American Thoracic Society

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In This Issue

Letter from the Editor

The October ATS Research News Quarterly features an interview with the Director of the National Center for Advancing Translational Sciences (NCATS), Christopher Austin, M.D. Dr. Austin shares his vision for the center over the next five years, how sequestration funding cuts are affecting NCATS research and how the center's programs address lung disease.

This month's Quarterly also features a report on the NHLBI's new multi-institutional Centers for Accelerated Innovations (NCAI's). The NCAI's are aimed at bridging the translational gap between scientific discovery and product development. Moving to the research advocacy area, we bring you news on the ATS Breathing Better Advocacy Alliance's first ever state congressional meeting, held with Rep. Chuck Fleischmann (R-TN) in Chattanooga, TN.

Next is an article on the new NIH and FDA Tobacco Centers of Regulatory Science (TCORS), coordinated by the NHLBI and other NIH institutes to support basic and applied research on tobacco and addiction, which is followed by a report on the Patient-Centered Outcomes Research Institute's (PCORI) research portfolio as it celebrates its third anniversary. The October Quarterly concludes with an update on health research funding.

Sincerely,

Linda Nici, MD
Editor

AGENCY SPOTLIGHT – NCATS

Interview with National Center for Advancing Translational Sciences Director, Christopher Austin, MD

Q. What is your vision for NCATS over the next five years?
A. A myriad of well-described and system-wide problems, both scientific and operational, is limiting the efficient creation and implementation of interventions that demonstrably improve human health. NCATS was created to address these roadblocks, and our aim for the next five years is to start transforming the translational process in all its stages, from target validation through public health impact. NCATS will focus on developing, demonstrating and disseminating new technologies and models that speed the delivery of new treatments and diagnostics to more people more quickly.

As I often say, translation is a team sport, so all our work will be done collaboratively, with partners and stakeholders in the public, private, government and non-profit sectors. Examples of NCATS priorities are the development of data and models that can more accurately predict drug efficacy and toxicology, new drug repurposing paradigms, provision of starting points for exploitation of novel targets and currently untreatable diseases, development of systematic resources for definition of clinical diagnostic and endpoint criteria, and improvement in the processes of clinical trial recruitment and execution.

Q. What impact is the sequestration funding cut having on the NCATS?
A. We know that investing in medical research translates to benefits for U.S. public health and the economy, and it certainly is more challenging for NCATS to meet its ambitious mission in this environment. NCATS is a new and distinct entity in the research ecosystem, and as such we have a long list of important priorities and opportunities, many of which we realistically cannot tackle with our current budget.

It's perhaps most concerning that the sequester that occurred last January was not a one-time event. If nothing is done, successive sequester cuts will lead to a nearly $19 billion loss to NIH-supported research over the next 10 years. Obviously, this will affect funding for

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Agency Spotlight *(Continued from page 2)*

NCATS, and sadly, have major consequences for the health of the American people.

Q. Lung diseases are now the third leading cause of death in the U.S. How are NCATS translational programs addressing lung disease?
A. NCATS does not target any particular disease, but rather focuses on problems that are common to the translational process for all diseases. That said, we believe that for the most part, problems are best solved in the context of particular scientific/medical problems, including those that are aimed at lung diseases. We like each NCATS project to be "dual use", serving to both address a particular scientific or medical problem, and demonstrating a generalizable solution to a translational roadblock.

Q. What are some of NCATS's collaborative initiatives with other NIH Institutes — such as NHLBI — on lung diseases?
A. NCATS has hundreds of ongoing projects with collaborators supported not only by every NIH Institute and Center, but also with investigators at biotechnology, pharmaceutical, government, and nonprofit organizations. I will mention just a few here.

NCATS researchers from the Probe Development Branch in the Division of Pre-Clinical Innovation (DPI) are working on several projects related to lung diseases. For example, NHLBI-funded researchers Dr. Julian Solway of the University of Chicago Institute for Translational Medicine and Dr. Jeffrey Fredberg of Harvard School Public Health are working with NCATS researchers to develop a compound that is being tested in human and mouse tissue models of asthma.

Another DPI project is focused on development of small molecule compounds that target the Nrf2 pathway, which is activated in lung cancers such as adenocarcinomas and squamous cell carcinomas. Collaborator Dr. Shyam Biswal of Johns Hopkins University was awarded support for this project through the NIH Common Fund's Molecular Libraries Program, giving him access to NCATS DPI collaborative assay development, high-throughput screening, informatics and medicinal chemistry resources. Other DPI projects are aimed at identifying starting points for therapeutics directed at novel approaches to arterial thrombosis and influenza.

