

Research News Quarterly

OCTOBER 2016

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Letter from the Editor

The October Research News Quarterly continues our interview series with NIH and other federal program leaders. In this issue's interview, Lanay M. Mudd, program director in the Division of Extramural Research at the National Center for Complementary and Integrative Health (NCCIH), discusses the Center's focus on studying the safety and effectiveness of complementary and integrative health interventions and how these efforts connect with ATS member and patient interests.

The Quarterly also features a commentary by ATS lung cancer specialists, Drs. Daniel Serman and Joachim Aerts, who report on recent advances in lung cancer immunotherapy. Moving to NIH news, Teresa Barnes, past chair of ATS PAR, reports on the NHLBI's final strategic research priorities related to pulmonary-critical care and sleep. Her article is followed by updates on the 50th anniversary of the National Institute of Environmental Health Sciences (NIEHS) and the 30th anniversary of the National Institute of Nursing Research (NINR). We also cover changes in the NIH's clinical trials policy that become effective beginning January 2017.

Moving to child health, we have an announcement on the naming of the new National Institute for Child Health and Development (NICHD) director, followed by an update on the availability of a new resource (CHEAR) to assist pediatric researchers studying child environmental exposures. The October Research News Quarterly concludes with an update from our Washington, DC, office on the process towards finalization of 2017 health research and services funding.

Sincerely,

Linda Nici, MD
Editor



INTERVIEW WITH Lanay M. Mudd, PhD

Program Director, Division of Extramural Research, National Center for Complementary and Integrative Health

Q: What is NCCIH's mission?

A: The mission of NCCIH is to define, through rigorous scientific investigation, the usefulness and safety of complementary and integrative health interventions and their roles in improving health and health care.

Q: What have been some victories and challenges for NCCIH, being a relatively new center at NIH?

A: NCCIH was founded 17 years ago and was preceded for 7 years by the NIH Office of Alternative Medicine, so we have an established history at the NIH. During the past 17 years, NCCIH's achievements have included:

- Supporting, and helping to design, three editions to date of the largest nationally representative survey ever conducted on Americans' use of complementary health approaches, a supplement to the CDC's annual National Health Interview Survey (NHIS). NCCIH has also funded, and in some cases conducted in-house, many studies of NHIS data on a wide range of topics, from how much Americans spend on these modalities to users' sociodemographic characteristics, and reasons for use.
- Discoveries in basic research aimed at understanding the biological effects and mechanisms of action of selected complementary interventions.
- Clinical trials, large and small, testing complementary therapies' efficacy and safety. The results have informed, for example, practice guidelines of professional medical societies; actions, at times, of the U.S. Food and Drug Administration (e.g., on ephedra); and, Americans' decisions about whether to purchase or use complementary health products and services (e.g., negative study findings on echinacea).
- Increasing broad recognition of evidence supporting that some complementary and integrative approaches have real contributions to make in health and medicine—for example, in some difficult-to-treat medical problems (such as acupuncture and yoga for back pain) and in symptom management. Chronic pain, especially, is a focus for the Center.

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Lanay M. Mudd Interview *(Continued from page 2)*

As we move ahead there is still much for NCCIH to do. First, we are taking a strategic approach to further building the evidence base on complementary approaches—including how they work and for whom, their safety, and the optimal methods of practicing and delivering them. Secondly, we are supporting a variety of high-quality research training and career development opportunities to build the workforce of investigators with knowledge and expertise in complementary health. A third commitment, also part of the Center’s charge from Congress, is providing objective and authoritative evidence-based information to the public and health care professionals.

Q: What are the priority/most pressing questions to be answered that bridge pulmonary/critical care/allergy/sleep medicine and integrative health medicine?

A: TNCCIH does not fund research on critical care specifically. We support scientific research on selected areas of high scientific priority. These areas are prioritized against four criteria: scientific opportunity and promise, amenability to rigorous scientific study, fostering discovery and innovation, and impact on public health and health care. The resulting priorities are captured in the five strategic objectives and the six areas of highest scientific priority in the Center’s [2016 Strategic Plan](#) and on our “What Research Will NCCIH Fund?” page at <https://nccih.nih.gov/grants/whatnccihfunds>. Examples relevant to your question could include the following:

- Improving care for hard-to-manage symptoms, particularly recurring or chronic symptoms [detailed on pages 19-21 of the Strategic Plan].
- Researching the potential benefit of certain complementary approaches to encourage better self-care, improve the sense of well-being, and promote greater commitment to a healthy lifestyle [pages 22-25 of the Plan].

