RFA for Data from the NHLBI study: PVDOMICS (Redefining Pulmonary Hypertension through Pulmonary Vascular Disease Phenomics) *(version 4, 10/6/23)*

Cleveland Clinic, PVDOMICS Data Coordinating Center

Part 1. Overview Information

PVDOMICS Clinical Data Access Proposal Request

Participating Organizations: Cleveland Clinic, 7 clinical sites (Brigham & Women's Hospital, Columbia University, Weill Cornell Medicine, Johns Hopkins University, Mayo Clinic, University of Arizona and Vanderbilt University), NHLBI, Pulmonary Hypertension Association

No funding will be provided.

See Section III. Information on Eligibility.

Purpose: This opportunity will disseminate PVDOMICS clinical data to research investigators external to PVDOMICS. This will allow many investigators to analyze the study's clinical data to address a broad range of specific aims and publish their findings. Omics data and biospecimens are not currently available.

Key Dates

Posted Date: June 10, 2022
First submission by August 1, 2022 by 5:00 PM local time of applicant organization.
Subsequent submission dates are: November 1, 2022, March 1 and July 1 2023, and **March 1, 2024.**

Applications that do not comply with these instructions may be delayed or not accepted for review.

You **must** submit the application electronically to: phrfa@ccf.org

Part 2. Announcement

Section I. Award Opportunity Description

Background

The background and design of the PVDOMICS study is given in: Hemnes AR, Leopold JA, Beck GJ, et al. PVDOMICS: a multi-center study to improve understanding of pulmonary vascular disease though phenomics. Circulation Research. 2017; 121:1136-1139. PMID: 2907434.

The PVDOMICS (Redefining Pulmonary Hypertension through Pulmonary Vascular Disease Phenomics, RFA-HL-14–027 and RFA-HL-14–030) initiative launched by the NIH/NHLBI in 2014 supported a national team of multidisciplinary investigators to perform comprehensive, deep phenotyping across WSPH (World Symposium on Pulmonary Hypertension) Groups 1 to 5 with the general hypothesis that epidemiological, biological, and hemodynamic features will allow differentiation of phenotypic similarities and differences among current WSPH group categories. This initiative included a Data Coordinating Center (Cleveland Clinic) and 6 clinical centers (Brigham and Women's Hospital, Columbia University/Cornell University, Johns Hopkins University, Mayo Clinic, University of Arizona, and Vanderbilt University). The instituted protocol was designed to lead to new understanding of patients with PH and right ventricular dysfunction, based on molecular, clinical, hemodynamic and radiographic characteristics.

A total of 1193 were enrolled from the clinical centers: 750 PH participants, 347 PVD at risk comparators, and 96 healthy controls (see table below). The study recruited individuals≥18 years of age who presented for evaluation of PH, heart failure, lung disease, dyspnea, and exercise intolerance. After a right heart catheterization, participants with PH were classified according to the traditional WSPH PH Groups 1 to 5 for adjudication purposes. Alternatively, patients with mild elevation in mean pulmonary arterial pressure (20–25 mm Hg) or normal pulmonary arterial pressure were assigned to WSPH 1 to 5 Comparator Groups who are at risk for PVD with similar underlying diseases or as healthy controls. Participants enrolled underwent a comprehensive clinical phenotyping protocol that included a rigorous assessment of pulmonary and right ventricular structure and function with collection of biospecimens for omic analysis. Subjects underwent quality of life assessment, sleep study, body compositional analysis, 6-minute walk testing, transthoracic echocardiography, cardiac MRI, cardiopulmonary exercise testing, pulmonary function testing, chest computed tomography, ventilation lung scan, and right heart catheterization with provocative maneuvers. Full details of each procedure are provided in the On-line Supplement to Hemnes et al, 2017. Clinical description results and outcomes of enrollees are provided in:
Hemnes AR, Leopold JA, Radeva MK, Beck GJ, et al and the PVDOMICS Study Group. Clinical characteristics and transplant-free survival across the spectrum of pulmonary vascular disease. Journal of the American College of Cardiology. 2022;80(7), 697-718. PMID: 35953136

PVDOMICS Study: Primary Groups

Primary Group[1]	WSPH	Comparators
Group 1	353	58
Group 2	136	140
Group 3	172	119
Group 4	57	23
Group 5	32	7
Total	**750**	**347**

[1] Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2013;62:D34-41.

