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
January 14, 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 Jan. 14, 2016, convening at 8:30 a.m. ET, in Conference Room 10, Building 31, on the National Institutes of Health (NIH) main campus. Christopher P. Austin, M.D., NCATS Advisory Council chair, and Freda C. Lewis-Hall, M.D., CAN Review Board 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. (by telephone)
Jorge L. Contreras, J.D.
Pamela B. Davis, M.D., Ph.D.
Louis J. DeGennaro, Ph.D.
Mary L. Disis, M.D.
Eric D. Kodish, M.D.
Geoffrey S. Ginsburg, M.D., Ph.D. (by telephone)
Freda C. Lewis-Hall, M.D.
Bernard H. Munos, M.B.A.
Harry P. Selker, M.D., M.S.P.H.
Anantha Shekhar, M.D., Ph.D.
Scott J. Weir, Pharm.D., Ph.D.

Representative Members

None present

Ad Hoc Members

Daniel L. Hartman, M.D., Bill and Melinda Gates Foundation
Richard E. Kuntz, M.D., Medtronic, Inc.
Geoffrey Shiu Fei Ling, M.D., Ph.D., Uniformed Services University of the Health Sciences
Matthew Might, Ph.D., University of Utah
Megan O'Boyle, Phelan-McDermid Syndrome Data Network
Paul G. Yock, M.D., Stanford University (by telephone)

Ex Officio Members

David Atkins, M.D., M.P.H., Department of Veterans Affairs (by telephone)

CAN REVIEW BOARD MEMBERS PRESENT

Chair

Freda C. Lewis-Hall, M.D., Executive Vice President and Chief Medical Officer, Pfizer

Vice Chair

Geoffrey S. Ginsburg, M.D., Ph.D., Director, Center for Applied Genomics & Precision Medicine, Duke Institute for Genome Sciences & Policy; and Professor of Medicine, Pathology and Biomedical Engineering, Duke University Medical Center (by telephone)

Executive Secretary

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

Board Members

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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.
Lawrence A. Soler, J.D.
Myrl Weinberg, M.A.
Scott J. Weir, Pharm.D., Ph.D.

Representative Members

None present

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Megan O'Boyle, Phelan-McDermid Syndrome Data Network
Sharon F. Terry, M.A., Genetic Alliance
Paul G. Yock, M.D., Stanford University (by telephone)

Ex Officio Members

David Atkins, M.D., M.P.H., Department of Veterans Affairs (by telephone)
S. Rao Kosaraju, Ph.D., National Science Foundation
Frank F. Weichold, M.D., Ph.D., Food and Drug Administration (attending in place of Stephen Ostroff, M.D.)

OTHERS PRESENT

NCATS leadership and staff

I. CALL TO ORDER

Christopher P. Austin, M.D., welcomed members and guests to the 11th meeting of the NCATS Advisory Council and the 14th meeting of the CAN Review Board. He reminded attendees that the open session was being videocast.

Dr. Austin welcomed Anna L. Ramsey-Ewing, Ph.D., as the new executive secretary of the NCATS Advisory Council and CAN Review Board. Dr. Ramsey-Ewing is the director of the NCATS Office of Grants Management and Scientific Review. Dr. Austin also introduced the *ad hoc* and *ex officio* members of the Advisory Council and CAN Review Board.

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 Sept. 3, 2015, 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 on May 12, 2016, and Sept. 15, 2016. The CAN Review Board also will meet by teleconference on Dec. 9, 2016.

New staff members who have joined NCATS since the last joint meeting were introduced:

- **Ilyas Singeç, M.D., Ph.D.,** is the new head of stem cell research within the Division of Pre-Clinical Innovation. He comes to NCATS from Pfizer, where he directed a laboratory for stem cell technologies.
- **Erica K. Rosemond, Ph.D.,** is a program officer at NCATS in its Division of Clinical Innovation. She manages several of the Clinical and Translational Science Awards (CTSA) Program hubs at NCATS.
- **Katherine A. Schwartz, M.S.,** is a program analyst for NCATS in its Division of Clinical Innovation. She previously served as a program analyst at the National Heart, Lung, and Blood Institute.

