

FYI from the NHLBI

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Recent Research Advances

This issue of the FYI from the NHLBI highlights several recent NHLBI-supported scientific advances.

Study Improves Risk Prediction in Individuals with Long QT Syndrome

Researchers have discovered that certain genetic mutations found in patients with long QT syndrome type 1 (LQT1), a rare genetic disorder that affects heart rhythm, are associated with a particularly high risk of sudden death. LQT1 can be caused by a number of different mutations that affect an ion channel found on heart muscle cells. Although all LQT1 mutations affect the same channel, their specific effects on channel function vary.

To determine how particular LQT1 mutations influence clinical outcomes, researchers gathered genetic and clinical data from 387 patients with LQT1. They then measured the effects of 17 different LQT1 mutations on ion channel function and correlated the findings with patient outcomes. Mutations that caused the ion channel to open more slowly than normal were associated with a higher risk for sudden death than mutations that did not affect the rate of channel opening.

Currently, risk assessment for patients with LQT1 is based primarily on factors such as age, gender, and measurements of the heart's electrical activity. The new findings on mutation-specific risk should enhance risk assessment for LQT1 patients and provide doctors with additional information needed to identify patients who might benefit from closer follow-up and more aggressive treatment.

Continued on page 2

The Heart Truth and the Red Dress

Many women are now aware of the Red Dress®, which was introduced as the national symbol for women and heart disease awareness in 2002, and of the primary message that it is intended to convey – that heart disease is the leading cause of death for women in the United States.

What many women may not know, however, is that The Heart Truth® campaign for which Red Dress® is the primary identifier is a product of NIH efforts. It was the NIH that developed the idea of a national program to educate women about their risks for heart disease and to recruit partner organizations to join in its sponsorship.

Although primarily directed toward women ages 40 to 60, the time when a woman's risk of heart disease starts to rise, the messages of The Heart Truth® are important for all women: for young women because heart disease develops gradually and can start at a young age, and for older women because it is never too late to take action to prevent and control the risk factors for heart disease. Even those who have heart disease can improve their heart health and quality of life.

National Wear Red Day, this year to be held on Friday, February 3, is an opportunity to show support for heart disease awareness among women.

Inside

NHLBI Workshops and Working Groups	2
Mark Your Calendar	2
NHLBI Research Initiatives	3
National Heart, Lung, and Blood Advisory Council September and October Meetings	4
News from Capitol Hill	4
Upcoming Events	5
Constituents' Corner	6
Need More Information?	6

Upcoming NHLBI Workshops and Working Groups*

No activities are scheduled for the period covering January through April 2012.

Continued from page 1

Protein Linked to Parkinson's Disease Found to Affect Fat Metabolism

A new study has shown that the protein Parkin, the product of a gene mutation that causes many early-onset cases of Parkinson's disease, regulates cellular uptake of dietary fat.

To study the potential role of Parkin in Parkinson's disease, researchers created genetically modified mice lacking the Parkin gene. Surprisingly, the mice did not display any obvious signs of Parkinson's disease. However, they differed from normal mice in one interesting respect: they did not gain weight as they aged or when fed a diet high in fat and cholesterol. Follow-up experiments revealed that Parkin-deficient mice have lower levels of proteins responsible for the transport of fat in the body.

The researchers went on to analyze cells from patients enrolled in the Parkinson's Clinic at the NIH, and discovered that the human cells also had a limited ability to absorb fat. Although it is not yet known how fat metabolism may be involved in the development of Parkinson's disease, the current study provides an important new avenue for understanding the disease.

Hydroxyurea Proves Safe and Effective for Young Children with Sickle Cell Disease

Results from a clinical trial indicate that hydroxyurea, a proven treatment for sickle cell disease (SCD) in adults, is also safe and effective in very young children. Hydroxyurea reactivates production of fetal hemoglobin, which typically is replaced by adult hemoglobin shortly after birth. Some people with SCD are able to produce normal fetal hemoglobin and their red blood cells show a reduced tendency to deform and clog blood vessels, with higher concentrations of normal fetal hemoglobin being associated with less-severe disease.

