Specialized Centers of Clinically Oriented Research Programs in Pulmonary Hypertension Reported Progress at the PHA Scientific Sessions

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Recently, the National Heart, Lung, and Blood Institute awarded 2 Specialized Centers of Clinically Oriented Research (SCCOR) program grants in pulmonary hypertension. The SCCOR program requires clinical and basic scientists with a broad range of skills to work together on a unified theme, with special emphasis on clinically relevant research.

The goal of the SCCOR program is to encourage multidisciplinary research on clinically relevant problems to allow basic science findings to be more rapidly applied to clinical situations. It is expected that over 50% of the funded research is clinical and interactions between clinical and basic scientists are expected to strengthen the research, enhance the translation of fundamental research findings to the clinical setting, and identify new research directions. In addition, each SCCOR project must have a defined organizational and administrative structure to enhance and enable interactions between investigators to increase the rate of translation of basic research findings to clinical applications.

At the recent Scientific Sessions at the Pulmonary Hypertension Association 8th International Conference, the principal investigators for the 2 SCCOR programs in pulmonary hypertension—Dr Paul Hassoun from Johns Hopkins University and Dr Kurt Stenmark from the University of Colorado Denver School of Medicine, reported on progress made in each of their research programs. These are summarized in the following reports.

National Heart Lung and Blood Institute Hopkins Specialized Center in Clinical Oriented Research (SCCOR): Molecular Determinants of Pulmonary Arterial Hypertension

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SCCOR Investigators: Paul M. Hassoun: overall Principal Investigator, Project 1 leader and administrative core leader; Hunter C. Champion: Project 2 leader; Fredrick Wigley: Project 3 leader; Roger A. Johns: Project 4 leader; Michael Crow: Project 5 leader; Noah Lechtzin: data management and statistics; Allen Myers: pathology core; Kathleen C. Barnes: genetics/genomics core; Jennifer van Eyk: proteomics core; and Jens Vogel-Claussen: imaging core.

Pulmonary arterial hypertension (PAH) is the leading cause of mortality in patients with the spectrum of scleroderma-related diseases. In addition, recent large clinical trials of PAH suggest that patients with scleroderma-related PAH have increased mortality and a significantly poorer response to therapy compared with patients who have idiopathic PAH. Although the reason for this discrepancy remains unclear, we hypothesized for this SCCOR that the overall worse outcome in scleroderma-related PAH is related to more severe structural changes involving the pulmonary vasculature (PV) and the right ventricle (RV), resulting in marked RV-PV dysfunction. Therefore, this SCCOR project is focused on understanding the complex PV and RV remodeling, resulting RV-PV uncoupling, and their crucial impact on morbidity and mortality in PAH.

In this SCCOR, we use scleroderma-related PAH as a clinical paradigm, contrasting it to idiopathic PAH, because of its particular severity, lack of response to available PAH therapy, and potential underlying genetic factors that dictate outcome. Because of the extensive expertise of our team in molecular and diagnostic pulmonary medicine and cardiology, we have the unique opportunity to not only characterize RV-PV responses in scleroderma-related PAH with increased sensitivity and clarity, but to also identify new molecular targets for potential therapy using state of the art imaging and genomic and proteomic technology. Relying on novel imaging systems and molecular tools, we proposed to conduct rigorous phenotypic characterization of patients who have scleroderma-related PAH. Our focus on animal models provides us with additional candidate genes and proteins for characterization and targeting in human studies.

We have the opportunity to validate the clinical importance of these genes in a large cohort of well-phenotyped patients with PAH, using functional genomics and proteomic approaches with characterization of potentially important polymorphisms. We hope