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National Biological Sample and Data Repository for Pulmonary Arterial Hypertension

K. Lutz, M. Pauciulo, C. Winslow, A. Walsworth, A. Gygi, A. Reponen, M. Barve, J. Harley, K. Marsolo, L. Martin, W. Nichols

Divisions of Human Genetics, Biomedical Informatics, and Center for Autoimmune Genetics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA

Purpose: To create a useful resource of patient material for the PAH research community that will enable well powered studies, the National Biological Sample and Data Repository for PAH (a.k.a PAH Biobank) has been established with funding from the NIH/NHLBI.

Background: The PAH Biobank represents an unparalleled collaboration among PH centers in the US to establish the largest cohort of PAH patients’ biological samples, clinical data, and genetic data available for study. This collection will allow for experiments with the statistical power to provide the insights from the state of the art technologies in genomics and proteomics.

Methods: Biological samples, clinical data, and genetic data are being collected on over 3,000 WHO Group 1 PAH patients. 28 PH centers, including five pediatric centers, across the United States have been enlisted to enroll patients, collect peripheral blood samples, and enter clinical data into a web-based eCRF. Enrollment includes treatment naïve patients to allow collection of serum/plasma samples both before and six months to one year after initiation of drug therapy. Serum and plasma are being banked using the patient blood samples shipped overnight from the enrolling centers. Additionally, both DNA and RNA are being isolated from a portion of the obtained lymphocytes. Immortalized lymphocyte cell lines are also being established. Genetic data are being generated for each patient including genotypes for genome wide SNPs (Illumina HumanOmni5) and coding sequence data for BMPR2, ALK1, ENG, CAV1, SMAD9, KCNK3 and EIF2AK4 (Illumina TruSeq Custom Amplicon). Additional genes causal for/associated with PAH can be added for screening as identified. MLPA (MRC Holland) is performed for BMPR2, ALK1, and ENG. Biological samples, clinical data, and genetic data for the patients are now available for request at www.pahbiobank.org. Samples and data will continue to be made available as processing of biological specimens and generation of genetic data is completed.

Results: To date, over 1,800 patients have been enrolled, with a goal of over 3,000 by the end of the project. Primary Diagnosis: 47% IPAH, 45% APAH, 3% HPAH, <1% PVOD, <1% PPHN, 2% drugs and toxins. Gender: 78% Female, 22% Male. Race: 83% White, 11% Black or African American, 3% Asian, 2% Other. 67 treatment naïve patients have been enrolled. Genome wide SNP and NextGen sequencing data have been generated for 1,549 patients. On average, >400 µg DNA and >15 µg RNA are banked per patient. In addition, ~36 200-µl plasma aliquots, ~27 200-µl serum aliquots and immortalized lymphoblastoid cell lines are stored for each patient.

Conclusion: This endeavor addresses a critical barrier of sample size to progress in the field of PAH research by providing the research community an unparalleled large patient cohort for here to now unprecedented hypothesis-driven studies. The cohort of patients and data can provide the much needed catalyst for tour de force research efforts aimed at accelerating the development of novel therapies through the identification of novel pathways or genetic factors contributing to the disorder.