The Pediatric Hydroxyurea Phase III Clinical Trial, known as BABY HUG, evaluated use of hydroxyurea in children 8 to 19 months of age. Hydroxyurea not only reduced pain episodes but also improved some measurements of spleen and kidney function relative to placebo. Moreover, children who received hydroxyurea also had less risk of swelling of the hands and feet and reduced incidence of acute chest syndrome, and they required fewer hospitalizations and fewer blood transfusions. All study participants will be followed through 2016 to assess the long-term effects of the treatment.

Broccoli Compound May Combat COPD

A compound called sulforaphane, which is found in broccoli, has been shown to stimulate metabolic factors needed to help COPD patients fight bacterial lung infections. Patients with COPD acquire lung infections due to a decreased ability of their macrophages to engulf and remove bacteria. The infections cause exacerbations of COPD and are a major source of morbidity and mortality.

NHLBI-funded investigators obtained macrophages from COPD patients and found that sulforaphane stimulated a factor called Nrf2, which then enhanced the ability of the macrophages to recognize and eliminate both *Haemophilus influenzae* and *Pseudomonas aeruginosa*, two types of bacteria frequently associated with pulmonary infections. In addition, mice treated with sulforaphane had increased Nrf2 levels, enhanced clearance of pulmonary bacteria, and decreased inflammation. The study results suggest that additional research on sulforaphane and its properties could lead to improved treatment for patients with COPD.

Continued on page 3

Mark Your Calendar . . .

February	American Heart Month (www.heart.org)
3	National Wear Red Day (www.nhlbi.nih.gov/educational/hearttruth/)
7-14	Congenital Heart Defect Awareness Week (www.tchin.org/aware/)
March	
5-11	National Sleep Awareness Week (www.sleepfoundation.org/event/national-sleep-awareness-week)
May	National High Blood Pressure Education Month (www.nhlbi.nih.gov/health/public/heart/hbp/prevhbp/index.htm)

NHLBI Research Initiatives

From time to time, the NHLBI invites investigators to submit grant applications or contract proposals for specific research programs. We are soliciting applications for the following new programs. Please visit the URL listed with each program to obtain information about application dates and deadlines. For full descriptions of these and other current research initiatives, visit www.nhlbi.nih.gov/funding/inits/index.htm.

Phase II Clinical Trials of Novel Therapies for Lung Diseases (UM1)

(RFA-HL-12-022)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-12-022.html>
Objective: Conduct Phase II clinical therapeutic trials that have the potential to advance development of novel therapies for a lung disease or a cardiopulmonary disorder of sleep.

NIH Competitive Revision Applications for Research Relevant to the Family Smoking Prevention and Tobacco Control Act (R01)

(PAR-12-010 and PAR-12-011)

<http://grants.nih.gov/grants/guide/pa-files/PAR-12-010.html>
Objective: Support an expansion of the scope of already approved and funded R01 projects involving smoking and tobacco products.

Virtual Reality Technologies for Research and Education in Obesity and Diabetes (R41/R42)

(RFA-HL-12-020 and RFA-HL-12-024)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-12-024.html>
Objective: Capitalize on the unique capabilities of virtual reality technologies to extend the health care and learning environments for patients with obesity and diabetes.

Clinical Trials Planning Studies for Rare Thrombotic and Hemostatic Disorders (U34)

(RFA-HL-12-023)

<http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-12-023.html>
Objective: Encourage the planning and development of feasible and well-designed multicenter clinical trials focused on rare hemostatic and thrombotic disorders.

Continued from page 2

Sirolimus Therapy Alleviates Symptoms of LAM

Investigators have found that sirolimus, a drug currently used to prevent transplant rejection, can improve lung function and quality of life in individuals with the lung disease lymphangioleiomyomatosis (LAM).

LAM is a rare and progressive disease in which cancer-like cells infiltrate the lung, leading to shortness of breath, cough, chest pain, and in many cases eventual respiratory failure. It affects almost exclusively women, primarily of child-bearing age.

Participants in the clinical study took daily oral doses of sirolimus or placebo over 12 months and had their lung function measured at regular intervals. The sirolimus group had stable lung function during the treatment period, whereas lung function declined about 12 percent in the placebo group. After stopping sirolimus, the rate of decline in lung function was similar in both groups, suggesting that treatment effectiveness requires continued use.