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

Christopher P. Austin, M.D., presented some recent NCATS highlights. In the interest of conserving paper, members received a flash drive containing the entire report, which is summarized below.

Organizational Update

- Anna L. Ramsey-Ewing, Ph.D., joined NCATS in September 2015 as the director of the Office of Grants Management and Scientific Review. She began her career at NIH as a scientific review officer and was most recently the director of the Office of Extramural Research Policy and Operations at the National Institute of Allergy and Infectious Diseases (NIAID).
- Dorit Zuk, Ph.D., is leaving her position as director of the NCATS Office of Policy, Communications and Strategic Alliances to return to a focus on basic research at the National Institute of General Medical Sciences.
- Penny W. Burgoon, Ph.D., will serve as the acting director of the Office of Policy, Communications and Strategic Alliances while retaining her role as director of the Office of Policy.

The following NCATS Advisory Council members' terms are set to expire: Pamela B. Davis, M.D., Ph.D.; Mary L. Disis, M.D.; and Todd B. Sherer, Ph.D. Two members of the CAN Review Board have completed their terms: Lawrence A. Soler, J.D.; and Myrl Weinberg, M.A. These members will receive certificates of appreciation from the U.S. Department of Health and Human Services Secretary Sylvia Matthews Burwell.

New members of the NCATS Advisory Council who were present as *ad hoc*, non-voting members were: Richard E. Kuntz, M.D.; Geoffrey Shiu Fei Ling, M.D., Ph.D.; Matthew Might, Ph.D.; Megan O'Boyle; and Sharon F. Terry, M.A.

Selected Translational Innovations Highlights

- **Matrix Drug Combination Screening Platform.** NCATS investigators have developed a high-throughput, combination drug-screening platform to identify promising drug combinations. This matrix screening method improves on the trial-and-error approach of testing thousands of drug combinations.
- **Drug Combination Dataset for Malaria.** A team of investigators led by NCATS screened almost 14,000 pairs of drugs using the matrix drug combination screening platform. The testing identified promising new antimalarial drug combinations and new information on mechanisms of action that could lead to new antimalarial therapies. NCATS made the data public to encourage the development of new treatments and drug combinations for malaria. The study appears in *Scientific Reports*.
- **The Toxicology in the 21st Century (Tox21) Transform Tox Testing Challenge: Innovating for Metabolism.** Three federal agencies — NCATS, the National Toxicology Program at the National Institute of Environmental Health Sciences and the Environmental Protection Agency — are offering up to $1 million in prizes to toxicology researchers who successfully retrofit commonly used high-throughput screening assays in order to predict the toxicity of chemicals on human health.
- **Pfizer's Centers for Therapeutic Innovation.** NIH joined Pfizer's Centers for Therapeutic Innovation in December 2014. The program bridges the gap between early scientific biologics discovery and clinical application through public-private resource sharing. This is the first NIH-wide biologics initiative with a pharmaceutical partner. In December 2015, the first proposal from NIH was approved. NIAID and Pfizer are currently finalizing the scope of work.
- **Gene Therapy.** NCATS supports gene therapy development through several projects, including projects in urea cycle disorders and primary immune deficiency. NCATS' Bridging Interventional Development Gaps scientists are working with a Mayo Clinic investigator on an adeno-associated virus therapy for osteoarthritis that had been found to be effective in large animal models. Within the Extracellular RNA (ExRNA) Communication Program (an NIH Common Fund program), there is a focus on a relatively new discovery: Cell membranes can form vesicles that bud off and can behave as signaling vessels by transporting RNA to other parts of the body. Projects funded by NCATS in this program support researchers trying to harness exRNA as a natural form of gene therapy, including a study to deliver drugs to the brains of people with Huntington's disease.
- **Niemann-Pick Type C1 Disease Project Update.** NCATS and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development entered into a cooperative research and development agreement with the biotechnology company Vtesse, Inc., to develop a drug to treat Niemann-Pick disease. The Food and Drug Administration (FDA) has designated this drug as a breakthrough therapy.
- **CTSA Program Common Metrics Initiative.** NCATS has been working with CTSA investigators and evaluators to develop metrics for the strategic management of the CTSA Program. They have come up with methods to measure the program's impact and are launching a pilot study to validate the metrics.

