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Title: Peripheral blood gene expression and airway morphology on CT scan: The MESA COPD study

Dr. Kathleen M. 20399 Donohue kd2128@columbia.edu MD [1], Ms. Tess 20400 Pottinger tdp2117@columbia.edu [1], Prof. Eric A. 20401 Hoffman eric-hoffman@uiowa.edu [2], Prof. Yongmei 20402 Liu oliu@wakehealth.edu [3], Dr. Charles 20403 Powell charles.powell@mssm.edu [4], Prof. Russ 20404 Tracy Russell.Tracy@uvm.edu [5], Dr. Benjamin M. 20405 Smith bs2723@columbia.edu [1], Prof. Daniel 20406 Rabinowitz dan@stat.columbia.edu [1] and Dr. R. Graham 20407 Barr rgb9@columbia.edu [1]. [1] Medicine, Columbia University, New York, NY, United States, 10029 ; [2] Radiology, University of Iowa, Iowa City, IA, United States ; [3] Genomics, Wake Forest University, Winston-Salem, NC, United States ; [4] Pulmonary, Mount Sinai, New York, NY, United States and [5] Pathology, University of Vermont, Colchester, VT, United States .

Body: RATIONALE: Small studies of the airway transcriptome in bronchial brushings from subjects with chronic obstructive pulmonary disease (COPD) suggest a role for oxidative response genes and notch pathways. We hypothesized that gene expression of these pathways in peripheral blood mononuclear cells (PBMC) would be associated with airway dimensions on CT scan. METHODS: The Multi-Ethnic Study of Atherosclerosis (MESA) COPD recruited participants with COPD and controls age 50–79 years with ≥10 packyears without clinical cardiovascular disease. Airway wall thickness and lumen area were measured using APOLLO software (VIDA Diagnostics) on full-lung CTs. mRNA expression in PBMCs was measured using Hu 133 Plus 2.0 array (Affymetrix). Models regressed airway dimensions on gene expression measures adjusting for age, sex, and race/ethnicity, cohort, cigarette smoking status, pack-years, height and weight and FDR was used to adjusted for multiple corrections. RESULTS: Among 101 participants, airway lumen area was associated with altered expression of histone cluster 1, H2ab (HIST1H2AB) (q=0.01), which is implicated in DNA repair-induced chromatin remodeling. Airway wall thickness was associated with altered expression of coiled-coil domain containing 24 (CCDC24) (q=0.002) and KIAA1244 (q=0.005). Less is known about the function of these two genes. There were (n=57) and (n=192) probe sets with differential expression related to lumen area and wall thickness, respectively, in genes such as dual specificity phosphatases, myosin light chain, and metallopeptidase inhibitors. CONCLUSIONS: Airway dimensions on CT scan were associated with altered gene expression levels in PBMCs of HIST1H2AB, CCDC24 and KIAA1244.