American Thoracic Society

Research News Quarterly

JUNE 2017

In This Issue

Letter from the Editor

The June *ATS Research News Quarterly* features an interview with the new Director of the National Institute of Child Health and Development, Diana Bianchi, MD. Dr. Bianchi discusses the institute's priorities in maternal and child health and human development, including NICHD's efforts to address respiratory problems in pre-term infants and collaborative research with other NIH institutes on rare diseases.

The *Quarterly* reports on the NIH's policy to redistribute funding to early and mid-career investigators. Next, we move to environmental health with a feature from *Quarterly* Editor Veena Antony, MD, on a resurgence of progressive massive fibrosis among coal miners, followed by a policy update on how the EPA and its scientific integrity are under attack by the Trump administration and Congress.

Moving to NHLBI programs, Research Advocacy Committee member Thomas Mariani, MD., provides a snapshot of the institute's Lung Development Molecular Atlas Program (LungMAP). In the next article, we provide a grant opportunities announcement for the Department of Defense's Medical Research Programs. The *Quarterly* concludes with an overview of the president's proposed budget for 2018, including recommendations for dramatic funding reductions to the NIH, CDC, and EPA.

Sincerely,

Veena Antony, MD
Editor

INTERVIEW WITH National Institute of Child Health and Development (NICHD) Director Dr. Diana Bianchi.

Q: Now that you've had some time to settle in as the new NICHD director, what can you tell us about the institute's mission and priorities for child health research?

A: Contrary to what people may think when they hear the name of our institute, child health is only one of our priorities. The "Child Health" in our name reflects a forward-thinking idea from the institute's founding in 1962: that children's health merited a research discipline of its own. Back then, people didn't think we needed to study children's health, as children were essentially healthy. Now, 55 years later, the idea of studying child health is mainstream. NICHD is the lead NIH institute for child health research—we fund almost 20 percent of the total. The rest of child health research at NIH is funded in part by nearly all the other institutes.

Going back to the institute's founding, another forward-thinking idea of the time was to study the life process as it unfolded. That accounts for the "Human Development" in our name. NICHD was established to study normal and abnormal development. Such research is the foundation that supports child health research, and so it is our central focus. Understanding and promoting normal development, however, requires research into reproductive health, pregnancy, and birth, and encompasses the use of basic science as well as clinical studies.

Q: Looking ahead in your tenure: what do you see as the most pressing needs for child health and human development research?

A: Human beings tend to measure progress as a series of incremental advances. But development is a continuum. It doesn't occur in discreet steps. Going forward, we need to integrate related disciplines and stress the importance of data science and sharing to leverage our investments. For example, take the problem of preterm birth. NICHD has 12 sites in its Maternal Fetal Medicine Units Network and 15 sites in its Neonatal Research Network. The networks have eight sites in common. We've encouraged the networks to share data, and they are collaborating on a joint secondary study to look at brain wave function in a subset of infants whose mothers received betamethasone during pregnancy to reduce the risk of late preterm delivery. We're hoping to see more such collaborations in the months and years ahead.

(Continued on page 3)

Diana Bianchi Interview *(Continued from page 2)*

Additionally, NICHD and its partners have made tremendous progress in increasing survival rates of preterm infants with very low birth weights. As more of these babies survive, they proceed through life with the consequences of their early birth. Recently, Tonse Raju, MD, chief of NICHD's Pregnancy and Perinatology Branch, reviewed the health of adults born prematurely. As adults, a small but significant portion had health problems; these included neurological abnormalities, hypertension, metabolic syndrome, diabetes, and limitations in cardiopulmonary function. Lung effects included higher airway resistance, lower exercise tolerance, and lower carbon monoxide diffusion capacity. What was initially considered to be solely a problem of early life has developmental ripples that occur all the way through to adulthood. For those individuals born preterm, we will need to explore possible interventions at later stages in the developmental process, not just in the perinatal period.

At the research level, sharing data can help us learn how events that occur in the womb or in the neonatal period affect long-term health. For example, NICHD has recently established the Data and Specimen Hub (DASH), at https://dash.nichd.nih.gov, which ultimately will be a central repository of de-identified clinical data and biospecimens for use in secondary research analyses. These resources will be available to investigators around the world and will be particularly useful for young investigators who want to get immediate experience with testing a hypothesis.

