

DNA variants may influence COPD patients' response to inhaled bronchodilators

October 25 2013

Several novel gene variants may help explain the response of patients with chronic obstructive pulmonary disease (COPD) to inhaled bronchodilators, according to a meta-analysis reported today (Oct. 25) at the American Society of Human Genetics 2013 meeting in Boston.

The meta-analysis used statistical methods to combine results from four individual studies with a total of 5,789 Caucasian [patients](#) with moderate to severe COPD.

Over 6.3 million unique [single nucleotide polymorphisms](#) (SNPs) were identified in the genotypes of the patients with COPD, which is a progressive breathing disorder that limits airflow in the lungs. The genotypes of over 700 African Americans with COPD also were analyzed.

"Identifying single nucleotide polymorphisms associated with bronchodilator responsiveness may reveal genetic pathways associated with the pathogenesis of COPD and may identify novel treatment methods," said Megan Hardin, M.D., Instructor of Medicine at Harvard Medical School and researcher in the Channing Division of Network Medicine at Brigham and Women's Hospital, Boston.

Dr. Hardin, who presented the research, added that multiple genetic determinants likely influence bronchodilator responsiveness. Functional analysis of the SNPs will be conducted, she added.

"As we continue to analyze the data, we expect to identify other important SNPs," said Craig P. Hersh, M.D., who headed the study and is Assistant Professor, Harvard Medical School, and faculty member in the Channing Division of Network Medicine at Brigham and Women's Hospital.

All of the subjects studied had significant histories of smoking, with most (4,561), over 10 pack-years. All patients were genotyped, and their lung function was tested by spirometry before and after they used the bronchodilator medication albuterol, which relaxes muscles in the airways and increases airflow to the lungs. Spirometry measures the volume and flow of air that is exhaled.

Each patient's bronchodilator responsiveness (BDR) was determined by three measures: absolute change in the volume of air exhaled during a forced breath in one second (FEV1); change as a percentage of predicted FEV1; and change as percentage of baseline FEV1.

In the presentation today, Dr. Hardin reported the top SNPs that thus far have been associated with each BDR outcome, but emphasized that additional analysis may reveal other SNPs with equally or greater influence on COPD patients' response.

SNPs in HS6ST3 were associated with the baseline measure while SNPs in XKR4 were associated with baseline and predicted measures. SNPs in the CUBN were associated with absolute and predicted measures. Among African American subjects, SNPs in CDH13 were significantly associated with the absolute measure.

More information: The ASHG 2013 abstract: "A genome-wide meta-analysis of the response to inhaled bronchodilators among subjects with chronic obstructive pulmonary disease".

Provided by American Society of Human Genetics

Citation: DNA variants may influence COPD patients' response to inhaled bronchodilators (2013, October 25) retrieved 23 April 2024 from <https://medicalxpress.com/news/2013-10-dna-variants-copd-patients-response.html>

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