Other pertinent examples from the Plan could include:

- Complementary and integrative health approaches have been commonly used by the general public to treat or manage disorders or

symptoms relevant to the nervous system, such as pain, sleep disturbance, stress, anxiety, and behavioral disorders. A key question is what the neural pathways are by which complementary approaches exert analgesic effects or therapeutic effects on various physiological systems.

- Managing symptoms—particularly recurring or chronic symptoms, which include insomnia and pain—is challenging. Current approaches to symptom management often have limitations, e.g., medications may have significant risks and side effects. Thus, one key question is how complementary health approaches may improve symptom management in both the short and long terms. We are also interested in better understanding the bidirectional relationship between sleep disturbance and chronic pain, and whether complementary approaches may help ameliorate both conditions.

Further, since a part of our mission is to provide science-based information on complementary approaches, the following key questions are among those within our information products on several of the topics you listed:

Allergy from [NCCIH Clinical Digest: Seasonal Allergies and Complementary Health Practices](#):

- Many complementary health approaches have been studied for allergic rhinitis. There is some evidence that the following might be helpful: (1) nasal irrigation with saline and (2) use of the dietary supplement [butterbur](#). While a variety of other natural products, as well as acupuncture, have also been studied, the scientific evidence on them is limited, conflicting, or demonstrates safety concerns with the therapies.
- Patients should discuss (and health care providers should ask their patients about) the best way to manage seasonal allergies, especially if the patient is considering or using a dietary supplement. Some supplements may interact with medications or other supplements or have side effects of their own (e.g., butterbur). In addition, most dietary supplements have not been tested in pregnant women, nursing mothers,

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Lanay M. Mudd Interview *(Continued from page 3)*

or children. No complementary health practice should be used as a reason to delay seeing one's health care provider about a medical problem or to replace scientifically proven treatments with unproven ones.

Sleep from [NCCIH Clinical Digest: Sleep Disorders and Complementary Health Approaches](#)

People who have trouble sleeping often try complementary approaches, such as dietary supplements, relaxation therapies, and other approaches. Research on complementary health practices and sleep disorders has produced promising results for relaxation techniques and melatonin. Current evidence about other products and practices is either too preliminary or inconsistent to draw conclusions. Safety concerns have been raised about a few of the herbs and dietary supplements used for this purpose (see our publication above).

Asthma from [Portal on Lung or Pulmonary Disease Information](#)

- NCCIH's information in this area focuses primarily on asthma and secondarily on integrative oncology in lung cancer. For asthma, some people turn to complementary practices to relieve the symptoms. According to reviewers who have assessed the research, there is not enough evidence to support the use of any complementary health practice for the relief of asthma. Although studies on a few practices have shown a trend toward symptom improvement in asthma, improvements in asthma symptoms do not always correlate with improvements in lung function.

Q: What is your perspective on the fact that many complementary and alternative medicines (exercise therapies like yoga, tai chi, music therapy, and herbal medicines) are already being used by the general public, while the data are still being generated or are lacking?

A: This is one of the challenges that NCCIH faces. Most of the approaches that we support research on are already in use with a wide array of purported benefits; however, the actual evidence base is lacking. Thus, our mission is to define, through rigorous

scientific investigation, the usefulness and safety of complementary and integrative health interventions and their roles in improving health and health care.

Q: What collaborations are there between NCCIH and NHLBI and VA ORD?

A: To help fulfill our mission and leverage our research investments, NCCIH works with a number of other NIH Institutes and Centers, the Department of Veterans Affairs, and the Department of Defense on designing studies of complementary and integrative approaches for the management of pain in military and Veteran populations. These studies bring together multidisciplinary teams of scientists working in either military or Veterans' health care systems. Some studies underway in our portfolio can be viewed at <https://nccih.nih.gov/news/press/09232014>. In early October, NCCIH, along with NHLBI, NIDDK, and NIEHS, awarded funding for a second study on chelation and heart disease (TACT2) - <https://nccih.nih.gov/health/chelation/TACT-questions>.

Q: What role would you like to see the ATS play in disseminating knowledge about integrative therapies and funding from NCCIH?