And, speaking of trainees, we have a pressing need to use our training dollars in a way that maximizes future success for early-stage investigators. NICHD has historically committed 5 to 7 percent of its total extramural budget to training grants. This will continue. However, based on an extensive review of the success in obtaining "R" series grants in a cohort of previously trained young clinician-investigators, the data have shown that MDs who were successfully funded by either an individual K award (K08 or K23), or an institutional K award (K12) plus an individual K, do better in the long term, compared to investigators who only received institutional K awards. These differences only apply to MDs, not to MD-PhDs. Based on this analysis, we anticipate gradually rebalancing some of the institutional K funding to make more money available for individual K awards.

Q: You have stated that one of your goals is to increase NICHD's collaboration with other NIH institutes and organizations. What are some of the specific areas of research in which you would like these collaborative efforts to focus?

A: Major focus areas for NICHD include structural birth defects, reproductive health, pregnancy outcomes, newborn conditions, and intellectual and developmental disabilities. As we share data and resources with other institutes and organizations around these avenues of research, we can optimize our investments and make the most of our opportunities.

The Gabriella Miller Kids First Pediatric Research Program (https://commonfund.nih.gov/kidsfirst/overview) is a good example. This is an NIH Common Fund program. NICHD shares leadership with the National Human Genome Research Institute, the National Cancer Institute, and others. Grants are awarded to sequence the genomes of families that include a child with cancer or with a structural birth defect. Many structural birth defects are associated with pediatric cancers, so learning about one condition may provide insights on the other. The plan is to assemble a centralized DNA database and share this resource with the scientific community, so other researchers can analyze these genetic data and potentially advance our understanding and treatment of these conditions.

There is also the matter of what to do about genetic variants once they're identified. NICHD has provided funding to create Genomic Clinical Variant Expert Review Panels to select genes and variants associated with conditions of high priority to the institute. The panels will rely on tools developed by NHGRI's Clinical Genomics Resource and the National Center

(Continued on page 4)

Diana Bianchi Interview *(Continued from page 3)*

for Biotechnology Information's ClinVar to look for candidate genes that can be targeted in clinical practice.

We are also collaborating with external groups such as the Gates Foundation to address global issues in maternal and child health.

Q: Are there specific areas of research related to child health and/or human development that you view as high priority or understudied?

A: I tend not to view priorities in terms of individual research areas, but as an overarching framework. NICHD's scope is incredibly broad: it spans much of human development, from preconception through pregnancy, childhood, and the reproductive years. NICHD also houses the National Center for Medical Rehabilitation Research. Disability occurs when the developmental process goes awry, and rehabilitation is an attempt to alleviate or correct what's gone wrong.

Obesity, cardiovascular disease, osteoporosis, and cancer are all chronic conditions with strong genetic and environmental components, often having roots in early life or even preconception. Our priority is to target these processes, finding markers that predict susceptibility and to identify targets for interventions.

At the moment, we're doing our best to understand the implications of Zika virus infection on human development. Given the catastrophic effects we've seen on the developing brain, we need to learn more about how the virus is transmitted and how it affects reproductive health, pregnancy, and the developing fetus. NICHD and others launched the Zika in Pregnancy (ZIP) study last year to evaluate the health risks Zika infection poses to pregnant women, their fetuses, and infants and to inform strategies to safeguard their health. The study is on its way to enrolling up to 10,000 pregnant women at sites in Puerto Rico, Brazil, Colombia, and other areas with active transmission of the virus.

Q: Many of the previous successes of NICHD projects have been related to early disease detection and intervention (ex. PKU, congenital hypothyroid disease), as newer treatments for other rare diseases emerge (ex. lumacaftor–ivacaftor for cystic fibrosis or nusinersen for spinal muscular atrophy.) How do you view the role of NICHD in developing systems to help identify and promote the treatment of these patients and others with rare diseases, given that rare disease research has gotten more difficult to study in the current funding environment?

A: Within NIH, the lead for rare diseases is the Office of Rare Disease Research in the National Center for Advancing Translation Sciences. The NICHD plays a major role in rare disease research because research on development and rare disorders often intersect. We are more involved in the basic science research that contributes to an understanding of the mechanisms underlying rare diseases. This is essential to developing treatment approaches. When we learn about a rare disease, we often find out information about pathways and systems that can help with other disorders. For example, studies of congenital leptin deficiency provided the framework for understanding the biochemical pathways influencing obesity.

Our intramural researchers study rare conditions such as Niemann-Pick type C, a disorder of cholesterol metabolism; Menkes disease, a disorder of copper metabolism; and adrenal gland disorders and tumors.

