Genetic Admixture and Asthma-Related Phenotypes in Mexican American and Puerto Rican Asthmatics

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Genetic association studies in admixed populations may be biased if individual ancestry varies within the population and the phenotype of interest is associated with ancestry. However, recently admixed populations also offer potential benefits in association studies since markers informative for ancestry may be in linkage disequilibrium across large distances. In particular, the enhanced LD in admixed populations may be used to identify alleles that underlie a genetically determined difference in a phenotype between two ancestral populations. Asthma is known to have different prevalence and severity among ancestrally distinct populations. We investigated several asthma-related phenotypes in two ancestrally admixed populations: Mexican Americans and Puerto Ricans. We used ancestry informative markers to estimate the individual ancestry of 181 Mexican American asthmatics and 181 Puerto Rican asthmatics and tested whether individual ancestry is associated with any of these phenotypes independently of known environmental factors. We found an association between higher European ancestry and more severe asthma as measured by both forced expiratory volume at 1 second (r2/C0.21, p=0.005) and by a clinical assessment of severity among Mexican Americans (OR: 1.55; 95% CI 1.25 to 1.93). We found no significant associations between ancestry and severity or drug responsiveness among Puerto Ricans. These results suggest that asthma severity may be influenced by genetic factors differentiating Europeans and Native Americans in Mexican Americans, although differing results for Puerto Ricans require further investigation. Genet. Epidemiol. 29:76–86, 2005. © 2005 Wiley-Liss, Inc.

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INTRODUCTION

Genetic association studies in unrelated individuals are currently being pursued for many diseases due to their power and relative efficiency. Genetic association studies directly test a variant believed to be either the true disease-variant or in linkage disequilibrium (LD) with the disease-variant. Recently, admixed populations such as African Americans and Latino ethnic groups are known to have areas of LD that can extend over large chromosomal regions due to allele frequency differences between the ancestral populations [Chakraborty and Weiss, 1988]. This increased LD among admixed populations can facilitate mapping complex trait genes in an approach generally referred to as admixture mapping [Risch, 1992; McKeigue, 1998; Zheng and Elston, 1999; McKeigue et al., 2000; Patterson et al., 2004; Smith et al., 2004].

A potential complication of studying admixed populations is the possibility of spurious associations due to population stratification [Pritchard and Rosenberg, 1999; Cardon and Palmer, 2003; Ziv and Burchard, 2003]. If the risk of disease varies with ancestry proportions, this will create associations of disease with genotypes at any locus where allele frequencies differ between ancestral populations. Thus, admixture mapping first requires appropriate adjustment for population stratification.

Asthma prevalence and severity vary widely among different racial and ethnic groups in the United States. Puerto Ricans have the highest asthma prevalence, morbidity, and mortality while Mexican Americans’ asthma prevalence, morbidity and mortality is lower than Caucasians’ and African Americans’ [Carter-Pokras and Gergen, 1993; Homa et al., 2000]. Within each of these Latino groups, individuals are descendants of highly diverse ancestral groups including Native-American, European, and African populations. Although Puerto Ricans and Mexicans share a common language and have arisen through several centuries of admixture, the relative proportions of these ancestral populations between the contemporary Puerto Rican and Mexican American population are different [Hanis et al., 1991]. Thus, we examined the association of individual ancestry with asthma severity and other asthma-related phenotypes in these two groups separately. Using 44 markers highly informative for ancestry, we estimated individual ancestry in 181 Puerto Rican and 181 Mexican American asthmatic subjects. In each population, we tested the association between individual ancestry and measures of airway dynamics, bronchodilator drug responsiveness, clinical assessments of severity, and serum IgE levels.