A: NCCIH's other selected collaborations have included some professional societies, patient advocacy groups, and organizations with an interest in improving health and well-being. These efforts allow us to expand our research portfolio and multidisciplinary expertise and gain a broader understanding of the health needs and perspectives of individuals using complementary health practices.

With respect to the ATS, we would welcome the Society linking to our website for dissemination of research results pertinent to your members. In addition, the ATS may wish to publicize results from NCCIH-funded studies conducted by ATS members. We would also welcome any efforts by the ATS to disseminate relevant NCCIH funding opportunities to your members through newsletters, etc. These funding opportunities are regularly updated on our website and publicized through our research blog. We encourage the ATS to maintain an interest group on complementary and

integrative research and promote collaborations with complimentary practitioners as well. ■

LUNG CANCER

Advances in Lung Cancer Immunotherapy

Dr. Daniel Sterman, director, Division of Pulmonary, Critical Care & Sleep Medicine, NYU School of Medicine/ NYU Langone Medical Centre, New York, USA, Dr. Joachim Aerts, director, Division of Thoracic Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Despite the progress made in the treatment of patients with advanced non-small cell lung cancer (NSCLC) with targetable driving mutations, minimal improvements have been made in the majority of patients who do not harbor these mutations. Chemotherapy, mostly platinum-based doublets, has been considered the standard-of-care treatment in patients with relatively good performance status, but median survival for the group of squamous and non-squamous as a whole still remains around one year, and longer-term survival is still extremely limited.

Recently, immunotherapy targeting the Programmed Death receptor 1 (PD-1) and its ligand (PD-L1) has altered this landscape dramatically. Initial clinical studies for advanced NSCLC in second-line and third-line treatments and beyond showed an impressive increase in long-term survival of patients compared with salvage chemotherapy. Recent results also show activity of these immunotherapy agents as a first-line treatment. Since the clinical results of checkpoint inhibitors acting on this PD-1 axis have been published, immunotherapy is now regarded as one of the standard treatments for patients with NSCLC without targetable mutations after progression on first-line chemotherapy.

PD-1 was originally detected in 1992ⁱ. However, it took many years before its role in cancer pathophysiology and ultimately in cancer treatment became apparent

and accepted. Anti-PD-L1 monoclonal antibodies were found to suppress the growth of a PD-L1+ murine tumorⁱⁱ. Although initially the effect of the PD-1 was only related to apoptosis of activated cytotoxic T-cells, the effects of PD-1 on the immune system are now considered much broader, with a complex interaction of different components of the immune response. For example, the effect of the PD-1/PDL-1 axis on regulatory T-cells is under active investigation.

Initial impressive results of the use of anti-PD-1 monoclonal antibodies (MAB) for advanced malignancies were published in a phase 1 study involving multiple tumor types, including melanoma, renal cell carcinoma, and NSCLC. In this study, the NSCLC cohort showed similar rates of durable responses as the other tumor types with acceptable toxicity.ⁱⁱⁱ This led to randomized trials in the second-line setting in NSCLC patients exploring PD-1/PD-L1 inhibitors as monotherapy in both efficacy studies and comparative studies versus standard treatment with chemotherapy (docetaxel). The first randomized studies published compared nivolumab (an anti-PD-1 MAB) in squamous and non-squamous cell lung cancer to docetaxel.^{iv v}

In both studies, nivolumab outperformed chemotherapy: in squamous cell carcinoma the hazard ratio was 0.59, increasing median survival from 6.0 to 9.2 months; in the non-squamous study, the hazard ratio was 0.73, increasing median overall survival from 9.4 to 12.2 months. In both clinical trials, the toxicity profile of the anti-PD-1 MAB was acceptable. Most striking was the increase in long-term survival due to immunotherapy demonstrated in the non-squamous trial, with an 18 month overall survival of 39 percent with nivolumab compared with only 23 percent in the docetaxel group. Studies have since been published using various anti-PD-1 or PD-L1 MABs showing similar levels of activity in advanced NSCLC and consistent superiority to chemotherapy.