NICHD partners with NCATS and other institutes to support the Rare Diseases Clinical Research Network, a collaboration of investigators and patient groups. Again, the idea is to integrate and share data. Under the program, there are now 22 consortia receiving funding to study more than 200 rare diseases. NICHD-supported researchers are investigating conditions such as brittle bone disorders, developmental synaptopathies, mitochondrial disease, Rett and MECP2-related disorders, and sterol and isoprenoid disorders.

Together with NHGRI, NICHD also funds the Newborn Sequencing In Genomic Medicine and Public Health—or NSIGHT—program. Genomic and exomic sequencing technologies are advancing rapidly, so we'd

(Continued on page 4)

Diana Bianchi Interview *(Continued from page 4)*

like to learn about the best ways to use these tools before they become widespread. It's reasonable to assume these technologies will identify many patients with rare disorders that might otherwise take a much longer time to diagnose. Researchers in the program also are looking at whether sequencing can provide information about conditions for which there are no formal screening recommendations.

Q: Given the huge economic burden of asthma and other pulmonary conditions in the US, how can NICHD research improve our understanding of lung development and asthma susceptibility?

A: At the NIH, the bulk of research pertaining to thoracic medicine falls under the purview of other institutes, most notably the National Institute of Allergy and Infectious Diseases and the National Heart, Lung, and Blood Institute.

As you might expect, NICHD has a strong interest in lung complications during the newborn period because of the respiratory issues facing preterm infants.

For example, NICHD's Neonatal Research Network is testing the effectiveness of hydrocortisone in reducing the incidence of bronchopulmonary dysplasia and improving survival in preterm infants. Infants under 30 weeks of gestational age (at birth) who are intubated at 14 to 28 days of life will be randomized to receive either hydrocortisone or a placebo. Researchers will then assess the participants' neurodevelopment at 22 to 26 months of age. Dexamethasone has been used for this purpose, but it carries the risk of side effects such as hyperglycemia, hypertension, and gastrointestinal bleeding. Data from other studies suggest that hydrocortisone may not pose these risks.

We're planning a follow-up to reassess the participants at five or six years of age to assess neurodevelopmental and respiratory outcomes.

NICHD is also supporting the Sustained Airway Inflation of the Lungs (SAIL) study, a multicenter randomized controlled trial that will compare sustained airway inflation of the lungs to standard PEEP/CPAP in reducing bronchopulmonary dysplasia and increasing survival. The study is planned to include 600 infants at 23 to 26 weeks gestational age.

A less common, but also very serious, pulmonary problem is congenital diaphragmatic hernia, a rare condition in which a hole in the diaphragm allows the liver and other organs to migrate into the chest and press against the lungs during development. This reduces oxygen capacity. Mortality is high, and pulmonary hypertension is a major complication for survivors. The Milrinone in Congenital Diaphragmatic Hernia trial is a Phase II pilot trial to determine if milrinone infusion can improve outcomes in newborns 36 weeks and older. The drug will be tested by itself and together with other pulmonary vasodilators like inhaled nitric oxide. The infants' status will be evaluated again at four-, eight, and twelve months of age.

Regarding maternal pulmonary health, Pauline Mendola, PhD, in our Division of Intramural Population Health Research is investigating the impact of maternal asthma on pregnancy and the newborn. For one of her analyses, she relied on a data set from the NICHD Data and Specimen Hub I mentioned earlier. She found that infants born to women with asthma had a higher risk for preterm delivery, newborn jaundice, and respiratory distress syndrome. Another analysis found that asthmatic women had a higher risk for preterm delivery after exposure to common air pollutants, compared to non-asthmatic women.

Finally, one of our grantees, Virender Rehan, MD, a neonatologist at Harbor-UCLA Medical Center, found evidence that maternal smoking could increase asthma risk not just in children, but also in grandchildren. His studies in rodent models found that this risk was much higher in male offspring than in female offspring.