Policy and Legislative Updates

- **Fiscal Year (FY) 2016 Budget.** NIH received a $2 billion increase for FY 2016; NCATS received a $52.7 million increase, including increases for the CTSA Program and CAN. The increases were finalized after the FY had begun, but NCATS had identified priorities and completed concept clearances in the event of increased funding. Robert J. Beall, Ph.D., asked whether the recent proposal by Vice President Joe Biden to mount a concerted effort to cure cancer would have any

effect on NCATS. Dr. Austin said the Cancer Moonshot proposal was still in development, and he will update the Advisory Council and CAN Review Board as the initiative moves forward.

- **Congressional Briefing.** Dr. Austin and CAN Review Board ad hoc member Dr. Might were among those who briefed the Rare Disease Congressional Caucus on "Precision Medicine: New Frontiers for Rare Diseases." The briefing was held in November 2015 and hosted by the Rare Disease Legislative Advocates.
- **Congressional Authorizing Activity.** The U.S. House of Representatives passed the 21st Century Cures Act, which authorizes $8.75 billion to NIH over the course of five years. The Senate authorizing committee has not yet released its version of the bill.
- **Precision Medicine Initiative (PMI) Cohort Program.** NCATS will administer the other transactions authority awards for the PMI Cohort Program, which is part of the NIH Common Fund. The program is designed to build a research cohort of 1 million volunteers. NIH announced multiple PMI funding opportunities in November 2015.
- **Notice of Proposed Rulemaking.** The deadline for comments on proposed rules to protect human research subjects — the Common Rule — closed on Jan. 6, 2016. CTSA Program representatives hosted a series of webinars about the proposed changes.
- **NIH Strategic Plan.** The congressionally mandated strategic plan was published in December 2015. NCATS programs highlighted in the report were: Tissue Chip for Drug Screening, Tox21, CTSA Program, and Discovering New Therapeutic Uses for Existing Molecules.
- **NIH Big Data to Knowledge (BD2K) Initiative.** NCATS program staff and CAN Review Board vice chair Geoffrey S. Ginsburg, M.D., Ph.D., are serving on the NIH BD2K Multi-Council Working Group.

Discussion

Dr. Davis said the matrix method for testing drug combinations may produce many new drug combinations that the FDA will be asked to approve. Has NCATS discussed this with the FDA? S. Rao Kosaraju, Ph.D., said this has not been discussed specifically with the FDA, but that FDA leadership is aware of the program. Dr. Austin said he will ask the investigators to contact the FDA staff.

Dr. Davis asked whether BD2K training will include undergraduates. Dr. Ginsburg said funding for the training will start with the pre- and postdoctoral levels. Petra Kaufmann, M.D., M.Sc., said there is an effort to reach trainees earlier in the pipeline, and that Erica K. Rosemond, Ph.D., has been working on BD2K training.

Dr. Beall asked Dr. Austin to prepare a slide for future presentations showing how much of the total NCATS budget each program receives. The Advisory Council and CAN Review Board members would find this information beneficial when comparing the relative effectiveness of different programs.