Although impressive achievements have been made with the introduction of immunotherapy in the treatment of NSCLC, we still have much to learn

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Lung Cancer *(Continued from page 5)*

regarding the optimal treatment paradigm and patient selection. Although long-term survival as a result of immunotherapy has been demonstrated in some, the majority of patients either fail to respond to the treatment or do so for shorter duration. Proper selection of patients the most likely to benefit from immunotherapy is essential. Beyond identifying those patients who will respond to monotherapy with anti-PD-1/PD-L1 MAbs, further research efforts must focus on non-responding patients, who may need other combinatorial immunotherapeutic paradigms to enhance anti-tumor immune activity. Unfortunately, there are currently no ideal biomarkers to sort out the potential responders from the non-responders. Immunohistochemical staining of tumor specimens for PD-L1 protein is the most studied mechanism, but has some significant caveats. In addition, for patients who initially demonstrated tumor response or disease stabilization, but subsequently had disease progression, future investigation will be necessary to identify resistance mechanisms.

One potential biomarker for response of NSCLC to anti-PD-1/PDL-1 MAbs is the presence of high numbers of mismatch repair gene mutations (as seen in cigarette smokers). The converse of this finding is that there is minimal efficacy of PD-1/PD-L1 checkpoint inhibition in patients harboring single “driving” mutations in EGFR or with ALK translocations.

Recently, preliminary findings of a first-line study with the PD-1 antibody, pembrolizumab compared to platinum doublet chemotherapy were reported as positive. In this study, only patients whose tumors highly expressed PD-L1 were included. A similar first-line study with nivolumab versus chemotherapy was reported as negative, but had a lower threshold for PD-L1 tumor staining. These preliminary results emphasize the importance of establishing a proper biomarker for checkpoint inhibitor therapies. Although PD-L1 testing is not considered the ultimate biomarker for clinical use in all the above mentioned studies, patients whose tumors highly express PD-L1 generally have better outcomes. Considering the high numbers of non-responding patients to PD-1/PD-L1 inhibition,

effective immunotherapy in these patients will depend upon the identification of reliable biomarkers, proper selection of patients, and implementation of novel combination immunotherapies guided by individual tumor immunophenotypes.

The clinical results with immunotherapy targeting PD-1/PD-L1 have created a whole new treatment paradigm for patients with advanced NSCLC, opening a pathway to long-term survival previously thought impossible. It is our task as a lung cancer research community to design and participate in research trials aiming to optimize immunotherapeutic treatment in patients with NSCLC. ■

NHLBI UPDATE

NHLBI’s Strategic Visioning Priorities and Their Importance to Pulmonary, Critical Care and Sleep

Teresa Barnes, past ATS PAR Chair and Member Emerita

Recently, the National Heart, Lung, and Blood Institute (NHLBI) announced its final strategic visioning priorities, created in large part by crowd-sourced input from the cardio-pulmonary-blood community. The document outlines some major interest areas to the pulmonary, critical care and sleep community (P-CC-S).

According to NHLBI Director Gary H. Gibbons, MD, “The research priorities in this Strategic Vision will enable us to accelerate our journey toward scientific and health advances over the next decade.”

The NHLBI made a different kind of request to the heart, lung and blood community in 2015, asking for input to set its research priorities. What was different is that the institute didn’t just ask for public comment: it launched an online forum to gather ideas and support (or non-support) for those ideas in real

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NHLBI Update *(Continued from page 6)*

time. The NHLBI’s online forum collected over 1,234 idea submissions. They even ranked the “popularity” of the ideas by tracking “leaders” within the forum. The forum idea and leader information is still available [here](#). NHLBI has said the priorities will be a dynamic document to be refreshed periodically using timely input from the scientific and patient communities.

The NHLBI Strategic Vision outlines four strategic goals and eight objectives with which to achieve them and

a final outcome that includes 132 Research Priorities. Many of the research priorities are important to the P-CC-S community, and some were consistent with recommendations from the ATS.

