

Research News Quarterly

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Letter from the Editor

The June Research News Quarterly continues our interview series with NIH institute and federal program heads with a conversation with the Director of the National Institute of Child Health and Development (NICHD), Alan Guttmacher, M.D. In this interview, Dr. Guttmacher outlines the institute's efforts to further our knowledge of rare pediatric diseases and the childhood origins of adult respiratory diseases, as well as the NICHD's programs to support pediatric pulmonary, critical care and sleep training.

Next, PAR member Teresa Barnes gives an overview of the NHLBI's new strategic planning process, followed by a report on exciting research opportunities available for the pulmonary, critical care and sleep community from the newly-expanded Department of Defense medical research program.

Moving to translational and comparative effectiveness research, we have an update on the National Center for Advancing Translational Research (NCATS) and Patient-Centered Outcomes Research Institute's (PCORI) joint effort to coordinate clinical trial site infrastructure. The June Research News Quarterly is rounded out with an update from our Washington office on the progress of 2016 health research funding legislation.

Sincerely,

Linda Nici, MD
Editor



INTERVIEW WITH ALAN E. GUTTMACHER, M.D., National Institute of Child Health and Development (NICHD) Director

Q: What is your vision for the institute over the next five years?

A: NICHD has an impressively broad mission, encompassing human development through the life span, child health, much of women's health, reproductive health, and medical rehabilitation. In 2012, we published the NICHD's Scientific Vision [statement](#) on the institute's web site. It's a complex and far-reaching document, focusing on the next 10 years. Some of the central concepts are:

- To develop the means to predict, identify and ameliorate the steps leading to birth defects and other variations in human structure and functioning.
- To gain sufficient knowledge of the complex interactions between biological and environmental factors— starting before conception— that influence development across the life span of the individual and of future generations, in order to predict, and act to prevent, treat, or reverse disease.
- To increase our understanding of the complications of pregnancy— among them gestational diabetes, hypertension, preterm birth, and stillbirth.
- To further our understanding of behavior and cognition in order to ameliorate developmental conditions or help individuals interact with the world in ways that can sustain or improve their health and well-being.
- To further our understanding of plasticity— the mechanisms underlying adaptive or maladaptive change at the cellular, organ, tissue, and system level.
- To understand how the forces that shape populations can influence health, together with understanding why some populations with similar genetic endowments and environmental exposures experience diverse health outcomes. Such understanding would inform the development of effective population- and community-based interventions and identify factors that can eliminate health disparities.

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Alan E. Guttmacher Interview *(Continued from page 2)*

- To harness the potential of transdisciplinary science-- collaboration and cooperation among researchers in diverse fields-- and to maximize the vast amount of information that will result from complex long term studies and repositories housing lifetimes of biological specimens.
- We're entering a promising new era in biomedical research and we believe the areas we've identified offer the greatest promise to improve the health of men, women, children and those with disabilities.

Q: Pharmacotherapy for children and pregnant women markedly lags behind what's available for adult men and for women who aren't pregnant. How is NICHD attempting to bridge this major gap?

A: Indeed, many pharmaceuticals have been tested and approved for use in adults but never studied in children or in pregnant women. This puts clinicians in the unenviable position of having to prescribe a necessary treatment off label, without the benefit of research findings applicable to these populations. However, one cannot simply extrapolate from studies of adult men and non-pregnant women. For example, because of their smaller size, generally more rapid metabolism and other physical differences from adults, children are affected differently by many drugs. Similar physiological concerns govern the use of pharmaceuticals for pregnant women—concerns not just for the mother, but also for the fetus.

These concerns have been around for some time. In 2002, Congress saw the great need for more information in this area and enacted the Best Pharmaceuticals for Children Act. To carry out its portion of the Act, the NIH supports research on off- and on-patent drugs to provide evidence to the FDA for pediatric labeling.

NICHD's Obstetric and Pediatric Pharmacology and Therapeutics Branch works to fulfill the provisions of the Act, through preclinical and clinical drug trials. Essentially, the NICHD works to identify and prioritize

the drugs that need further study, and conducts studies on priority drugs that the manufacturers have declined to study. Most recently, supported research networks demonstrated the effectiveness of the antibiotic meropenem for treating intestinal infections in children less than 3 months of age. As a result of these studies, the U.S. Food and Drug Administration granted approval for use of meropenem in this population.