NIH

Collins to Continue As NIH Director

On June 6, President Trump announced that Francis Collins, M.D., Ph.D., will continue as director of the National Institutes of Health, following Collins's request to the President to do so. Collins has served as Director of the NIH since 2009. Dr. Collins is a physician geneticist renowned for his discoveries of disease genes and his leadership of the international Human Genome Project. ■

NIH Scraps Controversial Grant Cap

On June 8, the NIH announced that it will not implement a controversial policy proposed in May, 2017, aimed at redistributing $250 million in funding to early and mid-career investigators that would have limited grant support to some later-stage investigators with at least 3 grants. Under the proposed policy, all NIH grants would have been scored according to a Grant Support Index (GSI) (a conversion from the previous Research Commitment Index) and those that exceeded a score of 21 would have been required to adjust their grant load. The GSI would assign point values to various kinds of grants based on type, complexity and size and it will only consider NIH support (not other agency grants).

In a statement announcing the proposal, Dr. Collins stated that he expected the new policy to ultimately enable the awarding of an additional 1,600 new grant awards to early and mid-career investigators while affecting an estimated 6 percent of NIH researchers whose grant awards may exceed the "21 score" threshold.

The research community, including the ATS, expressed serious concerns about how the policy would affect training grants, collaborative projects and ultimately, the NIH peer review system. Questions were also raised about how the data and metrics used to develop the GSI was assessed.

The ATS Research Advocacy Committee, chaired by Veena Antony, MD, which reviewed the policy on behalf of the ATS, approves of the NIH's final decision not to implement the GSI. She says that although the committee saw the benefit in more grants eventually becoming available to support early and mid-career professionals, they were very concerned about how the proposed policy might end of negatively impacting the overall peer review process in time. Dr. Antony was likewise concerned about how multi-disciplinary collaboration will be assessed in individual investigator GSI scores.

The NIH still plans to redistribute funding towards early and mid-career investigators through a New Generation Initiative and will continue to analyze optimal systems for evaluating faculty productivity and time commitments. The Advisory Committee to the NIH Director will review these efforts. The Next Generation Initiative will include the following mechanisms:

- Redirect funding from the NIH base budget to meritorious early-stage and mid-career investigators (those with 10 years as a principal investigator who are about to lose all NIH funding or are seeking a second award for highly meritorious research), beginning with $210 million in fiscal year 2017 and escalating $1.1 billion per year after five years, pending availability of funding
- Track NIH Institute and Center funding decisions for early- and mid-career investigators
- Utilize and potentially expand current NIH funding mechanisms aimed at early- and mid-career investigators, such as the NIH Common Fund New Innovator Awards the National Institute of General Medicine Sciences Maximizing Investigators' Research Award (MIRA), and other special awards from specific institutes, with an aim of funding most early-career investigators that score in the top 25th percentile

(Continued on page 7)

NIH Scraps Controversial Grant Cap *(Continued from page 8)*

- Develop and test new metrics for assessing the impact of NIH grant funding policy on scientific progress

The NIH has created a new web page for the Next Generation Researchers Initiative https://grants.nih.gov ngri.htm for the latest updates on this project. ■

ENVIRONMENTAL HEALTH

Environmental Health Perspective – A Resurgence of Progressive Massive Fibrosis in Coal Miners

Veena Antony, MD, Chair, ATS Research Advocacy Committeee

In response to a vigilant radiologist in Kentucky, the CDC recently reported a marked increase in the development of progressive massive fibrosis (PMF) in coal miners [(1)]. This increase is not limited to Kentucky where it was first noticed but is seen across the Appalachian mining community including Virginia, West Virginia and Alabama. Coal mine dust lung disease includes a spectrum of pulmonary pathology from emphysema, chronic bronchitis to coal worker's pneumoconiosis. PMF is an entirely preventable disease in patients with coal worker's pneumoconiosis. It is characterized by the presence of fibrotic nodules of varying sizes that coalesce and progress to larger nodules and subsequent destruction of lung tissue. At present, there is no known cure for the disease.

The National Institute for Occupational Safety and Health was required to implement a surveillance program to monitor disease prevalence following federal laws passed in 1969 that established respirable dust exposure limits. This resulted in a laudable drop in mortality from of more than 15 deaths per million to under 5 deaths per million in coal workers.

Unfortunately, over the last few years there has been a resurgence of coal worker's pneumoconiosis associated with PMF. The federal rules for surveillance did not apply to miners working in surface mines where several of the new cases of PMF have been found. Many workers are less than 50 years old and this increase has occurred in spite of the required surveillance of the underground coal miners. Some factors that are being considered as causative include longer working hours, the advanced mining techniques that produce more dust and long wall mining where a specialized machine cuts across the length of the coal face to extract coal. The use of helmet masks, years of employment and time spent in diesel cabs in surface mines are all possible contributors to the recent noted increase in patients with PMF.

