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# A genome-wide association study of severe asthma exacerbations in Latino children and adolescents

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**A novel SNP in *FLJ22447* is significantly associated with both severe asthma exacerbations in Latino youth and DNA methylation of a cis-CpG in nasal epithelium. This CpG is linked to nasal epithelial expression of a gene implicated in atopic asthma.** https://bit.ly/33D9Joc

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ABSTRACT Severe asthma exacerbations are a major cause of school absences and healthcare costs in children, particularly those in high-risk racial/ethnic groups.

To identify susceptibility genes for severe asthma exacerbations in Latino children and adolescents, we conducted a meta-analysis of genome-wide association studies (GWAS) in 4010 Latino youth with asthma in four independent cohorts, including 1693 Puerto Ricans, 1019 Costa Ricans, 640 Mexicans, 256 Brazilians and 402 members of other Latino subgroups. We then conducted methylation quantitative trait locus, expression quantitative trait locus and expression quantitative trait methylation analyses to

assess whether the top single nucleotide polymorphism (SNP) in the meta-analysis is linked to DNA methylation and gene expression in nasal (airway) epithelium in separate cohorts of Puerto Rican and Dutch children and adolescents.

In the meta-analysis of GWAS, an SNP in *FLJ22447* (rs2253681) was significantly associated with 1.55 increased odds of severe asthma exacerbation (95% CI 1.34–1.79, $p=6.3\times10^{-9}$). This SNP was significantly associated with DNA methylation of a CpG site (cg25024579) at the *FLJ22447* locus, which was in turn associated with increased expression of *KCNJ2-AS1* in nasal airway epithelium from Puerto Rican children and adolescents ($\beta=0.10$, $p=2.18\times10^{-7}$).

SNP rs2253681 was significantly associated with both DNA methylation of a cis-CpG in *FLJ22447* and severe asthma exacerbations in Latino youth. This may be partly explained by changes in airway epithelial expression of a gene recently implicated in atopic asthma in Puerto Rican children and adolescents (*KCNJ2-AS1*).