PRDM15 Is Associated with Risk of Chronic Obstructive Pulmonary Disease in a Rural Population in Chile

Dean Hosgood H.

III

Díaz-Peña R.

Blansky D.

Jaime S.

Parra V.

Boekstegers F.

Bermejo J.L.

García-Valero J.

Montes J.F.

Valdivia G.

Miravitlles M.

Agustí A.

Silva R.S.

Olloquequi J.

Background: Genome-wide association studies (GWAS) have accelerated our understanding of the genetic underpinnings of chronic obstructive pulmonary disease (COPD); however, GWAS populations have typically consisted of European descent, with ?1% of Latin American ancestry. Objective: To overcome this limitation, we conducted a GWAS in a rural Chilean population with increased COPD risk to investigate genetic variation of COPD risk in this understudied minority population. Method: We carried out a case-control study of 214 COPD patients (defined by the GOLD criteria) and 193 healthy controls in Talca, Chile. DNA was extracted from venous blood and genotyped on the Illumina Global Screening Array (n = 754,159 markers). After exclusion based on Hardy-Weinberg equilibrium (p ? 0.001), call rates (<95%), and minor allele frequencies (<0.5%)

in controls, 455,564 markers were available for logistic regression. Results: PRDM15 rs1054761 C allele (p = 2.22 × 10-7) was associated with decreased COPD risk. Three PRDM15 SNPs located on chromosome 21 were significantly associated with COPD risk (p < 10-6). Two of these SNPs, rs1054761 and rs4075967, were located on a noncoding transcript variant region of the gene. Conclusion: PRDM15 overexpression may play a role in the B-cell dysregulation in COPD pathogenesis. To the best of our knowledge, the association between PRDM15 and COPD risk was not previously found in GWAS studies in largely European populations, highlighting the importance of investigating novel variants associated with COPD risk among ethnically diverse populations.

Biomass

Chronic obstructive pulmonary disease

Genetics

Genome-wide association study

SNP

DNA

aged

Article

case control study

Chile

Chilean

chromosome 21

chronic obstructive lung disease

controlled study

DNA extraction

female

gene

gene frequency

gene overexpression

genetic association

genetic risk

genetic variation

genome-wide association study

genotype

human

major clinical study

male

pathogenesis

PRDM15 gene

priority journal

rural population

single nucleotide polymorphism