The symptoms of PMF are nonspecific and because there may be latency period of more than ten years a detailed work history is critical. Patients with abnormalities on a chest radiograph will need high resolution CT scans. Many of these patients have a history of smoking and nodules on lung scans will need to be monitored and biopsied. PMF nodules of >1cm in size can be metabolically active and give a false positive on positron emission tomography (PET) scans.

Prevention holds the key to limiting the ravages of PMF. A comprehensive monitoring of lung function and symptoms with aggressive limitation of exposure will remain a primary element in protection from disease. Personal exposure devices may be important and provide specific individualized prevention strategies. Since PMF can occur years after the exposure to coal dust continued monitoring even at the end of employment is recommended. Avoidance of all other respirable dusts including silica, cadmium and diesel fumes that can synergize with coal dust to produce PMF must be avoided. 6-7 percent of patients can develop tuberculosis if exposed and thus monitoring a change in immunological status is important.

The responsibility for stringently monitoring that standards for respirable dusts are met also falls upon the operators of the mines. Smaller mines where fewer

(Continued on page 8)

Environmental Health Perspective *(Continued from page 7)*

miners work longer hours must be closely monitored for their ability to follow regulatory guidelines. The U.S. will continue to operate coal mines even as attempts are made to turn towards renewable fuel sources. Given the chronicity and latency of the disease we expect to continue to encounter patients with this devastating disease.

The public health costs of the reversal of the decline in PMF are enormous. Adverse respiratory health outcomes in these patients need to be carefully documented and prospective studies where these patients are followed are needed. These studies should be incorporated into the ongoing surveillance that is presently being done for coal workers pneumoconiosis. It is surprising that we do not as yet know of the possible synergies between exposure to "coal dust" and other chemicals that may be present. It is also possible that genetic predisposing mutations render persons susceptible to this type of lung injury. Research in this field is urgently needed in the form of RFAs from the CDC, the NIH, and industry.

We can reverse the increase in PMF by bringing government, the coal mining industry and patients to the table to address and develop public health strategies to combat this preventable disease. ■

[1.] Blackley DJ, Crum JB, Halldin CN, Storey E, Laney AS. Resurgence of Progressive Massive Fibrosis in Coal Miners - Eastern Kentucky, 2016. *MMWR Morb Mortal Wkly Rep* 2016; 65: 1385-1389.

EPA Under Attack

The Environmental Protection Agency is under attack in the Trump Administration. In his fiscal year 2018 proposed budget, President Trump is requesting $5.6 billion for EPA—a 31 percent cut from the current $8.2 billion funding level. Also featured in the president's budget request is the elimination of 3,200 EPA staff positions, through early retirement and hiring freezes. While most observers don't think Congress will adopt the severe cuts proposed by President Trump, the budget numbers show the agency is held in low esteem by the Trump Administration.

But the attacks on the EPA aren't limited to the budget. The Trump Administration has rescinded several environmental regulations issued during the Obama Administration—the most prominent being the retraction of the EPA's Clean Power Plan to address carbon pollution emissions in the U.S. Staff in the Trump Administration have already removed or redirected information on climate data that was formerly housed on EPA websites.

And the attacks are not limited to the Administration. For several years, the House of Representatives has passed legislation that would, stop, weaken or delay EPA's authority to regulate the environment—with a particular focus on weakening EPA's authority to regulate air pollution. The House has adopted legislation that would delay by 10 years implementation of the 2015 EPA ozone standard of 70 ppb/8-hours. Similarly, legislation has been considered that would change the Clean Air Act to delay review of clean air standards from once every 5 years to once every 10 years – adding years of delay in addressing the health consequences caused by air pollution in our most polluted regions.

Its not just EPA's authority under the Clean Air Act that is under attack. How the EPA accesses outside scientific expert advice and how it uses scientific data are also under attack. The House passed two bills that would radically change how the EPA receives outside expert advice. The first bill, call the EPA Scientific Advisory Board Reform Act, would change EPA Scientific Advisory Board requirements to increase the number of industry representatives participating on the panel, allows participation of representatives from regulated industries as long as the conflicts are disclosed, prevents scientists who have received EPA grants in the past three years from participating on the panel, and bars panel members from reviewing or commenting on their own research. Further, the bill directs the board to "strive to avoid making policy determinations or recommendations," communicate uncertainties associated with the scientific advice provided to the EPA or Congress and encourage dissenting members

(Continued on page 9)

EPA Under Attack *(Continued from page 8)*

to make their views known. Effectively, the legislation is intended to reduce the voice of scientific experts on the EPA Scientific Advisory Board and preclude the board from making meaningful recommendations to the EPA.