The ATS has identified the areas of the NHLBI priorities that are of particular interest to the P-CC-S community and compiled them in [this resource](#). An abridged version of this extensive analysis is below. The full NHLBI Strategic Vision is available [here](#)

Objective 1: Understanding normal biological function and resilience

Compelling Questions	Critical Challenges/Research Barriers
How are normal cell functions regulated by complex gene networks and cell-to-cell interactions?	Reliable and diverse investigational models—from single cells to animals— that reflect individual variation as well as sex/gender-based differences are needed to reproduce normal functioning of HLBS systems and to reflect the activities of molecular targets in those systems and related diseases.
What are the key molecular and structural mechanisms that allow single cells and tissues to sense, integrate, and respond to mechanical cues and influences at local and systemic levels?	Development and application of comprehensive single-cell biology analytics are needed to facilitate an integrated understanding of cellular diversity, cell-to-cell interactions, and cellular phenomena in HLBS health and disease risk.
What are the mechanisms and range of normal physiologic responses to environmental, neuropsychiatric, social, and other stimuli that predict homeostatic resilience or transition to disease across the lifespan?	Advances in methods of and models for assessing and characterizing exposures (e.g., environmental, dietary, social) are needed to improve research on normal biologic function and resilience.
Does circadian regulation modify the effects of environmental exposures (e.g., cigarette smoke, particulates, pathogens, temperature, humidity) on mechanisms of HLBS function?	New investigative tools and knowledge of structural and matrix biology are needed to better understand injury, regeneration, and repair of the normal (or developing) heart, lung, and blood tissues and to enable regenerative medicine.

Objective 2: Investigate newly discovered pathobiological mechanisms important to the onset and progression of HLBS diseases

Compelling Questions	Critical Challenges/Research Barriers
What are the molecular mechanisms underlying dysregulation of homeostasis, and how do these mechanisms vary from individual to individual, leading to development of HLBS diseases in some but not in others?	Understanding the pathobiologic mechanisms that govern the conversion of chronic HLBS conditions into acute disease is critically needed, specifically identifying biomarkers to predict and therapies to prevent these transitions..
interstitial lung disease, hemoglobinopathies, congenital heart disease, cystic fibrosis, and asthma) be modified as affected individuals mature into adulthood?	dysfunction

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NHLBI Update *(Continued from page 7)*

Compelling Questions	Critical Challenges/Research Barriers
Do interventions to improve ventilation during sleep decrease morbidity and mortality in individuals with either heart failure (or other diseases associated with chronic hypoxemia) and sleep-disordered breathing?	

Objective 3: Investigate factors that account for differences in health among populations

Compelling Questions	Critical Challenges/Research Barriers
What community-based effectiveness and implementation research strategies can help address HLBS health inequities?	Sex/gender-specificity is needed in basic, translational, and clinical studies; data analyses; and management guidelines for HLBS conditions.
What are the environmental, genetic, and epigenetic factors and molecular, cellular, and systemic mechanisms that determine sex-related differences in HLBS health and disease?	Novel experimental strategies and tools are needed to evaluate the effect of sex differences on HLBS health, resilience, and disease.
Do the factors that render individuals or populations subjected to the same exposures (e.g., diet, smoking, other environmental and social exposures) resilient or susceptible to disease differ across the lifespan and by sex/ gender?	Advances in methods of and models for assessing and characterizing exposures (e.g., diet, smoking, other environmental and social exposures) are needed to understand differences in health among populations.

Objective 4: Investigate factors that account for differences in health among populations

Compelling Questions	Critical Challenges/Research Barriers
What factors render individuals or populations subjected to the same exposures (e.g., diet, smoking, other environmental and social exposures) resilient or susceptible to disease?	Predictive modeling and prevention trials are needed in populations at high risk for highly prevalent HLBS diseases.
What are biomarkers of pulmonary hypertension that could better identify individuals at high risk, reveal underlying mechanisms, and guide treatment?	
What are the major determinants of individual and sex differences in breathing patterns in sleep, susceptibility to insomnia, and other sleep behaviors?	

Objective 5: Develop and optimize novel diagnostic and therapeutic strategies to prevent, treat, and cure HLBS diseases

Compelling Questions	Critical Challenges/Research Barriers
Would interventions in pregnancy or early childhood designed to modulate immune development result in primary prevention of asthma?	An understanding of the immune system from a systems biology perspective is needed to design more efficacious treatment strategies for chronic inflammatory and autoimmune HLBS diseases.

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NHLBI Update *(Continued from page 8)*

Compelling Questions	Critical Challenges/Research Barriers
How should the management of diseases that typically develop in childhood (including childhood interstitial lung disease, hemoglobinopathies, congenital heart disease, cystic fibrosis, and asthma) be modified as affected individuals mature into adulthood?	Robust tools and algorithms are needed to evaluate objective biomarkers of sleep health and dysfunction
Do interventions to improve ventilation during sleep decrease morbidity and mortality in individuals with either heart failure (or other diseases associated with chronic hypoxemia) and sleep-disordered breathing?	