IV. CAN REVIEW BOARD UPDATE: Freda C. Lewis-Hall, M.D., Executive Vice President and Chief Medical Officer, Pfizer

CAN Review Board chair Freda C. Lewis-Hall, M.D., said the Board reviewed concepts for clearance at its December 2015 meeting in anticipation of receiving additional funding during FY 2016. The CAN Review Board approved seven concepts:

- Increasing Access to Compounds and Toxicity Data
- Proof-of-Principle Awards
- Sensors and Devices to Detect Clinical Outcomes

- Targeting Shared Molecular Etiologies (SaME) Underlying Multiple Diseases to Accelerate Translation
- 3-D Bioprinting of Human Tissues for Drug Screening
- Tissue Chip Testing Centers: Validating Proteomic Profiling for Clinical Applications
- Tissue Chip Testing Centers: Validating Microphysiological Systems and Proteomic Profiling for Clinical Applications

Discussion

Robert J. Beall, Ph.D., asked how many of the concepts are investigator-initiated. Christopher P. Austin, M.D., said the concepts are not generally investigator-initiated because the programs have many pieces and must be coordinated. However, many of the respondents are from the young investigator pool. Danilo A. Tagle, Ph.D., M.S., said NCATS wants to find the people with the best ideas and does not have preconceived thoughts about the investigators.

Scott J. Weir, Pharm. D., Ph.D., said the proof-of-principle awards could help young investigators who are missing only one key piece of data.

Geoffrey Shiu Fei Ling, M.D., Ph.D., said he likes the underlying etiology approach taken by the SaME Therapeutics program, which enables cancer investigators to populate clinical trials based on genetics, rather than on the tissue of origin of the cancer.

Dr. Ling said he believes in helping young investigators, but NCATS' mission is to get scientific discoveries to patients as quickly as possible. Investigators should be encouraged to find matching funds from commercial or philanthropic sources, which could move innovations to the clinic more quickly.

Dr. Austin said that with increased funding in FY 2016, NCATS can match up to $3 in funding for every $1 from another funder.

Anantha Shekhar, M.D., Ph.D., asked how to align CAN and the CTSA Program. Dr. Austin said NCATS has been working to form more collaborations between and among its programs and initiatives. Dr. Tagle noted the collaboration between the Tissue Chip program and the CTSA Program hubs.

V. NCATS STRATEGIC PLANNING UPDATE: Dorit Zuk, Ph.D., Director, Office of Policy, Communications and Strategic Alliances, NCATS

Dorit Zuk, Ph.D., said NCATS launched its strategic plan website in fall 2015, published a request for information (RFI) to solicit feedback and held town hall webinars. The RFI asks for input on the scientific and operational opportunities, challenges and research needs in translational science, including the following issues of interest:

- Breaking down silos
- Establishing interoperability of data systems
- Expanding research into new therapeutic modalities
- Achieving patient-driven research and patient/community engagement
- Forming innovative partnerships with a variety of stakeholders
- Identifying training needs of the next generation of translational scientists
- Identifying communication and dissemination tools to expand awareness of translational science

NCATS has received 40 stakeholder comments so far, and the deadline for comments has been extended to Feb. 8, 2016. An update will be provided at the next joint meeting on May 12, 2016.

VI. CLEARANCE OF CONCEPTS: Petra Kaufmann, M.D., M.Sc., Director, Office of Rare Diseases Research and Division of Clinical Innovation, NCATS; and Philip J. Brooks, Ph.D., Program Director, Division of Clinical Innovation, NCATS

CTSA Program Network Organizational Hub

NCATS proposes to create an organizational hub to help the CTSA Program sites standardize data and use common metrics across projects. The hub would help coordinate communication and collaboration among the more than 50 biomedical research centers and their stakeholders. Establishing an organizational hub is critical to making the network more efficient.

Discussion

Myrl Weinberg, M.A., asked whether the efforts of the organizational hub would duplicate efforts of other NCATS programs, such as in communications and common metrics. Petra Kaufmann, M.D., M.Sc., said NCATS will not duplicate efforts, but will adapt the NCATS programs to the needs of the CTSA Program.

Mary L. Disis, M.D., said the proposed hub could better coordinate the centers. Maintaining communication among more than 50 centers is very difficult.

Eric D. Kodish, M.D., asked how the common metrics would be used. Dr. Kaufmann said workforce training and development would be one area. Further discussion on common metrics was deferred to later in the meeting.