A second bill of concern is the Honest and Open New EPA Science Treatment Act. This bill bars the EPA from using any scientific information to base any risk, hazard assessment, criteria document, standard or rule making until that information is publicly available and is sufficient for independent analysis and has substantial reproduction of research results. This seemingly innocuous requirement is actually a powerful tool for opponents of regulation to stop the EPA from moving forward with policy. In general, the EPA bases all its policy decisions and regulation action on peer-reviewed data that is available in the public domain. However, this bill will give opponents of industry legal action to challenge any EPA action by saying the EPA did not provide enough information for the science to be independently analyzed or industry did their own study and came up with a different result—and therefore the science the agency used is not reproducible.

While the House has passed several pieces of legislation that would weaken and delay EPA's authority under the Clean Air Act, the Senate has not yet shown much interest in considering these bills. The ATS and our allies in the medical and public health community have taken a strong stand against these bills and will continue to urge Congress to reject these bills. ■

NHLBI

The Lung Development Molecular Atlas Program (LungMAP)

Thomas Mariani, MD, member, ATS Research Advocacy Committee

Over the past decade, various programmatic efforts have been initiated to develop comprehensive descriptions for development of multiple tissues and systems, including craniofacial (FaceBase; https://www.facebase.org) and genital-urinary tract (GUDMap;

http://www.gudmap.org) formation. Possibly the best known of these efforts is the privately-funded Allen Brain Atlas (http://www.brain-map.org), which has developed an anatomical, cellular and molecular atlas of brain formation in the mouse and non-human primate. The progress of the Allen Brain Atlas has led to substantial enthusiasm for supporting the NIH Brain Initiative (https://www.braininitiative.nih.gov)

launched in 2013 (PMID: 23661744). Seizing upon the opportunity and potential for impact of such efforts, the NHLBI initiated a national effort in 2015 to develop a structural, cellular and molecular atlas of the developing mammalian lung. This developing lung molecular atlas program (LungMAP) was conceptualized to focus on both the maturational phase of lung development, primarily encompassing the perinatal and postnatal period, and on the human system.

The LungMAP consortium, chosen through a competitive peer-review process, consists of a collaborative group of investigators organized into four Research Centers (RCs), a center for the acquisition and distribution of Human Tissues/cells (HTC), and a Data Coordinating Center (DCC). The RC at Cincinnati Children's Hospital Medical Center (CCHMC) is focused on using next generation technologies (e.g., single cell transcriptomics and molecular imaging) to define unique cells, based upon their expression profiles, and understand parenchymal cell-cell interactions. The RC at the Saban Research Institute of the Children's Hospital-Los Angeles is building a multi-scale structural and molecular atlas, by combining high-resolution imaging with characterization of the extracellular matrix.

An RC involving the Pacific Northwest National Laboratory, Baylor College of Medicine, the University of Washington, and the Texas Advanced Computing Center leverages state of the art techniques to spatially and/or temporally quantify the proteome, lipidome and metabolome during alveolar development. An RC

(Continued on page 10)

LungMAP *(Continued from page 9)*

involving The University of Alabama at Birmingham, Yale University, University of California-San Diego and Carnegie Mellon University is focused on integrating the dynamic and regional changes in epigenetic marks, microRNA, mRNA and proteins during alveolar septation, and using these data to generate a dynamic, temporal regulatory model of normal alveolar septation.

The University of Rochester, with support from Seattle Children's Research Institute, is responsible for obtaining healthy human lungs from Organ Donor Organizations, characterizing these lungs at the structural and cellular level, processing them and distributing samples to the RCs. All Centers collaborate to apply cutting edge bioinformatics analyses to these complex data sets. Duke University's Clinical Research Institute and RTI International serve as the DCC for LungMAP, and are responsible for helping to organize collaborative efforts, and for developing a comprehensive website that serves as the access point for LungMAP data.

One critical aspect of the LungMAP is the development of BREATH—a Bioinformatics REsource ATlas for the Healthy lung—database and website (https://www.lungmap.net). LungMAP.net is a public website with an interface for accessing LungMAP data, interpretations of the results, and tools for users to analyze the available data. Through BREATH and the LungMAP website, the DCC will help to develop a community of users who can share information freely and broadly. Another critical and related aspect of the LungMAP consortium is the commitment to delivering data to the public expeditiously, and prior to publication.