In NCATS' Therapeutics for Rare and Neglected Diseases (TRND) program, scientists are collaborating with researchers from Cincinnati Children's Hospital Medical Center to develop inhaled GM-CSF for pulmonary alveolar proteinosis, a rare disease marked by accumulation of proteins and lipids in the alveoli, leading to respiratory failure. The current treatment for this disease involves a periodic washing of the lungs under general anesthesia, a painful and invasive procedure.

Through our Tissue Chip for Drug Screening program, NCATS is funding a project led by Harvard University to develop a human cardio-pulmonary system on a microfluidic platform. The idea is to produce and connect "organoids" representing human myocardium, vascular system, and airway in a single microphysiological system that would allow for testing of drug efficacy and safety. The Tissue Chip program is also funding a project at the University of Texas Medical Branch at Galveston to create a human lung model that can be used to study lung development, microbial lung infections and diseases such as fibrosis.

Finally, through our Discovering New Therapeutic Uses for Existing Molecules pilot program, researchers at Virginia Commonwealth University and the University of Pittsburgh are working with Janssen Research & Development, LLC to repurpose a Janssen compound for smoking cessation.

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Q. In its June 2013 report on the CTSA program, the Institute of Medicine (IOM) made a number of recommendations to make the program more efficient and effective. One recommendation was to advance innovation in education and training programs. How do you envision NCATS addressing this recommendation?
A. NCATS is forming a Working Group of our Advisory Council to help advise me and the Council on implementation of all the IOM report recommendations. Each of the CTSAs have implemented education and training programs, and we will be building on these successes, encouraging innovations in education and training models and methodologies, including a strong emphasis on team science, leadership, community engagement and entrepreneurship. Dissemination of courses and education programs will ensure the clinical and translational science workforce broadly benefits the program.

Q. Another IOM recommendation that the ATS is particularly interested in concerns child health. Specifically, the IOM recommended strengthening clinical and translational research relevant to child health. How do you envision NCATS addressing this recommendation?
A. The IOM CTSA Report Working Group of our Council will be addressing this recommendation as well. We will be able to share more as discussions get underway.

Q. How can the ATS leadership better serve NCATS's goal to cultivate strong partnerships with medical societies and disease advocacy organizations?
A. Most important is to maintain the two-way dialogue to help NCATS address the most pressing translational problems. Every project NCATS does is collaborative, since it is only though collaboration that we can ensure that we are working on important problems which if successfully solved will have tangible health impact. I am grateful for ATS and other stakeholders who continue to provide expertise that advances NCATS' work. Serving on NCATS' review groups and project teams as subject matter experts, and ensuring that the ATS community is aware of all the collaborative opportunities that NCATS offers, are just a few examples of how we might work together more closely. ■

NHLBI

NHLBI Unveils New Translational Consortium Centers

In September, the National Heart, Lung and Blood Institute (NHLBI) announced three grant awards that will fund the creation of the NIH's new Centers for Accelerated Innovations (NCAI's), which are aimed at bridging the translational gap in the pipeline between scientific discovery and product development to move breakthrough innovations more quickly from bench to bedside for patients.

The NCAI's program was developed in response to an NHLBI/Small Business workgroup recommendation to develop strategies to provide pre-SBIR funding opportunities for products to improve the diagnosis, treatment and prevention of heart, lung and blood and sleep disorders and diseases. Each center is a consortium of academic, government, non-profit, and private sector organizations that will provide funding for feasibility studies; regulatory, legal, and business development expertise; and entrepreneurial training and mentorship. In order to leverage the NHLBI support, the centers have secured non-federal funding equal to or greater than the NHLBI grants.