Bernard H. Munos, M.B.A., said he knew nothing about the deliverables of the current coordinating center, even though he is an advisor to the program. Pamela M. McInnes, D.D.S., M.Sc. (Dent.), said the experience of the current coordinating center led NCATS staff to develop the idea of a coordination hub.

Louis J. DeGennaro, Ph.D., asked what authority the coordination hub would have to ensure that the CTSA Program hubs report and align data across the network. Dr. McInnes said the CTSA Program's primary direction comes from NCATS. The CTSA Program hubs recognize that changes are needed, and they are partners in the effort.

Robert J. Beall, Ph.D., said it will require much effort to make the hub work, both to collect the data and to disseminate usable data. He asked about the cost. Dr. McInnes said NCATS staff are aware of the cost because there are existing models, but the investment must be made.

Pamela B. Davis, M.D., Ph.D., said individual institutions involved in the CTSA Program network may balk at bearing the expense of coordinating the network. NCATS should find additional money to pay for that.

Scott J. Weir, Pharm.D., Ph.D., asked what role the hub would have in implementing new initiatives within the network. Dr. Kaufmann said the new hub, under the direction of NCATS, would help translate the innovations from the individual centers and would help disseminate the innovations.

There was a unanimous vote to close the discussion and to approve the concept.

Collaborative Innovation Exploratory Projects for the CTSA Program

Philip J. Brooks, Ph.D., said that this proposed initiative would enable teams of investigators to carry out exploratory projects to evaluate novel approaches to translational science. These would be for projects that are not well suited to the CTSA Collaborative Innovation Awards. The criteria for success will include quality and novelty of the application and the number of awards that lead to additional funding.

Discussion

Dr. Davis said she would prefer an administrative supplement because peer review takes too long — about nine months. She suggested trying out the concept and allowing the project investigators to compete for one of the larger innovation supplements. Dr. McInnes said this will not remove the option of administrative supplements, but it requires the grantees to work very closely with program staff.

Dr. DeGennaro said he supports the concept with peer review, but peer review must be speedier. He asked NCATS staff to rethink the criteria for evaluation, such as the impact that a project could have.

Geoffrey Shiu Fei Ling, M.D., Ph.D., said peer review ensures academic integrity, but there are ways to streamline the approach. He suggested placing NIH, FDA and National Science Foundation scientists on the peer review panels. They could be assigned more quickly and would avoid conflict of interest. Dr. McInnes said there is a limit on the number of federal employees allowed to sit on NIH peer review panels. Frank F. Weichold, M.D., Ph.D., suggested a hybrid form of review that would be quicker, such as an "expert review."

Megan O'Boyle asked whether CTSA Program hubs already are required to collaborate. Dr. Kaufmann said collaboration among the centers is a key part of the program, but the way in which the CTSA Program hubs are organized has made it difficult. The Collaborative Innovation Exploratory Projects would stimulate the collaboration.

Dr. Weir asked whether NCATS had considered reexamining the administrative functions of the CTSA Program hubs. Dr. Kaufmann said NCATS tries not to spend time on bureaucracy because the NCATS mission is to bring results to patients.

Dr. Beall asked whether CTSA Program hubs can partner with industry. Dr. McInnes said there are no preconceived notions about the types of organizations with which the CTSA Program hubs can partner. Dr. Davis said that partnering with industry is not necessarily a better option and that it is beneficial to the program to have the CTSA Program hubs partner with each other.

There was a unanimous vote to close the discussion and to approve the concept.

VII. NCATS PARTNERSHIPS WITH THE NIH COMMON FUND: Danilo A. Tagle, Ph.D., M.S., Associate Director for Special Initiatives, NCATS; Carson R. Loomis, Ph.D., Senior Advisor to the Director, NCATS; and David J. Eckstein, Ph.D., Senior Health Scientist Administrator, Office of Rare Diseases Research, NCATS

Christopher P. Austin, M.D., gave a brief overview of the NIH Common Fund, which began in 2003 to focus on trans-NIH scientific projects related to organs, technology and disease. Common Fund projects are overseen by two NIH Institute directors and an NIH project team. Danilo A. Tagle, Ph.D., M.S., presented two of the six NCATS programs funded by the Common Fund: the ExRNA Communication program and the Undiagnosed Diseases Network (UDN).

