same small group of proteins; almost two-fifths of proteins have received virtually no attention.
- Presumably, the more targets a drug binds to, the more side effects it will cause. Dr. Oprea's data suggest that either this may not be true or that our annotation of drugs target interactions is very sparse.
- There is a great deal of uncertainty about experimental data, and his team is trying to make sense of them.
- The FDA's Adverse Event Reporting System data may help prioritize druggable targets.

**Discussion**

Dr. Ginsburg asked whether Dr. Oprea plans to systematically profile the Tdark part of the genome. Dr. Oprea said he would like to do so. He is working with an international consortium that could conceivably conduct the experiments, but the work could take up to 15 years. Dr. Colvis said it is difficult to stimulate research on a particular gene unless it is associated with an interesting phenotype and the necessary reagents and tools exist to explore it.

In response to a question about next steps, Dr. Austin said the concept that Dr. Oprea discussed is not attractive to pharmaceutical companies because it takes too long to advance from a program to a drug. Dr. Colvis said Dr. Oprea’s work uncovers new areas of research but that it can be difficult to obtain funding because study sections do not want to fund research on a protein with which they are not familiar.

Alan D. Palkowitz, Ph.D., said this dataset is a good foundation and a tremendous asset. It is important to find more ways to leverage it, but he cautioned that this is a very complex area. Investments in both the disease science and approaches to drug targets must continue.

Dr. Shekhar commented that Dr. Oprea has an amazing amount of data. Dr. Oprea said his team also is tracing phenotype data, but he did not have time to cover that in his presentation.

**VIII. ADJOURNMENT OF JOINT MEETING**

Christopher P. Austin, M.D., thanked all participants for their input. He adjourned the open portion of the meeting at 2:26 p.m. ET.

**IX. CLOSED SESSION OF NCATS ADVISORY COUNCIL**

This portion of the Advisory Council meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

Advisory Council members discussed procedures and policies regarding voting and the confidentiality of application materials, committee discussions, and recommendations. Members did not participate in the discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent.

**X. ADJOURNMENT OF CLOSED SESSION OF THE NCATS ADVISORY COUNCIL MEETING**

Christopher P. Austin, M.D., adjourned the closed session of the NCATS Advisory Council meeting at 3:40 p.m. ET.

**CERTIFICATION**

We hereby certify that, to the best of our knowledge, the foregoing minutes and supplements are accurate and complete.

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Christopher P. Austin, M.D.

\_\_\_\_\_  
Date

Chair, NCATS Advisory Council  
and  
Director, National Center for Advancing Translational Sciences, NIH

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Anna L. Ramsey-Ewing, Ph.D.  
Executive Secretary, NCATS Advisory Council  
Executive Secretary, Cures Acceleration Network Review Board  
and  
Director, Office of Grants Management and Scientific Review, NCATS

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Date

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Geoffrey S. Ginsburg, M.D., Ph.D.  
Vice Chair, Cures Acceleration Network Review Board  
and  
Director, Duke Center for Applied Genomics & Precision Medicine;  
and Professor of Medicine, Pathology and Biomedical Engineering,  
Duke University Medical Center

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Date