Similarly, the Branch supports research to improve the safety and effective use of drugs during pregnancy and lactation. Currently, the branch has a number of active [Funding Opportunity Announcements](#) in translational research, pediatric and obstetric pharmacology, biomarkers, development of pediatric formulations and drug delivery systems, developmental pharmacology and toxicology, discovery and development of therapeutics for pregnancy-related diseases, and the development of instruments and devices for use in neonatal and pediatric care settings, among other areas.

Q: What initiatives is NICHD contemplating to further our knowledge and prevention of childhood antecedents of adult respiratory diseases?

A: This area is increasingly important, not just as it pertains to respiratory disease, but to all aspects of adult health. The NICHD Vision Statement that I mentioned earlier includes a section on the Developmental Origins of Health and Disease. The goal of this Vision concept is for developmental biology research to provide the means to identify—and, eventually, ameliorate—an array of structural and functional variations, including adult respiratory disease.

The NICHD's Pediatric Growth and Nutrition Branch supports a broad portfolio of research related to preventing chronic diseases. Many such chronic conditions result from gene-environmental interactions, and have their roots in infancy or childhood. The Branch emphasizes the need to identify childhood

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biomarkers of diseases with clinical onset later in life, and the steps that can be taken during childhood to mitigate or even prevent such conditions. Analyses of high-throughput “-omic” data offer the hope of identifying these biomarkers early. Similarly, gaining a better understanding of epigenetic processes could also provide insight into other developmental origins of health and disease.

The NICHD also is embarking upon a new undertaking that stands to advance our understanding of early life determinants of adult health and disease. Problems with the placenta have been linked to many health problems, perhaps most importantly, preterm birth. Extremely preterm infants are at higher risk for lung problems not only in infancy, but also early in life. Is it possible that improving placental function during pregnancy could head off preterm birth and resultant lung problems later in life? Probably. But we can't say for sure, because we don't have many techniques for in utero diagnosis of placental problems, let alone the means to fix them even if we could diagnose them.

Recently, the NICHD launched the Human Placenta Project, an effort to create tools and approaches and to recruit innovative scientists and clinicians to help us understand the role of the placenta in both health and disease. The placenta is the least understood human organ, yet an extremely important one that influences not only maternal health and fetal development, but the lifelong health of both the mother and the child who results from the pregnancy. Yet, because the placenta carries out its life sustaining functions hidden inside the uterus, we know comparatively little about it. The capacity to monitor the placenta noninvasively in real time, and intervene when necessary, would have the potential to improve dramatically not only the health of the mother and the fetus, but of the adult that fetus will eventually become.

We've issued an [RFA](#) seeking to support the development of new imaging or other assessment

technologies that will help us understand placental functioning in vivo, throughout gestation, and to determine how environmental influences might affect the placenta. Such technologies may well contribute to our understanding of the links between early fetal development and later-life health issues such as cardiovascular disease, diabetes, and yes, lung function.

However, as much as we'd like to prevent all health problems before birth, we also realize that there's an urgent need for postpartum solutions as well. The NICHD has joined with the National Institute of Biomedical Imaging and Bioengineering (NIBIB) to issue three related RFAs to monitor asthma in the community. The project is known collectively as the Pediatric Research using Integrated Sensor Monitoring Systems (PRISMS). The idea is to develop portable sensors that children at risk for asthma could wear. The sensors would collect environmental data and then relay this information to a central database where researchers could access it and undertake analyses. [The first RFA](#) seeks applications to develop wearable and non-wearable sensors to monitor pediatric environmental exposures and physiological signals. [The second](#) seeks applications to develop informatics platforms to warehouse the data that the sensors collect, and [the third](#) seeks to establish centers where the data would be compiled.

Q: What initiatives are being considered to elucidate rare diseases in children?

A: At NIH, the National Center for Advancing Translational Sciences administers the [Rare Diseases Clinical Consortia](#), a cooperative network of investigators studying rare disorders. The NICHD is a participant, and supports consortia investigating conditions including osteogenesis imperfecta, developmental synaptopathies, and disorders related to cholesterol metabolism.

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The NICHD also supports the Newborn Screening Translational Research Network, a resource for investigators engaged in newborn screening related research. Many of the disorders included in the screens are rare disorders. The Network helps researchers access collections of dried blood spots, evaluate the predictive value of biomarkers in early phase studies, develop new methods and technologies for newborn screening, identify diseases for inclusion in screening programs, and determine the effectiveness of treatments identified through screening.