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NHLBI *(Continued from page 4)*

NCAI grants totaling $31.5 million were awarded to the following multi-institutional centers:

- Boston Biomedical Innovation Center: Brigham and Women's Hospital, Boston Children's Hospital, Massachusetts General Hospital, and President and Fellows of Harvard College
- Cleveland Clinic Innovation Accelerator: The Cleveland Clinic Lerner College of Medicine; Case Western Reserve University, Cleveland; Cincinnati Children's Hospital; The Ohio State University, Columbus; and University of Cincinnati
- UC BRAID Center for Accelerated Innovation: University of California, Los Angeles; University of California, Davis; University of California, Irvine; University of California, San Diego; and University of California, San Francisco

NHLBI Director Gary H. Gibbons, M.D., said, "These centers essentially will offer a one-stop shop to accelerate the translation of early-stage technologies for further development by the private sector and ultimate commercialization. As a result, the public will gain access sooner to new biomedical products that improve human health while also benefiting from the economic growth associated with the creation of new companies and the expansion of existing ones." ■

RESEARCH ADVOCACY

ATS Holds First State Congressional Meeting in Tennessee

In August, the ATS Breathing Better Alliance (BBA) held its first-ever state congressional meeting in Chattanooga, TN. State congressional visits are a key goal of the BBA in order to strengthen grassroots advocacy efforts across the country and enable ATS members and patients to engage in advocacy close to home without requiring travel to Washington, DC.

From left: ATS member Rehan Kahloon, MD, ATS staff Nuala Moore, James Tumlin, MD, Director of Nephrology, Univ. of TN (UT) Medical School, David Seaberg, MD, Dean of the UT-Chattanooga School of Medicine, Congressman Chuck Fleischmann (R-TN), John Boldt, MD, Erlanger Hospital, Suresh Enjeti, MD, UT Pulmonary Div. Director, & Mukta Panda, MD, UT Training Director.

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Research Advocacy *(Continued from page 5)*

On August 12, a joint ATS/University of TN (UT) delegation met with Congressman Chuck Fleischmann (R-TN), a member of the House Labor-Health and Human Services (L-HHS) Appropriations subcommittee, to urge his support for NIH and CDC funding. The LHHS subcommittee determines annual funding levels for NIH and CDC proposed by the House of Representatives. In this important position, Rep. Fleischmann is a key congressional target for BBA advocacy.

The meeting was an effective partnership of ATS members and UT- Chattanooga School of Medicine faculty. The innovative research at UT, including in areas such as pulmonary fibrosis, lung cancer and sepsis and the need to foster this and the national research enterprise through NIH, was the focus of the discussion. ATS members also raised the need to support CDC funding through a discussion of tuberculosis (TB) in the U.S. and TB clinical drug research at Vanderbilt University funded through CDC's TB Clinical Trials Consortium (TBTC).

The BBA will continue holding state congressional meetings, with the next meetings being planned for Maryland and Ohio. Members and patient advocates interested in joining the BBA should contact advocacy@thoracic.org. ■

TOBACCO

FDA and NIH Launch First-Ever Tobacco Centers of Regulatory Science

The U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH) have launched an initiative to support tobacco regulatory research through new Tobacco Centers of Regulatory Science (TCORS). The program, the first of its kind, is coordinated by NIH's Office of Disease Prevention and administered by three NIH institutes, including the National Cancer Institute, the National Institute on Drug Abuse, and the National Heart, Lung, and Blood Institute, and will support research to ensure that U.S. tobacco regulatory efforts are based on sound and relevant scientific evidence.

Through the TCORS initiative, the FDA and NIH are awarding $53 million to create fourteen TCORS centers around the country to fund tobacco-related research in fiscal year 2013. Awarded sites include the University of Maryland at College Park, Yale University, University of Texas Health Sciences Center at Houston, the University of North Carolina at Chapel Hill and The Ohio State University at Columbus. TCORS scientists hold a broad range of expertise in specialty areas including epidemiology, economics, medicine, toxicology, public health, addictions, and marketing. TCORS is expected to provide more funding over the next 5 years for a total of $273 million to support federal tobacco regulatory science. TCORS was authorized under the Family Smoking Prevention and Tobacco Control Act, enacted in 2009.

Tobacco use in the U.S. continues to be the leading cause of preventable death and disease. TCORS sites will support basic and applied research on tobacco and addiction. The program will also provide young investigators with training opportunities to support the next generation of tobacco regulatory researchers. Designed to generate vital research in seven core areas, as well as ensure innovation in the field, the research supported by the initiative will provide scientific evidence within the following seven FDA tobacco-related research interest areas:

- Diversity of tobacco products
- Reducing addiction
- Reducing toxicity and carcinogenicity

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Tobacco *(Continued from page 6)*

- Adverse health consequences
- Communications
- Marketing of tobacco products
- Economics and policies

New and highly engineered formulations of cigarettes and smokeless tobacco products such as e-cigarettes, are now widely-available, with significant increases in their use by youth. TCORS research will study these new products and provide information about how variations between products and brands affect exposure to toxins, health outcomes, addiction potential and the ability to reduce tobacco use.