Objective 6: Optimize clinical and implementation research to improve health and reduce disease

Compelling Questions	Critical Challenges/Research Barriers
What methods and technologies are effective for increasing awareness of and participation in clinical research, as well as awareness of and access to evidence-based diagnostics and therapeutics, including emerging approaches to care?	Synergy and collaboration among people at the MD and PhD level for basic science; translational, patient-oriented researchers; community and population scientists; and individuals from multiple disciplines (e.g., engineers, clinicians, subspecialists, generalists, bioinformatics experts, academics, nonprofit organizations, industry) are needed to enhance and expedite advances in HLBS research.
How can we engage relevant stakeholders, including patients, private entities, and federal agencies, to improve the clinical research enterprise and address critical needs such as standardized informed consent and cost containment?	Innovative approaches to private sector collaborations and partnerships are needed early in therapeutic and diagnostic product development to bridge the gap between academic discoveries and product commercialization.
	Standardized approaches and resources, including data and biospecimen repositories, should be developed to facilitate collaboration between basic, clinical, and population scientists in clinical trials and population studies

Objective 7: Leverage emerging opportunities in data science to open new frontiers in HLBS research

Compelling Questions	Critical Challenges/Research Barriers
How do we encourage training in biostatistics, computer science, and bioinformatics to reach the entire biomedical community in this era of very large data sets?	<p>The development, application, and sharing of robust and multidimensional data-analytical and theoretical methods, mathematical modeling, and computational simulation techniques are needed.</p> <p>The development, application, and sharing of robust and multidimensional data-analytical and theoretical methods, mathematical modeling, and computational simulation techniques are needed for understanding fundamental mechanisms of HLBS systems, including gene, protein, and metabolic regulatory networks and the impact of environmental exposures on those networks.</p>

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NHLBI Update (Continued from page 9)

Objective 8: Further develop, diversify, and sustain a scientific workforce capable of accomplishing the NHLBI’s mission

Compelling Questions	Critical Challenges/Research Barriers
What kinds of exposures, beginning in early education, would stimulate and maintain students’ interest in and understanding of science, particularly students from diverse and disadvantaged backgrounds?	Sufficient numbers of clinical scientists are needed, particularly those interested in pursuing translation of breakthroughs from basic science laboratories into clinical settings.
How can we foster diversity among trainees and in the HLBS scientific workforce so that our research community reflects the makeup of the population at large and has ample participation of individuals from disadvantaged and medically underserved communities?	Programs of training, professional development, and mentoring are needed to help create a more diverse cadre of senior leaders in science and medicine.
How can clinical research training programs increase cultural competency about diseases or conditions that disproportionately affect underserved populations and attract and retain researchers who better understand the populations affected?	How can clinical research training programs increase cultural competency about diseases or conditions that disproportionately affect underserved populations and attract and retain researchers who better understand the populations affected?
How do we attract more students/trainees into traditional research fields (e.g., physiology, integrative biology) that are as critical to advancing science as emerging fields (e.g., “omics,” big data), but do not have the same cache and suffer from declining interest?	Better preparation of scientists for transitions between career stages (e.g., graduate/medical education stage, the postdoc/ fellowship period, the junior investigator stage) is needed.

NIEHS

NIEHS Celebrates 50th Anniversary

This year, the National Institute of Environmental Health Sciences (NIEHS) is celebrating its fiftieth anniversary of scientific discovery on the environmental influences on human health. For 50 years, the Institute has been advancing our understanding of how the environment affects lung health and many other areas encompassed in its broad mission, which includes a strong focus on prevention.

Some of the institute’s research has also provided the scientific basis for public policies on tobacco control and air pollution that have improved public health. NIEHS studies listed in the Environmental Protection Agency’s 1992 report [Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders](#) and the

National Toxicology Program’s reports on carcinogens, which identified tobacco smoke as a known human carcinogen, provided the research base that led to the enactment of smoking bans first on airplanes and in federal buildings, extending to workplaces and restaurants and finally to the enactment of 28 statewide smoking bans in all enclosed workplaces.