MATERIALS AND METHODS

STUDY PARTICIPANTS

As part of the ongoing Genetics of Asthma in Latino Americans (GALA) Study [Burchard et al., 2004], patients with asthma were enrolled in the San Francisco Bay Area, California (SF), Puerto Rico (PR), and Mexico City, Mexico (MX). Asthmatic subjects from the San Francisco Bay Area (n=181) and Puerto Rico (n=181) were included in this analysis, and their characteristics are shown in Table I. Subjects were recruited from community schools, clinics, and hospitals. In all health care centers, medical records were reviewed to identify patients with physician-diagnosed asthma, who then were contacted to participate in the study. Asthmatic subjects between the ages of 8 and 40 years, with physician-diagnosed asthma and two or more asthma symptoms (among wheezing, coughing, and shortness of breath) in the last two years, were eligible to participate. Recruitment was standardized across all clinical centers. Mexican Americans were recruited from five sites in Northern and Central California: San Francisco, Oakland, Redwood City, Salinas, and Fresno. Puerto Ricans were recruited from nine sites in Puerto Rico: Barceloneta, Barranquitas, Bayamón, Carolina, Catano, Corozal, Humacao, Mayaguez, and San Juan. Bilingual and bicultural physicians specializing in asthma were present at all interviews.

| TABLE I. Characteristics and pulmonary test results of study subjects* |
|-----------------|------------------|------------------|
| Characteristic  | Mexican Americans | Puerto Ricans     |
| Age, yr        | 11.9 (10:15)     | 12.2 (10:15)     |
| Sex, % Male    | 63.0             | 59.1             |
| Body mass index, kg/m² | 24.3 (20:29) | 21.2 (17:26)     |
| FEV₁, % predicted | 94.2 (86:103)   | 84.8 (76:95)     |
| ΔFEV₁, %       | 6.6 (3:10)       | 5.2 (1:10)       |
| Serum IgE, IU/ml | 251 (106:623)   | 280 (102:636)    |
| % Mild         | 43.1             | 39.2             |
| % US born      | 64.1             | 0                |

*Values are expressed as median (25th:75th percentile), and were missing for some subjects.
ASTHMA AND MEDICAL QUESTIONNAIRE

Asthmatic subjects were assessed using a modified version of the 1978 ATS-Division of Lung Disease Epidemiology Questionnaire [Ferris, 1978]. All subjects’ forms and questionnaires were available in English and Spanish. Ethnicity was self-reported. Subjects were enrolled only if both biological parents and all biological grandparents were of Puerto Rican (for the PR site) or Mexican ethnicity (for the SF sites and Mexico City). Local Institutional Review Boards approved the study, and all subjects signed forms indicating their consent to participate.

Pulmonary function tests and IgE measurements.

Asthma is characterized by recurrent episodes of wheeze, cough, and airway obstruction. Airway obstruction is an indicator of asthma severity and can be measured using spirometry. A standard measure of the severity of airway obstruction is forced expiratory volume in one second (FEV₁). The lower the FEV₁ is, the more severe the airway obstruction is. Airway obstruction is reversible with the inhalation of medications such as albuterol, the most commonly prescribed asthma medication in the world. The reversibility of airway obstruction is a measure of drug responsiveness. Reversibility can be measured by performing spirometry before and after the administration of albuterol and measuring the difference ($ΔFEV₁$).

Asthmatic subjects were instructed to withhold their bronchodilator medications for at least 8 hours before lung function tests. Spirometry was performed according to established standards (Standardization of Spirometry, 1995), and baseline FEV₁ is described herein as Pre-FEV₁. Bronchodilator drug responsiveness to albuterol is reported as percent change in forced FEV expiratory volume in 1 second from baseline ($ΔFEV₁$) after albuterol administration. Pulmonary function tests are expressed as a percentage of the predicted normal value using age-adjusted prediction equations from Hankinson and colleagues [Hankinson et al., 1999].

For this analysis, asthmatic subjects were classified as having “mild” or “moderate-severe” asthma based on three yes/no questions related to medication use and asthma symptoms: (1) is the patient’s only asthma medication a bronchodilator used on an as-needed basis? (2) without respect to medications used, has the patient had daily asthma symptoms for three or more months of the previous year? and (3) has the patient experienced nocturnal asthma >1 night per week for 3 or more months of the previous year? Asthmatic subjects were classified as mild if they answered yes to question 1 and no to all other questions. Subjects were classified as moderate-severe if they answered no to question 1 or yes to either question 2 or 3. Total plasma IgE was measured in duplicate using Uni-Cap technology (Pharmacia, Kalamazoo, MI).