To date, the program has generated substantive content that is available for interpretation and/or secondary analysis, both in print and on the LungMAP website (https://www.lungmap.net). Products from the research include 35 published articles and numerous abstracts and posters at scientific conferences, over 20 transcriptomic, proteomic, and lipidomic experimental data sets, 5000 high resolution images, close to a dozen 3D video reconstructions and a set of illustrative immunofluorescent images annotated using a customized tool developed by the DCC. Many future publications and data sets are certain to follow. Furthermore, resources including, but not limited to, human lung tissue-derived samples (e.g., cells, tissue blocks, molecular extracts; http://brindl.urmc.rochester.edu) and standardized protocols will be made available to the research community. ■

ATS WA, RI and OK Members Advocate for Research Funding on Capitol Hill, March 29, 2017

From Left to right Council on Chapter Representatives Chair Steve Kirtland, MD, Lynn Reinke, PhD, Sen. Jack Reed (D-RI), Linda Nici, MD, Cory Cross, MD.

DOD RESEARCH OPPORTUNITIES

Dept. of Defense Research Program Opens Respiratory Research Funding Opportunities

The Department of Defense has announced four individual open funding opportunities for its congressionally-directed medical research program (CDMRP). This program, overseen by the Secretary of Defense, in conjunction with the Service Surgeons General, is directed to select medical research projects of clear scientific merit and direct relevance to the

(Continued on page 11)

Respiratory Research Funding Opportunities *(Continued from page 10)*

healthcare needs of military service members, veterans and/or beneficiaries. The program challenges the scientific and clinical communities to address one of the congressionally directed topic areas with original ideas that foster new directions in basic science and translational research; novel product development leading to improved therapeutic or diagnostic tools; synergistic, multidisciplinary research program; or clinical trials that address an immediate clinical need.

The PRMRP program funding and disease eligibility increased significantly this year with $300 million in funding for 48 eligible disease/health areas, a 7.5 percent funding increase over the 2016 funding level. The $300 million in funding for 2017 is the largest in the PRMRP program's history.

The PRMRP program was originated by patient advocates. Lung disease-related research topics now include: Acute lung injury, burn pit exposure, constrictive bronchiolitis, influenza, pulmonary fibrosis, sleep disorders, respiratory health, tuberculosis, as well as diseases with a high incidence of pulmonary comorbidity including lupus, rheumatoid arthritis, and scleroderma.

CDMRP Medical Focused Program Award
Pre-application deadline: July 20, 2017

This award is intended to optimize research and accelerate the solution for a critical question related to at least one of the congressional directed topic areas (listed above) through a multi-disciplinary research program. Applicants are strongly encouraged to submit at least four synergistic research projects ranging from exploratory, hypothesis-developing studies through small-scale clinical trials with an intent to progress toward translational/clinical work.

Medical Focused Program Award Information

CDMPR Investigator-Initiated Research Award
Pre-application deadline: July 13, 2017

The investigator-initiated award supports studies that will make a key contribution toward research and/or patient care for a disease or condition related to at least one of the topic areas. Projects may focus on any research phase from basic laboratory through translational research, including animal and human model preclinical studies and correlative studies associated with an existing clinical trial; however, this award may not be used to conduct clinical trials.

Investigator-Initiated Research Award

CDMRP Discovery Award
Pre-application deadline: July 19, 2017

This award supports innovative, non-incremental, high-risk, potentially high-reward research that will provide new insights, technologies or applications that lay the groundwork for future avenues of investigation. Proposed research projects should include a well-formulated, testable hypothesis. This award is not intended to support a logical progression of an already established research project or other types of ongoing work; therefore, preliminary data are not required.

Discovery Award Information

CDMRP Technology/Therapeutic Development Award
Pre-application deadline: July 13, 2017

This is a product-driven mechanism intended to provide support for the translation of preclinical findings into products for clinical applications including prevention, diagnosis, and treatment in one of the CDMRP topic areas. Proof-of-concept should already be established.