The sirolimus group also showed other clinical improvements and reported a greater ability to carry out day-to-day functions and a better quality of life, suggesting a possible role for sirolimus in treating LAM.

New CPR Technique Benefits Cardiac Arrest Victims

A new cardiopulmonary resuscitation (CPR) technique that simultaneously incorporates two devices developed with funding from an NHLBI Small Business Innovation Research award has been shown to improve survival of people who experience cardiac arrest outside of a hospital setting.

One device, a suction cup with a handle and force gauge, is applied to a victim's chest. The person performing CPR pulls up on the handle to activate the suction cup, thereby ensuring that the chest rebounds fully after each chest compression in the CPR routine. The second device, which attaches to a facemask or breathing tube, prevents excess air from surging back into the lungs when the chest rebounds. When the devices are used together during CPR, blood flows more effectively to the heart and brain.

A recent clinical trial involving over 1,600 cardiac arrest victims compared standard CPR to CPR enhanced with both devices. Nine percent of those assigned at random to the enhanced CPR technique survived and were discharged from the hospital with good neurological function, as compared to six percent of those treated with standard CPR. The trial provides evidence for a promising strategy for improving out-of-hospital outcomes for cardiac arrest victims.

National Heart, Lung, and Blood Advisory Council Meetings

September 9, 2011

Dr. Shurin welcomed members to the 243rd meeting of the National Heart, Lung, and Blood Advisory Council (NHLBAC). The meeting was entirely a closed session. Council members attended via telephone.

The Council concurred on the award of numerous research grants to be supported with FY 2011 appropriated funds.

October 18, 2011

Dr. Shurin welcomed members to the 244th meeting of the NHLBAC. She recognized three Council members who are retiring: Dr. Noel Bairey-Merz, Dr. Andrew Marks, and Dr. Marlene Rabinovitch.

Three new Council members are expected to participate at the next Council meeting: Dr. Pamela Douglas, Professor of Research in Cardiovascular Diseases, Duke University School of Medicine; Dr. Ron King, President and Chief Scientific Officer, BioAccel; and Dr. Barbara Konkle, Director, Translational Research, Puget Sound Blood Center.

Dr. Shurin welcomed representatives of three NHLBI Advisory Committees: Dr. Sairam Parthasarathy, representing the Sleep Disorder Research Advisory Board; Dr. David Pinsky, representing the Heart, Lung, and Blood Program Project Review Committee; and Dr. Amy Shapiro, represent-

ing the Clinical Trials Review Committee. Dr. C. William Balke of the NHLBI Institutional Training Mechanism Review Committee and Dr. Edward Benz of the Sickle Cell Disease Advisory Committee were unable to attend.

Dr. Shurin noted with sadness the recent deaths of two important leaders of NHLBI activities: Dr. Bernadine Healy, a former NIH Director, who launched the Women's Health Initiative in 1991 and Dr. William Kannel, a former Director of the Framingham Heart Study.

Dr. Shurin discussed the NHLBI's concern about the impact of current budget constraints on the future of biomedical research. The NIH received a one percent cut in its budget for FY 2011 and is preparing for budget decreases again this year and next. The Institute plans to continue its policy of making strategic budget cuts as necessary, rather than across-the-board cuts. It will continue to look closely at potential investments and fund grants at full recommended levels.

Dr. Shurin summarized the Department of Health and Human Services (HHS) Sickle Cell Disease Initiative. The HHS has charged six agencies (NIH, Centers for Disease Control and Prevention, Health Resources and Services Administration, Food and Drug Administration, Agency for Healthcare Research and Quality, and Centers for Medicare

Continued on page 6

News from Capitol Hill

Appropriations for Fiscal Year (FY) 2012

On December 23, 2011, the President signed into law H.R. 2055 (Public Law 112-74), an omnibus appropriations bill. The law provides fiscal year 2012 funding for several Federal agencies, including \$30,689,000,000 for the National Institutes of Health. The law also establishes a new NIH center, the National Center for Advancing Translational Sciences (NCATS).