MARKER SELECTION

Forty-four autosomal ancestry informative markers (AIMs) were identified from the NCBI SNP database (dbSNP) or previously reported literature as being highly informative for ancestry and were genotyped in Mexican and Puerto Rican subjects. In addition, we genotyped our panel of 44 AIMs in African, European, and Native-American populations to estimate their allele frequencies in the ancestral populations. The ancestral allele frequencies were determined by genotyping the markers in populations collected from Sub-Saharan Africa (n=481): Nigeria, Central African Republic, Sierra Leone; Europe (n=243): Ireland, England, Germany and Spain; and Native-American populations indigenous to the United States and Mexico (n=148): Maya, Pima, Cheyenne and Pueblo. Delta ($δ$) determines ancestral informativeness and is defined as the absolute difference in allele frequency between two ancestral populations. A $δ$ value of 1 implies complete ancestry informativeness; a $δ$ value of 0 implies no informativeness for ancestry. Table II shows the AIMs used in this study, along with their chromosomal locations and delta values. These markers were selected because they exhibit high levels of allele frequency differences ($δ > 0.3$) between any two of the three parental populations. There were 31, 33, and 23 informative markers with $δ > 0.3$ between African and European ancestry, African and Native-American ancestry, and European and Native-American ancestry, respectively.

Information regarding primer sequences, polymorphic sites, and other relevant information has been submitted to the dbSNP NCBI database, under the submitter handle PSU-ANTH and/or KWOK; the dbSNP reference SNP (rs) numbers are indicated in Table II and further information can be found at (http://www.ncbi.nlm.nih.gov/SNP/).
The 44 AIMs were genotyped using the Acy cloPrime-FP tm (PerkinElmer) method [Chen et al., 1999]. PCR conditions were: 6 μl volume with Platinum Taq PCR buffer, 2.5 mM MgCl₂, 2.4–4.0 ng genomic DNA, 50 μM dNTPs, 0.1–0.2 μM primers, 0.1–0.2 U Platinum Taq (Invitrogen) plus 1 μl extra water to counteract evaporation. Cycling conditions were: 95°C for 2 min, 35 cycles of 92°C for 10 sec, 58°C for 20 sec, 68°C for 30 sec, and final extension at 68°C for 10 min. Enzymatic cleanup and single base extension genotyping reactions were performed with Acy cloPrime-FP.
kits. Plates were read on an EnVision fluorescence polarization plate reader (PerkinElmer).

STATISTICAL ANALYSIS

Individual admixture estimates were derived from a maximum likelihood algorithm, as implemented in the program IBGA [Parra et al., 2001]. Group admixture levels were calculated with the program ADMIX, which implements a weighted least squares method [Long, 1991]. To test the association between quantitative asthma-related traits (Pre-FEV1, ΔFEV1, and serum IgE) and ancestry, individual ancestry was incorporated as a continuous variable into linear regression models. Serum IgE levels were log-transformed to make the distribution approximately normal and all subsequent references to IgE levels indicate this transformation. We used logistic regression models to test the association between individual ancestry and asthma severity, defined as a qualitative phenotype. In each model, we used the maximum likelihood estimate of the individual ancestry as a predictor. We entered age, sex, asthma duration, regular use of asthma medication, and body mass index (BMI) into the model as covariates. Regular use of asthma medication was considered a covariate since it may be a marker of access to care and, thus, may confound the association between severity and ancestry. To adjust for potential environmental interactions, second-hand exposure to environmental tobacco smoke (ETS) and birthplace were also incorporated into models as covariates. ETS exposure was determined to be present if one or both parents reported current smoking and absent if both parents were current non-smokers. We also included the clinic or hospital from which the participant was recruited as a categorical covariate in the model as covariates. For Puerto Ricans, we were not able to characterize SES from the data collected.

We used a forward stepwise procedure to select covariates for each model. Tests for individual marker associations were performed using a linear regression model with the assumption of an additive genetic model (genotypes entered as 0, 1, or 2 alleles). We adjusted the associations for individual markers using a multivariate model in which individual ancestry was entered as a covariate. Regression models were estimated using the program STATA 8.0 S/E (College Station, TX). We present nominal p values in the text and tables. However, for associations that meet a nominal significance level, we also consider a more conservative Bonferroni correction as noted in the text.