ExRNA Communication Program
Until recently, scientists believed that the microvesicles that bud off from cells contained only cellular debris and that RNA is not secreted from cells. But research has shown that microvesicles and exosomes are filled with regulatory RNA, RNA protein complexes and lipids. The secreted RNA mediates cell-to-cell communication.

Healthy cells make different exRNA from disease cells. The content of exosomes can transform the recipient cell to the phenotype of the donor cell. This finding suggests the possibility that these vesicles could be harnessed to block diseases such as cancer or to diagnose disease at an earlier stage.

NIH will invest $130 million over the course of six years in the exRNA program to support a consortium of investigators. The program will make 30 awards to help move the field forward in several ways:

- Discovering more about exRNA generation, secretion and transport
- Developing a catalog of exRNA found in body fluids
- Investigating the potential for exRNAs for use as therapeutics and biomarkers

The ExRNA Communication Consortium is a network of investigators that includes an external scientific panel, an NIH project team and FDA staff. Consortium members share pre-publication data and resources. The consortium makes awards in five categories: data management and resource repository, biogenesis, profiling, clinical therapeutic utility and biomarkers.

- The **Data Management and Resource Repository** at Baylor College of Medicine will support data deposition, management, analysis and sharing within the consortium. The repository will set exRNA standards and protocols. The data will be made available to the general scientific community at http://www.exrna.org.
- **Biogenesis** projects will enable investigators to examine the principles that guide the selection of regulatory RNA molecules for extracellular transport and determine the function of the exRNAs.
- **Profiling** will produce a reference list of noncoding exRNAs from healthy human body fluids. The catalog will include all types of extracellular regulatory RNA, including microRNA and messenger RNA.
- **Clinical therapeutic utility** projects will enable investigators to develop exRNA-based therapies and demonstrate proof-of-concept pre-clinical studies during the initial UH2 stage, leading to studies that enable Investigational New Drug applications during the UH3 phase. These projects also will enable researchers to investigate the exosomes themselves as potential vessels for drug delivery.
- **Biomarker** projects will enable investigators to identify and validate exRNA biomarkers from body fluids. The 10 biomarker projects investigate various diseases and conditions, including Alzheimer's disease, multiple sclerosis, myocardial infarction and high-risk pregnancy preeclampsia.

These projects are limited to five years, with the first two years focused on exRNA biomarker discovery and the final three years on clinical validation of the biomarkers.

Dr. Tagle provided several examples of ongoing projects, including the discovery of a novel biomarker of heart failure, microRNA (miR-30d). Another group is using a grape-derived nanovector to deliver miR17 intranasally to the brain to inhibit tumor progression. There also are ongoing clinical trials using plant exosomes, including one to deliver curcumin to colon cancer tissue. The project team is led by NCATS Director Dr. Austin and Dinah S. Singer, Ph.D., of the National Cancer Institute.

Discussion

Matthew Might, Ph.D., asked whether there is a size limit on the RNAs that are transported in the vesicles. Dr. Tagle said there is no known size limit. Curcumin is a large molecule that would not normally cross the blood-brain barrier, but does when enclosed in the vesicle. The vesicles also can get miRNAs across the blood-brain barrier.

Undiagnosed Diseases Network

David J. Eckstein, Ph.D., said the UDN began in 2008 to help patients with unknown disorders reach a diagnosis and to discover new rare diseases. Of the 900 patients with complex disorders accepted into the program, 360 are children. UDN has diagnosed about 225 of the patients.

Gene function studies of the variants identified in some of the rare diseases are an important part of the network's work. The extremely rare diseases diagnosed include myoclonus epilepsy due to SCARB2 mutations and neurodegeneration with brain iron due to c19orf12 mutations. Among the new disease genes discovered was one that causes arterial calcification due to deficiency of CD73 (NT5E mutations) and one that causes short stature and osteoporosis (ATP6V1H).

