European Respiratory Society
Annual Congress 2012

Abstract Number: 3519

Publication Number: P3908

Abstract Group: 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

Keyword 1: Pulmonary hypertension **Keyword 2:** Genetics **Keyword 3:** Pharmacology

Title: Applying pharmacogenomics to pulmonary arterial hypertension (PAH): A target-based approach to therapy

Sami 21208 Said sami.i.said@stonybrook.edu MD [1,2] and Sayyed 21209 Hamidi sayyed.hamidi@stonybrook.edu MD [1,2]. [1] Medicine, SUNY at Stony Brook, Stony Brook, NY, United States and [2] Medicine Service, Northport VA Medical Center, Northport, NY, United States .

Body: INTRODUCTION & AIMS: Pharmacogenomics, the study of how genetic variations influence the response to drugs, has the desirable objective of tailor-making drugs for each individual genetic makeup. The successful application of this concept in oncology provided the rationale for this study. Like cancer, PAH is a heterogeneous disorder with an unsatisfactory outlook, where responses to drugs often differ in different forms of the disease. METHODS: We examined 2 experimental models of PH: mice with deletion of the Vasoactive Intestinal Peptide gene ($VIP^{-/-}$), and rats injected with monocrotaline (MCT), 2 models with comparable, though not identical, phenotypic features. We analyzed their particular gene alterations, with special reference to genes related to vascular remodeling and inflammation, and compared phenotypic and genotypic responses in each model to treatment with VIP. RESULTS: $VIP^{-/-}$ mice showed overexpression of genes promoting vascular proliferation and inflammation, with underexpression of anti-proliferative genes. VIP fully corrected all PH features and matching gene expression alterations. MCT rats, however, showed complex gene expression alterations: As in $VIP^{-/-}$ mice, those promoting vascular remodeling and inflammation, and others tending to modulate the PH. Further, VIP treatment failed to correct many of the genotypic abnormalities, and only partially corrected the phenotype. CONCLUSIONS: This preliminary proof-of-concept study demonstrates the importance of genomic information in determining the therapeutic response to a given drug. Full validation of the role of pharmacogenomics in PAH must await comparable studies in patients with different forms of the disease.