Technology/Therapeutic Development Award Information

Trump Budget Cuts *(Continued from page 11)*

RESEARCH FUNDING UPDATE

Trump Budget Proposes Radical Cuts to NIH, EPA and Other Agencies

On May 23, 2017 President Trump released his full proposed budget outline for fiscal year (FY) 2018 which proposes radical funding cuts to federal research and health programs. As reported in March, when a partial fiscal year 2018 budget was released, the administration has proposed a 19 percent funding reduction to the NIH for 2018. The proposed cut would apply across all institutes. Specifically, the administration's FY2018 budget proposes the following for the NIH institutes that the ATS monitors:

- A $575 million or 18 percent funding cut for the National Heart, Lung and Blood Institute
- An $838 million or 18 percent funding cut for the National Institute of Allergy and Infectious Disease
- A $323 million or 12 percent funding cut to the National Institute of General Medical Sciences
- A $159 million or 23 percent funding cut to the National Institute of Environmental Health Sciences
- A $305 million or 22 percent funding cut to the National Institute for Child Health and Development
- A $33 million or 22 percent funding cut to the National Institute for Nursing Research

Another budget proposal that would impact U.S. biomedical health infrastructure significantly if enacted is a proposal to cap indirect costs for NIH grants at 10 percent of total research for all types of NIH grants. This proposal would have serious damaging effects for many institutions across the country. While we do not expect a 10 percent indirect cap to be enacted, the issue of capping indirect costs in some manner will be discussed in Congress. The ATS will monitor these discussions closely and keep members informed.

Notably, the President's budget proposes eliminating the Fogarty International Center, the NIH's global health research and training institute. The Fogarty Center supports research on tuberculosis, HIV/AIDS and other global health threats and activities to build research capacity in low and middle-income countries.

Proposed CDC Funding Cuts

The administration's budget also proposes to eliminate the Agency for Health Research and Quality (AHRQ) and create a new National Institute for Research on Safety and Quality at the NIH, to improve the efficiency and coordination of health services research, which would be funded at $272 million, an 18 percent reduction from AHRQ's FY2017 budget of $324 million. Previous administrations have proposed virtual elimination of AHRQ, so this proposal is not necessarily novel and the AHRQ is expected to be maintained.

The FY2018 budget proposes a radical $1.2 billion or 16.7 percent funding reduction to the Centers for Disease Control and Prevention (CDC) and a complete elimination of the CDC's Office of Smoking and Health. The administration proposes folding tobacco control activities into a new "America's Health" block grant funded at $500,000 million annually for state public health departments to address leading causes of death and disability such as heart disease, diabetes and tobacco use. The ATS is deeply concerned about this proposal to eliminate the CDC's national tobacco control program in favor of a state block grant from which states could choose public health priorities and fund them accordingly. This approach would erode tobacco use and prevention as a national public health priority and permit states to significantly cut back or even eliminate tobacco use cessation, prevention and education efforts. The successful Tips from Former

(Continued on page 13)

CDC Funding Cuts *(Continued from page 12)*

Smokers national campaign would be eliminated under this proposal.

The FY2018 budget proposes funding reductions for the following other CDC programs that the ATS monitors:

- A $4 million or 13.8 percent funding reduction to CDC's asthma program
- A $12.2 million or 8.6 percent funding reduction to the CDC's domestic tuberculosis program
- A $135.2 million or 40 percent funding reduction to the CDC's National Institute of Occupational Safety and Research

The budget proposes to slash the EPA by 31 percent. Specifically for EPA programs, it proposes:

- Discontinuing funding for the clean power plan
- Eliminating funding for international climate change programs
- Eliminates funding for climate change research and partnership programs and "all related efforts"
- Proposes to "reorient the EPA's air program to protect the air we breathe without unduly burdening the American economy."
- Cuts the EPA Office of Research and Development by nearly 45 percent

Concerning international affairs and global health, the State Department would see a 28 percent funding cut overall under the proposed budget and the U.S. Agency for International Development's global tuberculosis program would be cut by 26.5 percent.

Finally, the Department of Veterans Affairs Medical Research program, which has seen funding increases over the past few years would be cut by $35.3 million or just over 5 percent.

While the President's budget contains a number of very problematic proposals such as the NIH indirect policy and elimination of the CDC's tobacco control program, it is important to note that this budget proposal, though of serious concern, is only the first step in the fiscal year 2018 funding and appropriations process. Annual government spending is determined by Congress. We expect that Congress will reject most of these proposed funding reductions and proposals, including the NIH indirect cap. The ATS is actively advocating with Congress and with our sister organizations to oppose President Trump's FY2018 budget. We will alert ATS members when action is needed to support NIH, CDC, EPA and other ATS priority programs.