UDN has three objectives:

- Improve diagnosis and care for people with undiagnosed disease
- Facilitate research into the etiology of the disease
- Create a research community to improve patient management

UDN has seven clinical sites, a Coordinating Center, two DNA Sequencing Cores, a Metabolomics Core, a Model Organism Screening Center and a Central Biorepository. The clinical sites can complete a clinical evaluation in one week.

Carson R. Loomis, Ph.D., said the Metabolomics Core and the Model Organism Screening Center follow the patients and monitor their treatments after they are diagnosed. This process will lead to better understanding of gene function and the pathophysiology of abnormal gene function.

The Model Organism Screening Center can investigate 200 variants per year by using zebrafish, *Drosophila*, mice and yeast. The Metabolomics Core provides expertise to aid in clinical diagnosis. The Central Biorepository coordinates sample shipments and organizes and stores half of the collected samples of blood, urine, cerebrospinal fluid and sputum. The other half of the collected samples stay at the clinical site.

There is a lot of interest nationally and internationally in this network. The program is funded through 2017, after which it will undergo review to determine whether it should be funded for another five years.

Discussion

Geoffrey S. Ginsburg, M.D., Ph.D., asked that the network share its data with other rare disease programs around the world. Dr. Austin said this is the intention of the network. Researchers in Japan have started an undiagnosed disease network and want to share data. Also, Dr. Austin now is chair of the International Rare Diseases Research Consortium's Executive Committee.

Scott J. Weir, Pharm.D., Ph.D., asked whether UDN and SaME are complementary. The response was that they are. The National Human Genome Research Institute is a partner in the program. UDN has a central institutional review board (IRB).

VIII. UPDATES FROM THE CTSA PROGRAM AND OFFICE OF RARE DISEASES RESEARCH: Petra Kaufmann, M.D., M.Sc., Director, Office of Rare Diseases Research and Division of Clinical Innovation, NCATS

CTSA Program

Clinical trials are inefficient, costly and often ineffective. NCATS' efforts to resolve this problem include:

- Establishing a centralized IRB for multisite studies. NCATS has run a pilot test by using a centralized IRB that has worked well.
- Streamlining contracting using a pre-negotiated master agreement that is used across the sites and includes acceleration of three areas:
    - Confidential disclosure agreement
    - Clinical trial agreement
    - Subcontracting

Through the CTSA Program, NCATS has harmonized training across sites to streamline training. The investigators have drawn up a list of research competencies and clinical practice standards. CTSA Program investigators have shared curriculum and training opportunities for first-time principal investigators (PIs), research coordinators, other personnel and community members.

NCATS also is improving participant recruitment to clinical trials by developing, through the CTSA Program, a recruitment protocol and a way to find qualified participants from electronic health records. NCATS wants to disseminate these methods more widely to accelerate translational science and improve health.

NCATS plans to launch three trial innovation centers (TICs) and recruitment innovation centers (RICs) this year. RICs could begin as early as February 2016 and will be funded for up to five years, at a total cost of $3 million per center. TICs could begin as early as June 2016 and will have up to seven years of funding, at a total cost of $4 million per center.

To reach the strategic goals, CTSA Program communications have been streamlined through the use of five task forces, more than 50 program hubs and a steering committee. Each task force has a lead team, and a member of the lead team is on the steering committee. The task forces are focused in the following areas:

- Workforce development
- Collaboration and engagement
- Integration across the life span
- Methods and processes
- Informatics

Louis J. DeGennaro, Ph.D., asked whether the communications structure should include one project communications team. Petra Kaufmann, M.D., M.Sc., said the CTSA Program network organizational hub, discussed earlier in the meeting, would perform that function.