Research Objectives and Scope

This opportunity will allow access to the PVDOMICS study clinical data results so that investigators can evaluate specific hypotheses. Information about the PVDOMICS study is available on the website: https://lriapps.ccf.org/pvdrfa/

Specifically, the following is available on this website:

1) Protocol v1.3

2) Clinical data forms

3) Data Dictionary

4) Current analysis topics by PVDOMICS investigators

Research Proposal

Proposed projects should be consistent with the overarching PVDOMICS goal to identify sub-phenotypes and biomarkers of pulmonary vascular disease that will enhance early diagnosis, and assessment of interventions to prevent or treat this debilitating condition. Omic signatures will be available in the future but are NOT included in the current RFA.

Proposed studies should contain the information below (by completing and submitting the Data Proposal Form on https://lriapps.ccf.org/pvdrfa/

1. Proposal Title

2. Principal Investigator, Institution and Contact Information

3. Other Key Personnel, Their Role and Institution

4. Proposal Description

a) Background/Rationale (including literature findings and any preliminary data)

b) Research Question(s)/Hypotheses/Specific Aims

c) Primary Outcomes (if appropriate)

d) Brief Analysis Plan

5. PVDOMICS data requested, including what PH disease or Comparator group(s) are requested.

Use the PVDOMICS Data Dictionary to specify each variable requested by listing the Form # and variable name. If all the items for a specific form are requested, please say "all" for the given form instead of listing each item. Please limit your data requests to only data that are necessary to carry out your proposal. Data items that are currently available are indicated in the Table of Contents worksheet. Additional items available for request will be posted subsequently.

Study Team

A description of key personnel in the study team and their roles should be provided along with an NIH biosketch for each.

Section II. Information

Funding and Anticipated Number of Awards:

PVDOMICS will not provide any funding for proposed studies. The number of awards is not limited.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations:

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

Nonprofits Other Than Institutions of Higher Education

For-Profit Organizations are permitted

Principal Investigator (PI)

Eligible Principal Investigator:

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research as the PI and with their study team.

2. Additional Information on Eligibility

Number of Applications:

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

Section IV. Application and Submission Information

Page Limitations

Four pages, not including list of requested data and biosketches

Provide:

1) A specific study proposal (as described in Section I) using the Proposal Request Form.

2) NIH Biosketch of PI and Key Personnel

Submission Requirements and Information

Applications must be electronically submitted by March 1, 2024 to: phrfa@ccf.org

Please name your emailed file: PILastName.InstitutionName.Proposal # (# =1 if submitting only 1 application). For example: SmithDuke1

Paper applications will not be accepted.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

The proposal will be evaluated on:

1) Appropriate rationale/justification for the proposed work

2) Clear specific aims with hypotheses

3) Clear and appropriate analysis plan

4) Investigator(s) expertise

Results obtained and manuscripts should be in line with the approved aims. A drift in aims requires notification and re-discussion with the PVDOMICS Steering Committee. A copy of a draft abstract, poster/talk or manuscript should be sent the PVDOMICS Data Coordinating Center for review by the PVDOMICS investigators before submission to professional meetings or to a journal. The PVDOMICS study needs to be acknowledged in any presentation, abstract or publication. The PVDOMICS Data Coordinating Center should be sent a final copy of any abstract or publication.

2. Review and Selection Process

Applications will be evaluated on scientific and technical merit by the PVDOMICS Steering Committee. If there is a significant overlap with a proposed topic and one being done by PVDOMICS investigators, the proposal will not be approved, although the investigators may be invited to collaborate with the PVDOMICS investigators on this topic. External investigators who have an approved topic are encouraged to collaborate with PVDOMICS investigators.

3. Anticipated Approval Dates

After the peer review of the application is completed, the P.I. will be emailed a letter within one month of the submission deadline that will state approval or not. After approval, the Data Coordinating Center (DCC) at the Cleveland Clinic will work with the Principal Investigator of the proposal to execute a Data Use Agreement. IRB approval of the proposed study will be

needed by the Principal Investigator's institution. The PVDOMICS DCC will then provide the approved data to the P.I. Note that this will be a Limited Data Set (with dates).

Section VI. Contacts

We encourage inquiries concerning this opportunity and will be glad to answer questions from potential applicants.

Contact: phrfa@ccf.org