RESULTS

ADMIXTURE ESTIMATES

Among the Mexican Americans as a group, ancestry was estimated to be 3.4 ± 0.97% African, 44.9 ± 1.7% European, and 51.7 ± 1.7% Native American. Among Puerto Ricans, ancestry was estimated as 16.2 ± 1.6% African, 65.5 ± 2.2% European, and 18.3 ± 2.1% Native American. Estimates for individual admixture demonstrate a very wide range of genetic ancestry among individuals in these two highly admixed Latino populations (Fig. 1), although the standard errors on individual admixture estimates are large.

MEXICAN-AMERICAN POPULATION

We found a significant relationship between individual ancestry and asthma severity (as defined by Pre-FEV1) in our Mexican-American population (Table III, Fig. 2). European ancestry was associated with more severe asthma [defined by lower Pre-FEV1 (Pearson: r = −0.211, p = 0.0051; Spearman: rho = −0.228, p = 0.0024)]. European ancestry remained a significant predictor of Pre-FEV1 in a multivariate regression model after adjustment for age, sex, asthma duration, regular use of asthma medication, ETS exposure, birthplace, socioeconomic status, recruitment site, and BMI. The forward stepwise regression model identified age and ETS exposure as the only other significant effectors of Pre-FEV1. A decrease of 1.7% (95% CI: 0.6%–2.8%) Pre-FEV1 was observed per 10% increase in European ancestry (Table III). There is a strong inverse correlation between Native-American and European ancestry. Therefore, any negative association with European ancestry would be expected to have a positive association with Native-American ancestry. As expected, in models where Native-American ancestry was the main predictor, Native-American ancestry was associated with
Fig. 1. Individual ancestry (IA) estimates. Estimates for 181 Mexican-American asthmatics (top) and 181 Puerto-Rican asthmatics (bottom) are shown, clustered by admixture level. The distribution of individual ancestry estimates in Mexican Americans covers the range of European and Native-American proportions, while African ancestry contributes very little to this population. However, in Puerto Ricans, African and European ancestries show a high degree of variability, while Native-American ancestry exhibits a more restricted pattern of variation.
milder asthma [defined as higher measures of Pre-FEV\textsubscript{1} (Pearson: $r=0.176$, $p=0.0197$; Spearman: $\rho=0.186$, $p=0.0139$)]. After correction for the aforementioned potential confounders, Native-American ancestry remained significantly associated with higher Pre-FEV\textsubscript{1} values. Additionally, ETS exposure was found to be associated with Pre-FEV\textsubscript{1}. We found no association between Pre-FEV\textsubscript{1} and African ancestry ($r=0.092$, $p=0.224$). No associations were found between individual ancestry and either $\Delta$FEV\textsubscript{1} or IgE levels among Mexican Americans.

We also tested the association between ancestry and asthma severity, comparing the proportion of ancestry among mild versus severe asthmatics, as defined by asthma medication use and clinical symptoms. We found an association between higher European ancestry and asthma severity (Table IV). For each 10% increase in European ancestry there was an approximate 37% risk increase for severe asthma. Adjustment for Pre-FEV\textsubscript{1}, age, sex, asthma duration, ETS exposure, birthplace, and BMI did not affect the association. Conversely, Native-American ancestry was associated with decreased risk of asthma severity, with an odds ratio of 0.66 (95% CI 0.54–0.81, $p=0.00006$) for having severe asthma versus mild asthma per 10% increase in Native-American admixture. Both of the associations between European ancestry and lower Pre-FEV\textsubscript{1} and increased clinical severity are significant after adjustment for multiple hypothesis testing, considering that 4 phenotypes were tested against ancestry (Bonferroni adjusted cutoff for significance is $p=0.0125$).

We also noted that there was a higher European admixture in U.S.-born Mexicans ($n=116$) than in Mexico-born Mexicans ($n=65$; 44.7% vs. 38.6%, $p=0.036$), although the adjustment for birthplace did not change the strength of the association between ancestry and asthma severity.