CTSA Program Common Metrics Initiative leads are working with the PIs, evaluators, administrators and coordinators to identify the metrics of success. The PIs want to be able to measure the overall impact of the program. The first set of measures was adopted in December 2015. The metrics come under four categories:

1. Hub resources and services
2. Workforce development

3. Consortium 2.0
4. Collective impact of the hubs

The key to measuring the success of the program is to focus on concise, high-level metrics. These measures can be captured in a reasonable time frame, and the program personnel will want to analyze them.

Dr. Kaufmann said the CTSA Program hubs will use the data in several ways:

- Measure how well the program is doing
- Identify the underlying factors behind the program's performance
- Implement the most promising management strategies

Office of Rare Diseases Research

Dr. Kaufmann shared the following updates and plans:

- The Rare Diseases Clinical Research Network includes 22 consortia at 250 institutions worldwide. Network-supported investigators study 282 rare diseases, with the participation of more than 130 patient advocacy groups. There are 90 active protocols.
- The Genetic and Rare Diseases Information Center provides information to patients and their families, researchers, and the public about rare or genetic diseases.
- The NCATS Scientific Conferences program brings people together to identify scientific opportunities and evaluate applications.
- The NIH/NCATS Global Rare Diseases Patient Registry Data Repository/GRDR® will serve as a one-stop shop for rare diseases data from around the world.
- The NCATS Toolkit Project will help patients and patient advocacy groups find researchers and clinical trials. This toolkit will feature translational research tools and resources to help identify where gaps exist.
- Rare Disease Day at NIH 2016 will take place on Feb. 29.

Discussion

Dr. DeGennaro asked about the common metrics that would measure the performance of the multisite clinical trials. Dr. Kaufmann said the metrics initiative she presented would measure the performance of the CTSA Program network itself, locally and regionally. Currently, those data exist, but they are not in one place, which is why the organizational hub is needed: to have the data in one place.

Myrl Weinberg, M.A., said she is pleased with NCATS' progress in involving patients in these projects.

Pamela B. Davis, M.D., Ph.D., said if this is no more than a clinical trials network, then NCATS is missing the boat. The network should provide training, support, advice on best practices and more.

Anantha Shekhar, M.D., Ph.D., said that RICs and TICs will provide the kinds of metrics about which Dr. DeGennaro asked, but those centers are just being set up.

Harry P. Selker, M.D., M.S.P.H., noted that these metrics will be difficult to develop because the aim is to measure how research is done across many disciplines, involving a very large number of researchers. The CTSA Program hubs are trying to find ways to measure the many intangibles that are important to good research.

Daniel L. Hartman, M.D., asked whether there has been resistance to these changes from CTSA Program investigators. He also said the Bill and Melinda Gates Foundation has done a great deal of work in sub-

Saharan Africa on harmonization of regulations. He offered to speak with Dr. Kaufmann about the lessons they have learned.

Dr. Kaufmann said that while change is challenging, CTSA Program investigators recognize the value of change and have been partners in these changes. She also said it is important for NCATS to harmonize its efforts with other groups working globally and to make its work public and sharable. She will further discuss the issue with Dr. Hartman outside the meeting.

David Atkins, M.D., M.P.H., noted there are many other things that slow down research, and the IRB time to approval is only a short piece of that. Are there other tasks that could be sped up to get clinical trial results out more quickly?

Dr. Kaufmann said that a series of steps in the process could be done more quickly, leading to much less time from study conception to publication. IRB approval times can take one year, but NCATS has cut that to four months. NCATS, with the investigators, also is looking for innovative methods to make the process much shorter.

IX. ADJOURNMENT OF JOINT MEETING

Christopher P. Austin, M.D., thanked all participants for their input. He adjourned the open portion of the meeting at 2:51 p.m. ET.

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 absented themselves from the meeting during 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.

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 3:45 p.m. ET.

CERTIFICATION

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

_____ _____

Christopher P. Austin, M.D. Date
Chair, NCATS Advisory Council
and
Director, National Center for Advancing Translational Sciences, NIH

_____ _____

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

_____ _____

Freda C. Lewis-Hall, M.D. Date
Chair, Cures Acceleration Network Review Board
and
Executive Vice President and Chief Medical Officer, Pfizer