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## ***Advances in PH Journal***

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"//connect.facebook.net/en_US/all.js#xfbml=1"; fjs.parentNode.insertBefore(js, fjs);
})(document, 'script', 'facebook-jssdk');
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## NIH Mission

The National Institutes of Health (NIH), a part of the US Department of Health and Human Services, is the nation's biomedical research agency. The NIH is the largest source of funding for biomedical research in the world, funding thousands of scientists in universities and research institutions. The NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. The NIH is composed of

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27 institutes and centers, each with a specific mission, often focusing on particular diseases or body systems. The National Heart, Lung, and Blood Institute (NHLBI) is one of the component institutes, whose mission is to provide global leadership for research, training, and education programs that promote the prevention and treatment of heart, lung, and blood diseases. The Division of Lung Diseases (DLD) within the NHLBI is responsible for administration of the extramural grant and contract portfolio in lung diseases research, which includes diseases of the airways, lung tissues, including the interstitial compartments and cells, the lung vascular systems, and sleep. Additional information about the NIH and its mission, its collective institutes and centers, and the DLD can be found by accessing the following Web site and its associated links: <http://www.nih.gov/index.html>.

Five areas of promise for advancing biomedical research are currently identified by the NIH.<sup>1</sup> The NHLBI strategic plan is aligned to these 5 areas, which include: 1) capitalizing on high-throughput technologies, 2) fostering translational medicine, 3) performing research beneficiary to the cause of US health care reform, 4) performing research focused on global health, and 5) improving the research base by reinvigorating and empowering the biomedical research community. NHLBI-sponsored research programs and initiatives are designed to foster ongoing efforts in these areas of promise specific to heart, lung, and blood diseases. Programs and initiatives originating from within the DLD likewise align to the strategic plan and goals of the NHLBI and NIH. Furthermore, the DLD strategic plan for advancing lung disease research involves a multidisciplinary approach to program development to generate support mechanisms for the lung investigative community.

The NHLBI currently supports a robust program in lung vascular and pulmonary hypertension (PH) research. The NHLBI funded approximately \$32.9 million in fiscal year 2010 and \$37.2 million in fiscal year 2011 in PH and related research projects. The NHLBI supports basic science in lung vascular biology and disease with projects that: 1) discover and define lung vascular biology and factors contributing to development of lung vascular disease; 2) focus on cellular, molecular, and genetic factors contributing to PH pathogenesis including high-throughput, technology-based projects; 3) advance the paradigm of PH as a vasculoproliferative disease; and 4) define right ventricular biology and pathophysiology in the context of lung vascular function and disease. In addition, translational projects are: 1) advancing diagnostics, therapeutics, and disease monitoring; 2) testing novel hypotheses of disease etiology using human tissues; and 3) identifying novel endpoint measures for use in clinical trials.

## **ACTIVITIES IN LUNG VASCULAR RESEARCH**

While the breadth of the entire NIH portfolio cannot be presented in this article, the following are selected examples of NHLBI-supported research projects. The NHLBI continues to build off the strategic plan for lung vascular research in order to identify priority areas for future activities.<sup>2</sup> The NHLBI has implemented programs in response to the strategic plan. These include: 1) Utilization of a Human Lung Tissue Resource for Vascular Research, and 2) the Pulmonary Vascular-Right Ventricular Axis Research Program (PV-RV); both are designed to fill gaps in pulmonary vascular disease (PVD) translational research. Researchers supported by the Lung Tissue Resource Program have the opportunity to leverage tissues and cells comprised in a biorepository supported by the Pulmonary Hypertension Breakthrough Initiative (PHBI). This program also introduces young investigators to lung vascular translational research, and presents an opportunity to test mechanistic hypotheses derived from animal models in human specimens. Researchers supported by the PV-RV are better

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defining the relationship between the “sick” lung vasculature and its impact on right heart function and failure. This program brings together multi-disciplinary teams of investigators who are studying questions such as: 1) how does infant and childhood lung vascular disease affect lung vascular and right heart function in later life? 2) Can stem cells treat lung vascular and right heart disease? 3) Are beta-blockers effective in treating right heart disease? 4) What are ideal noninvasive measures for diagnosing and monitoring right heart disease in adults and children who have PVD? Both the Lung Tissue Resource Program and the PV-RV are very early in their progress.

In addition to the translational programs, the NHLBI held a workshop in August 2011, to focus on 21st century clinical research priorities in PVD.<sup>3</sup> Experts with diverse experience in pediatric and adult PH clinical research, as well as experts from other fields reviewed the state of scientific knowledge forming the basis for current treatment of children and adults with PVD. Recommendations on how to fill gaps in clinical research included: 1) improved methods of phenotyping to identify subjects for appropriate PVD clinical studies; 2) validation of new, meaningful endpoints; and 3) priorities for specific clinical research needed to advance care of patients with various subsets of PVD from childhood through adulthood. The recommendations from this workshop will help to inform future activities and research opportunities.

As a final example, the NHLBI recently supported an investigator-initiated resource in PVD, the “National Biological Sample and Data Repository for Pulmonary Arterial Hypertension (PAH).” This resource will significantly enhance the conduct of basic, translational, and clinical research for PAH, and the biological samples collected and genetic data generated from these samples will enable unprecedented hypothesis-driven science for all forms of PH. This resource represents collaboration between academic PH centers to leverage an industry-sponsored patient registry (the REVEAL registry). Upon full implementation, the resource will collect and maintain biologic material from no less than 2500 World Health Organization (WHO) Group 1 PAH patients, including total genomic lymphocyte DNA; EBV transformed peripheral blood lymphocytes and plasma; and genome-wide SNP genotype data and BMPR2/ALK1 sequence/MLPA data. All biological samples, clinical data, as well as the SNP genotype and sequencing data for the patients will be made available to the entire scientific community.

For a comprehensive summary of PH-related research ongoing at the NIH, please utilize the NIH Research Portfolio Online Reporting Tools (RePORT) to obtain reports, data, and analyses of NIH research activities (<http://report.nih.gov>).

## **CONCLUSION**

Advances in treating PH patients have come as a result of collective efforts by physicians, scientists, patient advocacy, pharmaceutical companies, and public and private grant-awarding agencies. NHLBI-supported basic science research on the physiologic and cellular mechanisms responsible for pulmonary vascular tone regulation and abnormal vasoconstriction have been important in identifying the therapeutic potential of the drugs now in clinical practice for PAH. However, a new era in our understanding of PH pathogenesis is emerging, and with this new understanding novel challenges and exciting research opportunities will arise. The NHLBI will strive to work with and support the research community to meet the challenges ahead.

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