**TABLE III. Association of ancestry with asthma severity (Pre-FEV\textsubscript{1})**

<table>
<thead>
<tr>
<th>Population</th>
<th>Significant predictors</th>
<th>Regression coefficient</th>
<th>95% Confidence interval</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mexican Americans</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>European IA</td>
<td>$-1.50^a$</td>
<td>$-2.54$ to $-0.45$</td>
<td>0.005</td>
</tr>
<tr>
<td>Adjusted$^b$</td>
<td>European IA</td>
<td>$-1.71^a$</td>
<td>$-2.83$ to $-0.59$</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>ETS exposure</td>
<td>6.41</td>
<td>1.68 to 11.1</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Puerto Ricans</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted$^b$</td>
<td>Age</td>
<td>$-0.35$</td>
<td>$-1.67$ to $1.32$</td>
<td>0.82</td>
</tr>
</tbody>
</table>

$^a$Individual ancestry coefficients are reported as change in Pre-FEV\textsubscript{1} per 10% increase in individual ancestry.

$^b$Variables included in each multivariable model were determined using a forward stepwise selection approach.

![Fig. 2. Association between European ancestry and asthma severity (defined as baseline Pre-FEV\textsubscript{1}) among Mexican Americans. The regression model shows a significant negative correlation between European admixture and asthma severity ($r=-0.211$, $p=0.0051$); that is, European ancestry is associated with more severe asthma as defined by Pre-FEV\textsubscript{1}.

**PUERTO RICAN POPULATION**

Among Puerto Rican asthmatics, we found no significant association between African ancestry and asthma-related phenotypes after adjustment for multiple hypothesis testing. There was a borderline association between African ancestry and higher bronchodilator drug responsiveness [$\Delta$FEV\textsubscript{1} (Pearson: $r=0.163$, $p=0.0321$) at the nominal level of significance (Table V). However, this association became non-significant when we adjusted for known potential confounders ($\beta$ Coefficient: 0.63; 95% CI: $-0.27$ to 1.54, $p=0.16$) and was not included in the final model (Table V).
We found no significant associations between bronchodilator drug responsiveness and European ancestry (r = −0.0589, p = 0.44) or Native-American ancestry (r = −0.0814, p = 0.29). No associations between ancestry and quantitative or qualitative measures of asthma severity or IgE levels were observed in Puerto Ricans.

**INDIVIDUAL MARKER ASSOCIATIONS**

Associations between individual AIMs and asthma phenotypes were evaluated with and without correction for individual ancestry estimates. Table VI shows the independent associations between single-locus genotypes and the quantitative and qualitative measures of asthma severity in Mexican Americans and Puerto Ricans.
phenotypes Pre-FEV$_1$ or ΔFEV$_1$ among Mexican Americans and Puerto Ricans. In the unadjusted regression model, three out of 44 markers (7%) were nominally associated with Pre-FEV$_1$ in Mexican Americans at the 0.05 significance level. After correction for individual ancestry, only one marker was significantly associated with Pre-FEV$_1$, suggesting some degree of confounding between ancestry and Pre-FEV$_1$, consistent with the association between European ancestry and Pre-FEV$_1$ among Mexican Americans. There were several other modest associations between individual markers and other phenotypes at the nominal level of significance. However, none of these would be considered significant once the number of tests is taken into consideration.

**DISCUSSION**

Using 44 ancestry informative genetic markers (AIMs), we estimated individual ancestry among 181 Puerto Rican and 181 Mexican American asthmatics. Among Mexican Americans, we found an association between European ancestry and asthma severity, as defined by lower Pre-FEV$_1$. Interestingly, an independent qualitative measure of asthma severity, based on asthma medication use and clinical symptoms, was also associated with European ancestry and, thus, corroborated our initial findings. The observation of greater asthma severity in individuals with higher European ancestry suggests that one or more alleles at higher frequency among Europeans may increase asthma severity in Mexican American populations. However, this association may also be due to unmeasured environmental factors. For example, a certain environmental factor may be more common in regions of Mexico that have higher European ancestry. This may lead to an association between European ancestry and asthma severity, even though there may be no genetic factors that underlie this association [Risch et al., 2002]. In addition, the association we observed may be due to a bias if asthmatic patients with higher European ancestry and less severe asthma are less likely to use the community clinics from which the patients in this study were recruited.

Thus, additional studies of the Mexican population accounting for other potential environmental risk factors for asthma and studying this group in diverse regions may help to clarify this association.