Resolutions

On November 14, 2011, the Senate passed a resolution (S. Res. 322), introduced by Senator Mike Crapo (R-ID), designating November 2011 as Chronic Obstructive Pulmonary Disease (COPD) Awareness Month. The resolution encourages all people of the United States to become more informed about COPD and get screened if they are at risk. It also encourages further partnership between the Federal government and private entities to enhance patient education about COPD.

NHLBI Division of Lung Disease Director Speaks at Congressional Briefings

On October 11, 2011, Dr. James Kiley, Director of the Division of Lung Diseases, NHLBI, spoke at a congressional briefing sponsored by the U.S. COPD Coalition. In addition to Dr. Kiley, speakers included Senator Mike Crapo (R-ID), NHLBI grantee Dr. James Crapo, Dr. Wayne Giles, CDC, and Ms. Danica Patrick, the DRIVE4COPD Campaign Ambassador. Dr. Kiley discussed research on COPD and the NHLBI-sponsored national COPD awareness campaign, COPD Learn More Breathe Better®.

On October 13, 2011, Dr. Kiley spoke at a congressional briefing sponsored by the Allergy and Asthma Network Mothers of Asthmatics (AANMA). Representative Bill Cassidy (R-LA) and Representative Nita Lowey (D-NY), two of the co-chairs of the Congressional Allergy and Asthma Caucus, also spoke at the event. Other speakers included Dr. Paul Garbe, CDC, and Ms. Karen Myerson, Asthma Network of West Michigan.

Upcoming Events

Activity	Date/Location	More Information
Parent Heart Watch 2012 National Conference	January 13 – 15, 2012 New Orleans, LA	http://www.parentheartwatch.org/ActionAdvocacy/Events.aspx
National Heart, Lung, and Blood Advisory Council 245th Meeting	February 15, 2012 Bethesda, MD	http://www.nhlbi.nih.gov/meetings/nhlbac/index.htm
National Sleep Foundation Sleep Health and Safety 2012	March 2 – 3, 2012 Washington, DC	http://www.sleepfoundation.org/events-activities
Hermansky-Pudlak Syndrome Network, Inc. 19th Annual HPS Conference	March 16 – 18, 2012 Uniondale, NY	http://www.hpsnetwork.org/en/events/2012-03-16/19th-annual-hps-conference
Aplastic Anemia and MDS International Foundation, Inc. 2012 Patient and Family Conference	March 24, 2012 Washington, DC	http://www.aamds.org/support-and-community/conferences
Hemophilia Federation of America Symposium 2012	March 30 – 31, 2012 Santa Clara, CA	http://hemophiliafed.org/what-we-do/meetings-events/symposium/
Parent Project Muscular Dystrophy 2012 West Coast Connect Meeting	April 13 – 15, 2012 San Diego, CA	http://www.parentprojectmd.org/site/PageServer?pagename=Connect_conference
The LAM Foundation LAMposium	April 20 – 22, 2012 Cincinnati, OH	http://www.thelamfoundation.org/index.php
American Autoimmune Related Diseases Association, Inc. 8th International Congress on Autoimmunity	May 9 – 13, 2012 Granada, Spain	http://www2.kenes.com/autoimmunity/Pages/Home.aspx
Mended Hearts Annual Convention	May 16 – 21, 2012 Dallas, TX	http://mendedhearts.org/events
Alpha-1 Association 21st Annual National Education Conference	June 8 – 10, 2012 Seattle, WA	http://www.alpha1.org/education/nateduconf.php
Pulmonary Hypertension Association 10th International PH Conference and Scientific Sessions	June 22 – 24, 2012 Orlando, FL	http://www.phassociation.org/
Barth Syndrome Foundation 6th International Scientific, Medical, and Family Conference	June 25 – 30, 2012 St. Pete Beach, FL	http://barthsyndrome.org/english/View.asp?x=1670
Parent Project Muscular Dystrophy 2012 Connect Conference	June 28 – July 1, 2012 Ft. Lauderdale, FL	http://www.parentprojectmd.org/site/PageServer?pagename=Connect_conference
Scleroderma Foundation 2012 National Patient Education Conference	July 27 – 29, 2012 Grapevine, TX	http://www.scleroderma.org/national_conference_2012.htm

Constituents' Corner

No constituents' submissions were received for this issue.