In 2013, the NICHD and the National Human Genome Research Institute (NHGRI) funded a series of [pilot projects](#) to determine the feasibility of genomic sequencing in newborns. This powerful technology has the potential to diagnose a vast array of disorders and conditions, many of them rare. But, deciphering an individual's genetic code brings with it a host of clinical and ethical issues. We funded four pilot projects which will proceed over five years. In addition to genomic sequencing and analysis, the investigators are focusing on how their findings relate to patient care, and to the ethical, legal, and social implications of using genomic information in the newborn period.

The NICHD Division of Intramural Research program supports researchers on the NIH campus, a number of who study rare disorders. These include cancers of the adrenal glands and other adrenal disorders.

I'd also like to mention a project on childhood onset [tracheomalacia](#). Narrowing or closure of the airways can be extremely debilitating, even life threatening. NICHD funds Glenn Green and Scott Hollister at the University of Michigan to develop a 3D printed [bioresorbable splint](#) for treating the condition, an effort with the potential to transform treatment of this condition.

Q: What are the major processes adopted by NICHD and aimed at securing the pipeline of outstanding investigators in the field of pediatric lung, critical care and sleep medicine?

A: Through its extramural branches, the NICHD offers support for a number of training and career development opportunities. These include [Individual Research Fellowships](#) for graduate students and postdoctoral fellows, [Career Development Awards](#), for senior level postdoctoral fellows and junior faculty, [Institutional Training Grants](#), to support groups of pre and postdoctoral fellows in basic, clinical and behavioral sciences, and [Education Grants](#), for summer research experiences and methods-based short courses.

NICHD also supports the [Pediatric Critical Care and Trauma Scientist Development Program](#), a national faculty training program to develop successful pediatric critical care and pediatric physician scientists. Emphasis is on pediatric critical care medicine, with a focus on multi-organ dysfunction syndrome, sepsis, traumatic brain injury, and acute lung injury.

NICHD's [Child Health Research Career Development Award](#) Program provides for "Centers of Excellence" in pediatric research, to train junior faculty planning careers in academic pediatrics. The program matches talented junior faculty members at each center with appropriate scientific mentors who provide the background, techniques, and tools to help them become productive scientists and secure independent research funding. Participants enhance their basic research skills and generate preliminary data that can provide the basis for funding applications of their own. ■

NEWS FROM NHLBI

NHLBI Gathers Input from Stakeholders to Focus Future Research Priorities

By Teresa Barnes, Member, Research Advocacy Committee & Patient Advisory Roundtable

The National Heart, Lung, and Blood Institute (NHLBI) launched a “Strategic Visioning Initiative” earlier this spring to gather input from the public and as the word got out to stakeholders, the ideas came pouring in.

The NHLBI’s objective was to collect as many ideas from various stakeholders as possible to help guide the institute’s research focus for the next decade. The strategic visioning framework published by the institute outlined the following 4 goals:

- Promote Human Health - To expand knowledge of the molecular and physiological mechanisms governing the normal function of heart, lung, blood, and sleep systems as essential elements for sustaining human health.
- Reduce Human Disease - To extend our knowledge of the pathobiology of heart, lung, blood, and sleep disorders and enable clinical investigations that advance the prediction, prevention, preemption, treatment, and cures of human disease.
- Advance Translational Research - To facilitate innovation and accelerate research translation, knowledge dissemination, and implementation science that enhances public health.
- Develop Workforce and Resources - To enable and develop a diverse biomedical workforce equipped with the essential research resources to pursue emerging opportunities in science.

Using an online software platform called Ideascale to collect input from stakeholders, NHLBI sought input until May 15th.

The institute requested feedback specifically in the form of “compelling questions” and “critical challenges.” In defining what it meant by the two areas, NHLBI explained, “When you identify a particular gap in knowledge that needs to be filled, express it as a Compelling Question (e.g., “What pathobiology underlies the interaction of ...”)...when you identify a technical challenge or needed resource, express that as a Critical Challenge (e.g., “Investigators need validated non-rodent animal models of ...”).”

Much of the push for participation came from leaders of NHLBI itself and communications included personal emails to researchers and patient advocates alike. In one email sent by NHLBI’s Director of Science Policy, Engagement, Education and Communications, Lenora E. Johnson, DrPH, MPH, she stressed “the success of this Initiative depends upon your participation”.

Initially, it was largely the research community, primarily individual researchers, that responded to the requests and began posting their ideas. However, in the last weeks of the campaign, NHLBI made a push to increase input from other stakeholders, particularly patients and patient advocates. The institute wanted advocates to know the value it placed on the patient perspective and of their interest in gaining truly innovative and thought provoking ideas from all stakeholders.