We did not observe a similar trend towards increased asthma severity with European ancestry or decreased asthma severity with Native-American ancestry in Puerto Ricans. This may be due to the fact that the association between European ancestry and more severe asthma among Mexican Americans is due to an unmeasured environmental confounder as discussed above. Alternatively, there may be a gene–environment interaction that underlies this difference. For example, there may be an environmental factor that increases the severity of asthma only in the presence of a certain genotype, which is higher among people of European ancestry. Furthermore, the Puerto Rican population is somewhat more complex in genetic ancestry. Puerto Ricans participating in the GALA study have substantial contributions from three different ancestral populations, while Mexican Americans are primarily European and Native American, with little African ancestry. Thus, more complex interactions between these ancestries may have altered the association. Moreover, the Native-American ancestral population of Puerto Rico may be distinct from that of Mexico, as genetic distance between Native-American groups has been shown to be relatively high [Rosenberg et al., 2002]. A reliable estimate for the Native-American ancestral population of Puerto Rico is also difficult to ascertain, as very few individuals of the indigenous Taíno Indian tribe survived after the European conquest of the island [Rouse, 1993].

A genetic interpretation of the association that we observed of more severe asthma among Mexican Americans with higher European ancestry suggests that Native Americans have less severe asthma compared to European-American populations. There are limited reports of asthma prevalence among the Native Americans. American Indian and Alaskan Native children who were cared for by the Indian Health Services between 1979 and 1989 had rates of asthma diagnosis at the time of hospital discharge similar to rates seen in white children [Hisnanick et al., 1994]. A more recent study found a non-significant lower rate of asthma among Native Americans compared with European Americans in a survey of school age children [Stout et al., 1999]. However, the data comparing the phenotypes we analyzed, clinical and spirometry-based measures of asthma severity among diagnosed asthmatics, is even more limited than prevalence data and thus it is difficult to make any conclusions about asthma severity among European-American
asthmatics vs. Native-American asthmatics. Since our Puerto Rican data does not demonstrate an association between increased European ancestry and severity, our results in Mexican Americans should be interpreted with caution. Eventually, only identification of a locus that underlies a severity difference between Europeans and Native Americans can confirm that this difference is due to a genetic rather than an environmental difference.

The individual ancestry estimates that we obtained are statistical estimates, and for each individual these estimates may have considerable statistical error. However, since the error should be random with respect to the phenotypes of interest, the estimates of association should be biased towards the null hypothesis. Therefore, the error in estimating the associations in our analysis likely led to underestimating the strength of the associations with individual ancestry and reduced power.

In addition to associations between ancestry and asthma phenotypes, we found several individual AIMs to be associated with asthma severity (Pre-FEV$_1$) and bronchodilator drug responsiveness (ΔFEV$_1$) in our Latino ethnic groups, even after correction for individual ancestry. The markers that were associated with severity among Mexican Americans in univariate analyses were no longer significantly associated after correction for individual ancestry, suggesting that these associations were false positives due to stratification. Some of the other associations were not eliminated after correction for individual ancestry. These associations are all of marginal significance and are likely the result of type I error. None of these markers would meet significance after correction for multiple hypotheses testing. However, since only a very small fraction of the genome was covered with the markers used in this study, we would not expect to find loci for asthma severity. Once adequate coverage of the genome is achieved with AIMs, we should be able to more definitively determine whether there are any specific loci that underlie the associations with ancestry that we describe here. Global studies of allele frequency differences among different racial/ethnic populations suggest that genes that modify immune response are more likely to have large allele frequency differences, presumably due to selection [Akey et al., 2002]. Since such genes may affect asthma severity, then admixture mapping for asthma severity modifiers may be a feasible approach.

In summary, our results demonstrate that recently admixed populations, such as Latino ethnic groups, provide both a challenge and opportunity for genetic association studies. The presence of population stratification in admixed populations leads to spurious associations between unlinked markers and disease. However, such populations offer a potential advantage in disease gene mapping. Given that linkage disequilibrium in highly admixed populations spans extended regions of the genome, relatively few markers that are informative for ancestry may provide coverage for detecting linkage to disease alleles across the entire genome, compared to the number of random markers required for traditional LD mapping [Shriver et al., 2003; McKeigue 2005; Patterson et al., 2004; Smith et al., 2004]. Therefore, with the use of ancestry informative markers, admixture mapping may be a feasible method for discovering genes underlying asthma severity in admixed populations.

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**ELECTRONIC DATABASE INFORMATION**


**REFERENCES**


