Introducing PVDOMICS: A Novel, NHLBI Research Initiative in Pulmonary Hypertension

The National Institutes of Health (NIH) Pulmonary Arterial Hypertension (PAH) Registry was instrumental in characterizing the devastating nature of PAH almost 25 years ago. Since then, significant advances in treating PAH patients have occurred. These advances have come as a result of collective efforts by physicians, scientists, patient advocacy organizations, pharmaceutical companies, and public and private grants-awarding agencies. There are now 11 approved therapies for Group 1 pulmonary hypertension in the U.S., and they are making a difference in the lives of patients living with this disease. However, there is still no cure for this disease. The limitations of current therapeutic options, such as wide differences in patients’ responses to treatment, necessitate that lung vascular disease and PH research remains a high priority for the National Heart, Lung, and Blood Institute (NHLBI).

Significant advances in scientific knowledge and opportunities for applying that knowledge have also occurred during the past 25 years. A new initiative launched in 2014 by NHLBI is designed to ask research questions about PH in a way that will lead to developing therapeutics that are more precise and that enhance the promise of personalized treatments. This program, called Redefining Pulmonary Hypertension through Pulmonary Vascular Disease Phenomics (PVDOMICS), will support a national team of multidisciplinary investigators to perform comprehensive, “deep phenotyping” across Groups 1-5 PH. Phenotyping research is performed similarly to how data are collected through a registry. But deep phenotyping uses modern, molecular techniques to evaluate collected data and biospecimens in a more integrated manner. PVDOMICS will measure and integrate genomics, transcriptomics, proteomics, metabolomics, cell biology and tissue functioning, imaging, and other clinical traits deemed necessary to fully describe a lung vascular disease phenotype. PVDOMICS will not only improve understanding of the molecular factors causing PAH (Group 1 PH), but will also expand understanding of lung vascular disease to include patients suffering from PH due to congestive heart failure and those with PH in combination with other chronic lung diseases, such as COPD and pulmonary fibrosis.

Many benefits accrue from a better understanding of PH phenotypes. First, more sensitive measures of disease may be found, allowing for earlier diagnosis of disease, enabling trials of interventions intended to prevent or forestall early disease, and identifying novel factors suggesting disease risk. Second, novel, holistic-based features of disease may be identified, allowing clinical-trial enrollment of patients who respond more uniformly to mechanism-based therapies. Third, measures of disease severity that include biomarkers as well as clinical characteristics may prove useful as surrogate outcome measures in clinical trials. For example, outcome measures may be identified that are more sensitive and specific than a six-minute walk-distance test. More specific outcome measures will improve the efficiency and fidelity of clinical trials. Overall, PVDOMICS will generate a more precise classification of lung vascular disease and foster novel biological concepts to catalyze associated innovative research into preventing lung vascular disease and developing more efficacious, precision approaches to individual therapy.

PVDOMICS plans to enroll and phenotype approximately 1,500 PH subjects during a five-year project period. The infrastructure of PVDOMICS will consist of a central data coordinating center, the Cleveland Clinic, supporting enrollment and phenotyping activities being conducted at seven academic medical institutions across the U.S. Those institutions include Brigham and Women’s Hospital, Columbia University, Cornell University, Johns Hopkins University, Mayo Clinic, University of Arizona and Vanderbilt University. The PVDOMICS consortium of investigators will develop a common phenotyping protocol in the first stages of PVDOMICS, and eligibility criteria will be determined for inclusion in the study. Because PVDOMICS is not conducting interventional trials, it is anticipated that most Group 1-5 PH patients who want to participate in this research study may be able to enroll, even if already enrolled in a drug trial or other studies. NHLBI also welcomes partnering opportunity discussions with PH mission-dedicated organizations and interested pharmaceutical industries. NHLBI is very pleased that PHA is an active partner in this research program.

PVDOMICS has begun initial organization and protocol development activities and active recruitment for enrollment into the study is anticipated to begin mid-2015. For more information, please contact Dr. Lei Xiao at 301-435-0222 or email lei.xiao@nih.gov.

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