NIEHS-supported research, including the Harvard Six Cities Study, published in 1993, identified the cardiopulmonary health effects, including deaths from lung cancer, of outdoor particulate matter. These and other NIEHS-supported studies provided the EPA with the science base to issue stronger National Ambient Air Quality Standards in 1997, which, together with updated air quality standards set in 1990, have resulted in cleaner air in the U.S.

NIEHS is also the lead NIH institute researching the health effects of climate change and has been a key partner for the ATS in this area. The Institute supported the 2010 ATS workshop, the *Respiratory Health Effects of Global Climate Change*.

The Institute has also maintained a strong commitment to research training, fostering the careers of respiratory health investigators through various fellowship, training, and career development awards such as the Ruth L. Kirchstein National Research Service Awards and Individual Career Development Awards.

Under the leadership of Director Linda S. Birnbaum, PhD, NIEHS is poised to generate many new and exciting discoveries that will protect public health. The ATS is proud to co-chair the Friends of the NIEHS (FNIEHS), a coalition of over 30 public and environmental health and patient organizations that advocates for NIEHS funding. FNIEHS is holding events to commemorate the Institute's 50th anniversary, including a Capitol Hill reception and a congressional briefing on Nov. 16. [Learn more about NIEHS's 50th anniversary.](#) ■

NINR

ATS Nursing Assembly Chair Lauds New NINR Strategic Plan

In September, the National Institute of Nursing Research (NINR), which is also celebrating its 30th anniversary in 2016, launched a new strategic plan outlining the Institute's priorities for future nursing science. "Advancing Science, Improving Lives: A Vision for Nursing Science" features four research focus areas: symptom science, wellness, self-management, and end-of-life and palliative care.

The Research News Quarterly interviewed ATS Nursing Assembly Chair Eileen G. Collins, PhD, RN, for her thoughts on the new plan. She said, "The four scientific areas identified by NINR in the plan are areas of great interest to many ATS scientists. For example, researching the physiological basis for co-occurring symptoms or symptom clusters such as dyspnea and fatigue are key areas that we can focus on to help our patients manage their disease." Dr. Collins continued, "Additionally, NINR continues to focus on helping health professionals manage the symptoms of the seriously ill and plan for end-of-life decisions."

Dr. Collins also noted the NINR's focus on innovation as a particular strength of the Institute. She said, "NINR has identified promoting innovation as a cross-cutting area necessary for the advancement of nursing science. The Institute wants to maximize the use of innovative methodologies through interprofessional partnerships." She cited example of innovations as ranging from smart devices to system infrastructure. Dr. Collins concluded, "NINR is focusing their strategic plan on areas important to our patients. It is also certainly worth taking a look at the plan to see what NINR can offer in the way of research funding." [Click here to view the NINR Strategic Plan](#) ■

NIH

NIH Releases Final Clinical Trials Policy Changes

In September, the Department of Health and Human Services released a final rule mandating new changes to NIH and FDA clinical trials requirements and procedures. The changes are the culmination of an effort previously reported on by the Quarterly, which included input from the ATS on modernizing and improving the efficiency and quality of clinical trials and providing more information to patients to enhance their ability to participate in studies. The changes are also intended to improve the application and award process and enhance NIH's ability to determine the merits and viability of studies. The NIH's new clinical trial policies will begin going into effect in Jan. 2017. One widely expected policy proposed by NIH last year that will go into effect in May 2017 is use of single-Institutional Review Board review of multi-site studies. NIH will provide standardized agreements for institutions to use the single review.

One of the key changes aimed at informing both the public and researchers more quickly about clinical trial results and reducing duplication will require all NIH-funded trials to register and submit summary results to ClinicalTrials.gov within 21 days of enrollment of the

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NIH (Continued from page 11)

first study participant. This regulation will go into effect on Jan. 18, 2017, with compliance required by the end of April 2017. NIH is working on formatting and feature changes to ClinicalTrials.gov to make it more user-friendly to professionals and patients. In most cases, registration and trial results information will be posted within 30 days of receipt. Trials will also need to be submitted in response to a specific Funding Opportunity Announcement (FOA). New NIH clinical trial FOA's will now include review criteria centered on the rationale, design, and operational plans in order to facilitate study assessments. Applications submitted under broader "parent funding announcements" will no longer be accepted. Trial applications will need to include information about protocols and other information needed for peer and programmatic review.