In another email message from NHLBI to researchers, a staffer wrote “I am writing to ask you to provide input to our Strategic Visioning process, through which NHLBI is attempting to identify the most critical directions for future heart, lung, blood, and sleep research – especially those areas that may need an extra push to succeed.”

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New from NHLBI *(Continued from page 6)*

The Ideascale software allowed the contributors to describe their ideas (in the two categories as defined by NHLBI) and post them to the public forum. As others visited the forum and perused the posted ideas, they could “vote” on others’ ideas – either by voting positively or negatively and could provide suggestions to improve ideas already submitted. Ultimately, each idea would have a total of ‘net’ votes that indicated support of the community or lack thereof.

Idea contributors were “rewarded” for their ideas that produced support from other stakeholders by the Ideascale software by getting “earned badges” for their good work. Badges included titles such as “Apprentice” which told the user “You’re now an apprentice. Welcome to the magical world of IdeaScale”, and “Team Player” that told users “Way to bring hoop dreams to life!” as well as “Candidate” that told users “The people have spoken. Your idea has earned you a candidacy badge”.

NHLBI held at least two webinars to inform the community about how to participate in the strategic visioning initiative. NHLBI staff also posted to social media site LinkedIn to gain last minute input from stakeholders.

The ATS Research Advocacy Committee submitted a set of critical research questions and challenges for the institute’s strategic vision. NHLBI is currently reviewing and evaluating input from the stakeholder community. Lamont Williams of the NHLBI press office said the institute is “happy with the response” to the strategic visioning forum. NHLBI plans to open up a comment opportunity for stakeholders later this summer to comment on the research priorities that emerge from this first phase of the process. ■

DOD RESEARCH OPPORTUNITIES

Pulmonary Researchers Gain Access to Defense Department Research

by Teresa Barnes, Member, Research Advocacy Committee & Patient Advisory Roundtable

This spring, the Department of Defense (DOD) announced legislatively appropriated funding for the Congressionally Directed Medical Research Programs (CDMRP) including the Peer Reviewed Medical Research Program (PRMRP) for fiscal year 2015. The PRMRP program has more than doubled the number of disease areas included in this year’s grant opportunities and increased funding. Researchers need to prepare quickly as deadlines are looming.

The PRMRP is the official determination of disease areas that can be funded through the DOD. 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 healthcare needs of military service members, veterans and/or beneficiaries. The PRMRP challenges the scientific and clinical communities to address one of the FY15 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 \$247.5 million in funding for 41 eligible disease areas. Funding in 2014

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New DOD Research Opportunities *(Continued from page 7)*

was \$200 million for 25 eligible disease areas. The nearly \$250 million in funding for 2015 is the largest in the PRMRP program's history.

The PRMRP program was originated by patient advocates. As a result of patient organization advocacy efforts, including members of the ATS Public Advisory Roundtable (PAR) some diseases such as Pulmonary Fibrosis are included in the 2015 program for the first time. Lung disease-related research topics now include: Acute Lung Injury, Pulmonary Fibrosis, Sleep Disorders and a topic called "Respiratory Health" as well as diseases with a high incidence of pulmonary comorbidity including Lupus, Rheumatoid Arthritis, and Scleroderma.

There were three areas within the CDMRP that have specific restricted allocations that provide obvious opportunities for pulmonary researchers including: Gulf War Illness (including respiratory illness), which will provide \$20 million in 2015; Lung Cancer, which will provide \$10.5 million in fiscal year 2015 and Tuberos Sclerosis which will provide \$6 million in funding for 2015.

Each area of disease has separate program announcements from the DOD and some have already been announced with deadlines coming up as early as the first week of June. Current program announcements for PRMRP can be found at: <http://cdmrp.army.mil/funding/prgdefault.shtml>. Requests for email notification of the Program Announcements release may be sent to help@cdmrp.org.

