Amerindian ancestry influences genetic susceptibility to chronic obstructive pulmonary disease

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The contribution of genetic ancestry on chronic obstructive pulmonary disease (COPD) predisposition remains unclear. To explore this relationship, we analyzed the associations between 754,159 single nucleotide polymorphisms (SNPs) and risk of COPD (n = 214 cases, 193 healthy controls) in Talca, Chile, considering the genetic ancestry and established risk factors. The proportion of Mapuche ancestry (PMA) was based on a panel of 45 Mapuche reference individuals. Five PRDM15 SNPs and two PPP1R12B SNPs were associate with COPD risk (p = 0.05 to 5×10?4) in those individuals with lower PMA. Based on linkage disequilibrium and sliding window analyses, an adjacent PRDM15 SNPs were associated with COPD risk in the lower PMA group (p = 10?3 to 3.77×10?8). Our study is the first to report an association between PPP1R12B and COPD risk, as well as effect modification between ethnicity and PRDM15 SNPs in determining COPD risk. Our results are biologically plausible given that PPP1R12B and PRDM15 are involved in immune dysfunction and autoimmunity, providing mechanistic evidence for COPD pathogenesis and highlighting the importance to conduct more genome wide association studies (GWAS) in admixed populations with Amerindian descent.

Ancestry

Autoimmunity

Chronic obstructive pulmonary disease (COPD)

Genome wide association studies (GWAS)

Hispanic paradox

Immune dysfunction

Personalized medicine

genomic DNA

aged

American Indian

Article

biomass

body mass

carbon monoxide diffusing capacity of the lung

Chile

chronic obstructive lung disease

clinical assessment

cohort analysis

controlled study

disease predisposition

dyspnea

exercise

female

forced expiratory volume

forced vital capacity

gene frequency

gene linkage disequilibrium

genetic association

genetic risk

genetic susceptibility

genome-wide association study

genotyping technique

hospitalization

human

lung function

lung function test

major clinical study

male

modified medical research council scale

oxygen saturation

principal component analysis

pulse oximetry

quality of life

risk factor

single nucleotide polymorphism

six minute walk test

smoking