NIH will now require "good clinical practice" (GCP) training in the new procedures for both NIH-funded clinical trials investigators and NIH staff who conduct or oversee clinical trials. The intent of this training is to ensure that those involved in clinical trials are informed about the design, conduct, monitoring, analysis, and reporting of trials. The GCP training requirement will go into effect on Jan. 1, 2017.

A new trial policy aimed at reducing delays will harmonize the NIH and FDA investigational new drug (IND) application process by encouraging the use of a clinical trial protocol template. The template will help investigators draft protocols that include all information needed to facilitate speedier IRB review and FDA IND regulations.

NIH leaders have stated that efforts to continue modernizing and improving the clinical trials infrastructure will be ongoing. Below are web links to specific NIH clinical trial policy requirements and the full NIH policy.

- [Clinical trial \(CT\)-Specific FOA's](#)
- [CT Registration and Results Submission](#)
- [Single-IRB Review](#)
- [GCP Training](#)
- [Full NIH Policy](#) ■

CHILD HEALTH

New NICHD Director Named

Diana W. Bianchi, MD, has been named the new director at the NIH National Institute of Child Health and Development (NICHD). Dr. Bianchi comes to the NIH from the Tufts University School of Medicine, where she was vice-chair for pediatric research and executive director of the Mother Infant Research Institute. She is a practicing geneticist with a focus on prenatal genomics, including development of non-invasive parental FDA screening and diagnostics, and new treatments for genetic disorders. Dr. Bianchi will join the NICHD on October 31, 2016.

Child Health Exposure Study Resource Now Available for Investigators

A new National Institute of Environmental Health Sciences (NIEHS) resource that enables NIH-funded pediatric investigators to include environmental exposure measurements in their research studies is now available free of charge. The Children's Health Exposure Analysis Resource (CHEAR) program is aimed at expanding the number of scientists examining child environmental health.

CHEAR will provide laboratory and data analytical services for targeted and untargeted assessment of various environmental exposures and associated biological response indicators in biological samples.

Some examples of the criteria that a study may include to be eligible for using CHEAR:

- Have an ongoing or completed epidemiological or clinical study on child health
- Desire to add environmental exposure data to a study or need for more extensive analysis of exposures

- Open to researchers funded at least in part by NIH extramural funds, and the applicant is eligible to apply for an NIH grant at his/her home institution
- Agree to share experimental design details and supporting data, including phenotypic data at the individual level to facilitate analysis by the CHEAR consortium, including both the CHEAR Data Center and Laboratory Network

Interested investigators can create an account and request CHEAR services [at this link](#). The first request is shorter than a grant application, and if accepted, will be followed by a consultation with one of the CHEAR network laboratories before a full application is submitted. ■

RESEARCH FUNDING

Congress Passes Temporary 2017 Spending Measure; Finalization of 2017 Spending to Follow Election

Just two days before the expiration of fiscal year 2016, the House of Representatives passed the short-term spending measure for fiscal year 2017 by a vote of 342 - 85, averting a government shutdown that would have gone into effect on October 1. The Senate passed the bill earlier the same day by a vote of 72 - 26, and President Obama quickly signed the bill into law. The measure includes a 7.1 percent funding increase for the VA Research Program--a significant success.

The bill flat funds the government at the current FY 2016 level through Dec. 9, with a minor 0.5 percent across the board cut to all programs. It also includes \$1.1 billion in funding to combat the Zika virus and \$500 million in funding to Louisiana and other states for disaster relief.

When Congress returns to Washington following the November 8 election, it will need to pass additional

legislation to finalize FY 2017 funding. NIH has a good chance of receiving a funding increase, as both the Senate and House Appropriations Committees passed health spending bills that provided NIH increases of \$2 billion and \$1.25 billion respectively.

Election Update

The full House of Representatives is up for re-election on Nov. 8, 2016. On the Senate side, 34 seats are up for re-election, and there is a chance Democrats could take control of the Senate. Senators up for re-election include the key committee chairman and members, among them Roy Blunt (R-MO), chair of the Senate Labor-Health and Human Services Appropriations Subcommittee, which provides funding for NIH and the CDC; and the committee's top Democrat, ranking member Patty Murray (D-WA). In the House, Labor-Health and Human Services Appropriations Subcommittee Chairman Tom Cole (R-OK) is expected to both win re-election and retain his subcommittee chairmanship. The new Congress will open in January 2017. ■

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