For more information about the PRMRP or other CDMRP-administered programs, please visit the CDMRP website (<http://cdmrp.army.mil>) or contact help@eBRAP.org or 301-682-5507

Important award opportunities and deadlines include (but are not limited to):

Gulf War Illness Pre-application Deadline: July 9, 2015
Link: <http://cdmrp.army.mil/funding/gwirp.shtml>

Lung Cancer Pre-application Deadlines: July 2, 2015
Link: <http://cdmrp.army.mil/lcrp/default.shtml>

Tuberos Sclerosis Pre-application Deadline: July 27, 2015
Link: <http://cdmrp.army.mil/tscrp/default.shtml>

Other Grant Opportunities (Details at <http://cdmrp.army.mil/funding/gwirp.shtml>):

- **New Gulf War Illness (GWI) Epidemiology Research Award (NEW for FY15!) - Preapplication due July 9, 2015**
Open to: Independent Investigators at all academic levels (or equivalent).
- **Investigator-Initiated Research Award - Preapplication due July 9, 2015**
Open to: Independent Investigators at all academic levels (or equivalent). Supports new ideas in basic and clinical developmental research focusing on GWI.
- **Innovative Treatment Evaluation Award - Preapplication due July 9, 2015**
Open to: Independent Investigators at all academic levels (or equivalent). Supports small-scale, early clinical trial evaluations of innovative treatments not previously studied in GWI.
- **Clinical Trial Award - Preapplication due July 9, 2015**
Open to: Independent Investigators at all academic levels (or equivalent). Supports larger, more definitive (Phase II or III or FDA device class I-III) clinical trials focusing on treatments for GWI.
- **New Investigator Award – Letter of Intent due October 15, 2015**
Open to Transitioning Postdoctoral Fellows, Early-Career Investigators & New GWI Researchers (Established independent investigators who have received less than \$300,000 in federally funded, non-mentored GWI research funding). Previous experience in GWI research is not required. ■

NEWS FROM NCATS & PCORI

NCATS and PCORI Partner to Streamline Clinical Trials

NCATS and the Patient-Centered Clinical Outcomes Research Institute (PCORI) recently began working together to better coordinate clinical trial research. Both agencies support infrastructure and funding for conducting multisite clinical trials. The NCATS' Clinical and Translational Science Awards (CTSA) program supports research for earlier stage trials while PCORI funds later stage trials. CTSA and PCORI staff are working together to coordinate activities and prevent duplication across the following three areas of interest:

- Streamlining regulatory oversight through shared institutional review board agreements
- Building electronic health records/informatics tools to conduct trial feasibility assessments and enhance trial recruitment capabilities
- Improving the contracting process

NCATS and PCORI workgroups met on May 27 to begin planning to develop shared tools and resources that will be compatible with PCORI and CTSA clinical trial operations. These efforts will move both agencies closer to seamless trial infrastructure that can serve all CTSA hubs and beyond. ■

RESEARCH ADVOCACY

Research Advocacy Committee Advocates for Increased Health Research Funding



Daniel Salerno, M.D., Aaron Hamvas, M.D., Rep. Danny Davis (D-IL), Jeff Jacobson, M.D., Kari Rosbeck, PAR member and Usha Raj, M.D.

On January 28, the ATS, the National Heart, Lung and Blood Institute (NHLBI) and its patient partners the LAM Foundation and the COPD Foundation sponsored a successful educational briefing for congressional staff, entitled Women's Lung Health: Advances & Challenges. The event was held in cooperation with Representative Rosa DeLauro (D-CT) and House COPD Caucus co-chairs Representatives David Joyce (R-OH) and John Lewis (D-GA).

The briefing featured an overview of NHLBI research on women's lung health by institute Director Gary Gibbons, MD. Kathryn Steele, a LAM patient, spoke movingly of her experience being diagnosed with LAM and living with the disease. NHLBI scientist Joel Moss, MD, PhD, outlined how research on LAM over the past decade has transformed patient lives and MeiLan K. Han, MD, MS, associate professor of medicine at the University of Michigan, discussed the burden of COPD among women. ■

RESEARCH FUNDING

2016 Health Research Funding Update

The House and Senate Appropriations subcommittees have started moving FY2016 spending bills. As we go to press, the Labor-Health and Human Services (Labor-HHS) subcommittee, chaired by Rep. Tom Cole (R-OK), has scheduled a June 17 vote on the 2016 health research and services spending bill, known as the Labor-HHS bill. On the Senate side, subcommittee chairman Sen. Roy Blunt (R-MO) has scheduled a panel vote on the Senate's June 24 vote on the 2016 Labor-HHS bill. ATS members are urged to contact their House Representative and senators to urge their support for NIH and CDC funding. Use the ATS website to send an email to your members of Congress by clicking on www.thoracic.org/advocacy.

Following subcommittee action, the Labor-HHS bills will be voted on by the full Appropriations committees. The Labor-HHS bill is expected to be a difficult spending bill to resolve because the House's overall funding allocation is over \$3.5 billion lower than FY2015, so the final outcome of the health spending bill is unclear. ■