"While we've made tremendous strides in reducing the use of tobacco products in the U.S., smoking still accounts for one in five deaths each year, which is far too many," said NIH Director Francis S. Collins, M.D., Ph.D. "FDA/NIH partnerships like the Tobacco Centers of Regulatory Science keep us focused on reducing the burden and devastation of preventable disease caused by tobacco use." ■

PCORI

PCORI Marks Third Anniversary of Support for Patient-Centered Outcomes Research

The Patient-Centered Outcomes Research Institute (PCORI), the independent research institute set up under the Affordable Care Act (ACA), is marking its third anniversary by showcasing the growth of its research portfolio since creation of the institute. At a time when other sources of federal research funding are shrinking, PCORI offers opportunities for supporting patient-centered comparative effectiveness research (CER). The institute awarded 71 new project grants in September, bringing total award funding to $243.5 million for 147 studies in FY2013. The distribution of funding is spread across the following 5 program focus areas:

- Assessment of Prevention, Diagnosis and Treatment Options – 24 projects totaling $45.6 million
- Improving Healthcare Systems – 13 projects totaling $24.5 million
- Communications and Dissemination Research – 6 projects totaling $10.9 million
- Addressing Disparities – 9 projects totaling over $15 million
- Accelerating Patient-Centered Outcomes Research and Methodological Research – 19 projects totaling over $18 million.

So far asthma is the main area of emphasis for PCORI within respiratory, critical care and sleep research, which indicates significant potential for support of projects in these areas. PCORI's overall funding is scheduled to increase from $425 million currently to $500 million in fiscal year 2014, which may open additional funding opportunities. The bulk of studies funded by the institute are currently focusing on mental disorders, cardiovascular diseases and cancer.

The PCORI institute supports research studies that determine which treatments and interventions are most effective, funding projects that are most likely to provide evidence that will change current practices and improve patient health outcomes. PCORI's Director of Stakeholder Engagement, Susan Hildebrandt, recently provided guidance for investigators on the type of questions the institute is seeking in research proposals. She says, "In short, we're interested in those questions that people ask when deciding between two or more healthcare choices…" She elaborated, "Most importantly, PCORI wants studies that will produce information that allows patients to weigh benefits and risks of treatments according to their individual preferences."

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PCORI *(Continued from page 7)*

The institute does not fund studies on the causes of diseases or how they work or, as expressly prohibited by Congress in its authorizing legislation under the ACA, research on the cost or cost effectiveness of different treatments or studies on insurance coverage. PCORI can, however, look at how out-of-pocket costs affect patient adherence to treatment or their decision-making on treatment options.

To view the full blog discussing PCORI research question guidance, visit PCORI blog. ■

RESEARCH FUNDING

Agreement Between Congress and President Reopens Federal Government; Sequestration Still Looms

On October 16, a deal was finalized between the House, Senate and President Obama that reopened federal government agencies and increased the debt ceiling. The agreement funds government programs at current funding levels through January 15, 2014 and raises the debt ceiling until February 7, 2014. The measure also requires additional income verification for individuals receiving health insurance subsidies provided through the Affordable Care Act's health insurance exchanges and back pay for federal employees furloughed during the two week government shutdown.

The agreement also created a bicameral conference committee to determine final FY2014 spending and other budget issues by a new deadline of December 13, 2013. This committee, co-chaired by the House and Senate Budget committee chairs, Sen. Patty Murray (D-WA) and Rep. Paul Ryan (R-WI), is tasked with determining whether budget sequestration funding cuts will be implemented in FY2014. If a new plan is not produced by this committee by December 13, budget sequestration funding cuts of 5 – 7% will be implemented across the board to all federal agencies on January 15, 2014, with the exception of the Veterans Dept. and some safety net programs such as food stamps.

While there is a collective sigh of relief that the current budget impasse is behind us, the current budget agreement does not address, let alone resolve, any of the long-term budget issues that have divided Congress and the Administration. And the possibility of another round of sequestration funding cuts for NIH, CDC and most other health programs in fiscal year 2014 still looms large. ATS members are urged to continue educating their members of Congress about the damaging effects 2013 sequestration cuts have had on research and public health and how additional reductions will devastate both systems. The ATS Washington Office will keep members informed of the spending process, including when ATS member action is need to support health research and services funding. ■