We invite you to use this space that we reserve for you to share your successes and opinions. You may submit your ideas and articles to nhlbi.listens@nih.gov or Public Interest News, Office of Science and Technology, Building 31, Room 5A07, 31 Center Drive, MSC-2482, Bethesda, MD 20892-2482.

October 2011 Advisory Council Meeting

Continued from page 4

& Medicaid Services) and the Offices of Minority Health and Planning and Evaluation to improve the health of people with sickle cell disease. Each agency is taking action to enhance implementation of research advances; provide evidence-based guidelines to families, health care providers, and payers; facilitate new drug development; and provide public health data to inform both the health care delivery and research agendas.

Dr. Shurin offered Council members an opportunity to discuss their concerns about the effects of the new NIH policy to allow only one resubmission of a grant application (i.e., no A2s). Dr. Shurin offered to raise the issue with NIH leadership and to convey the concerns and suggestions of Council members.

Dr. Cynthia Dunbar, Hematology Branch, NHLBI Division of Intramural Research, discussed three areas of research involving cell therapy in which her lab has been involved: hematopoietic stem cell gene therapy and insights gained from a non-human primate model; stem cell-niche interactions and research on improving mobilization, homing, and engraftment for transplant and gene therapy; and induced pluripotent stem cells and their utility as regenerative medicine models and suitability for preclinical development.

Dr. Robert S. Balaban, Scientific Director, NHLBI Division of Intramural Research, summarized NHLBI collaborative activities with the new NIH Center for Regenerative Medicine, which was established to accelerate the development of cell-based therapies for repairing or replacing tissue damaged by disease or injury.

Dr. Balaban described the success of the NIH Stadtman Tenure-Track Investigator Program to recruit outstanding tenure-track scientists and the Lasker Clinical Research Scholars Program to help increase the pool of talented clinical/translational researchers. He also discussed the Intramural Division's new Clinical Research Strategic Plan.

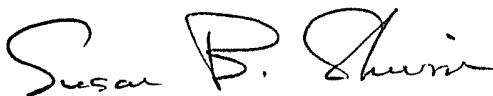
Dr. Lawrence Tabak, Principal Deputy Director, NIH, discussed the continuing efforts of the NIH to improve the diversity of its scientific workforce. He reported that despite efforts spanning 30 years, the NIH has had a less-than-impressive impact on the diversity of the NIH-funded workforce. He emphasized the commitment of the NIH to a diverse biomedical workforce and discussed the steps it is taking to address the situation.

Dr. Shurin discussed the possibility of using the K99/R00 mechanism to support Early Stage Investigators (ESIs) who do not have much preliminary data. She reminded Council members that the Institute will no longer participate in the NIH Exploratory Developmental Research Grant Program (R21) because the Institute determined that although the R21 mechanism may have seemed an attractive opportunity for ESIs, it provided insufficient time for them to obtain results needed to support an R01 grant application.

NHLBI staff presented seven new initiatives, seven renewals, and one request by another IC for secondary support, all of which had been reviewed in September by the Board of External Experts. The Council was mostly supportive of the initiatives presented, but made a number of specific recommendations for consideration prior to their release.

Need More Information?

We are always interested in receiving comments and suggestions from the community. If you or your organization have questions for me or for the Institute, please contact me at shurinsb@nhlbi.nih.gov or Dr. Carl Roth at rothc@nhlbi.nih.gov.



Susan B. Shurin, M.D.
Acting Director, NHLBI

For information on specific issues, the following contacts may be helpful:

- For health-related questions, information about publications, or communications pertaining to NHLBI policies and priorities, please contact the trained information specialists of the NHLBI Information Center at 301-592-8573, or write to the Information Center at P.O. Box 30105, Bethesda, MD 20824-0105, or email inquiries to nhlbiinfo@nhlbi.nih.gov.
- For additional information regarding NHLBI events, consult the references provided or www.nhlbi.nih.gov/calendar/nhcal.htm. Most other NIH Institutes and Centers also maintain calendars on their Web sites. Links to their Web pages are at www.nih.gov/icd.