Association Analysis in African Americans of European-Derived Type 2 Diabetes Single Nucleotide Polymorphisms From Whole-Genome Association Studies

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OBJECTIVE—Several whole-genome association studies have reported identification of type 2 diabetes susceptibility genes in various European-derived study populations. Little investigation of these loci has been reported in other ethnic groups, specifically African Americans. Striking differences exist between these populations, suggesting they may not share identical genetic risk factors. Our objective was to examine the influence of type 2 diabetes genes identified in whole-genome association studies in a large African American case-control population.

RESEARCH DESIGN AND METHODS—Single nucleotide polymorphisms (SNPs) in 12 loci (e.g., TCF7L2, IDE/KIF11/ HHEX, SLC30A8, CDKAL1, PKN2, IGF2BP2, FLJ39370, and EXT2/ALX4) associated with type 2 diabetes in European-derived populations were genotyped in 993 African American type 2 diabetic and 1,054 African American control subjects. Additionally, 68 ancestry-informative markers were genotyped to account for the impact of admixture on association results.

RESULTS—Little evidence of association was observed between SNPs, with the exception of those in TCF7L2 and type 2 diabetes in African Americans. One TCF7L2 SNP (rs7903146) showed compelling evidence of association with type 2 diabetes (admixture-adjusted additive \( P \) \( [P_a] \) \( = 1.59 \times 10^{-8} \)). Only the intragenic SNP on 11p12 (rs9300039, dominant \( P [P_d] \) \( = 0.029 \)) was also associated with type 2 diabetes after admixture adjustments. Interestingly, four of the SNPs are monomorphic in the Yoruba population of the HAPMAP project, with only the risk allele from the populations of European descent present.

CONCLUSIONS—Results suggest that these variants do not significantly contribute to interindividual susceptibility to type 2 diabetes in African Americans. Consequently, genes contributing to type 2 diabetes in African Americans may, in part, be different from those in European-derived study populations. High frequency of risk alleles in several of these genes may, however, contribute to the increased prevalence of type 2 diabetes in African Americans. Diabetes 57:2220–2225, 2008

RESEARCH DESIGN AND METHODS

Recently, several whole-genome association (WGA) studies have reported evidence for the existence of multiple type 2 diabetes susceptibility genes. These results were primarily observed in different European-derived study populations. Included in these loci are polymorphisms in TCF7L2 (1–5), HHEX (1–6), SLC30A8 (1–4,6), CDKAL1 (2–6), IGF2BP2 (3–6), FTO (4–7), PKN2 (3,4), FLJ39370 (3), EXT2/ALX4 (1), and LOC387761 (1). Despite the compelling evidence of association of many of these genes in European-derived study populations, little or no investigation of association has been reported for African Americans.

Differences between European-derived and African American populations (e.g., haplotype block structure and allele frequency discrepancies) suggest that the genetic risk factors of each may not be identical. Previously, we have reported that common genetic variants in TCF7L2 and HNF4A contribute to type 2 diabetes in African Americans, whereas polymorphisms in CAPN10, TCF1, and PPARG have little or no evidence of association (8). Lack of association with other type 2 diabetes susceptibility loci in African Americans has also been observed (9). In addition, differences in allele frequencies of risk polymorphisms between ethnicities have been shown (e.g., Chandala et al. [10]). These substantial discrepancies could contribute to the differences in overall prevalence of type 2 diabetes within these ethnic groups. Consequently, we examined the influence of single nucleotide polymorphisms (SNPs) recently identified in WGA studies on type 2 diabetes susceptibility in a large African American case-control population.
of Medicine and was in accordance with the principles of the Declaration of Helsinki.

Candidate gene genotyping. SNPs PKN2 rs6698181; IF2BP2 rs4402060; FLJ39370 rs17044137; CDKAL1 rs10945388 and rs7754840; SLC30A8 rs13266634; CDKN2A/CDKN2B rs564308 and rs10811661; HHEX/IDE/KIF11 rs1111875, rs5015480, and rs7923837; EXT2/ALX4 rs3740878, rs16079099, and rs1183192; FTO rs8050136; LOC387761 rs7488916; intragenic rs8000939; and TCF7L2 rs7903146 were genotyped using iPLEX technology (Sequenom, San Diego, CA) (12). Primer sequences are available on request. SNP genotyping success rates were >98.6% in case and >98.4% in control subjects. Concordance between blind duplicate samples included in the genotyping was >99.5%.

Admixture analyses genotyping. Sixty-eight bi-allelic ancestry-informative markers were genotyped using iPLEX technology (Sequenom, San Diego, CA) in 993 African American case, 1,054 African American control, 44 Yoruba Nigerian, and 36 European-American subjects. Both the Yoruba Nigerian and European-American individuals were utilized only for admixture analyses. Primer sequences are available on request. Genotyping success rates for ancestry-informative markers were >99.0% in African American case and >98.5% in African American control subjects.

Statistical analyses. Hardy-Weinberg equilibrium (HWE) values were determined by calculating a $\chi^2$ statistic and corresponding P-value. Structures of the haplotype blocks for the SNPs genotyped in CDKAL1, EXT2/ALX4, and IDE/KIF11/HHEX were ascertained using Haploview 3.2 (13) using the criteria outlined by Gabriel et al. (14).

Measures of linkage disequilibrium and association were calculated using the program SNPGWA (15). For each tandem pair of SNPs, the linkage disequilibrium statistics $D'$ and $r^2$ were computed. Multiple tests of association including the overall 2 d.f. (genotypic), additive (Cochran-Armitage trend test), and corresponding lack of fit to additivity were calculated. Tests of association under the dominant and recessive genetic models are also reported. Haplotypic association was calculated using the expectation-maximization algorithm implemented in this program. Initially, tests were performed using 1,000 permutations. Where association tests indicated possible significance (empirical $P < 0.10$), permutations were increased to 10,000. The quantitative trait (BMI) association analysis for FTO SNP rs8050136 was performed using a module of SNPGWA (QSNGWA). Association values adjusted for age or sex were calculated using the program SNPADDMIX. Estimates of case and control haplotype frequency were obtained using Dandelion 1.20 (16).

To provide context for these tests of association, power analyses were computed using QUANTO (17). Specifically, power estimates to detect the range of reported odds ratios (ORs) from the European-derived samples were computed assuming a type 2 diabetic population prevalence of 0.15 (consistent with African American populations) and polymorphism-specific type 1 error rates of $\alpha = 0.05$ and $\alpha = 0.10$. Power was calculated based on the risk allele frequency observed in our African American sample.

Individual ancestral proportions were calculated using an expectation-maximization algorithm (FRAPPE) (18) under a two-population model. Estimates of ancestral allele frequencies were obtained from the genotyped African American and European-derived samples. Logistic regression tests of additive, dominant, and recessive genetic models included adjustments for individual estimates of African ancestry (19).

RESULTS

Eighteen SNPs in 12 type 2 diabetes loci previously associated in European-derived populations were genotyped in a sample of 993 African American type 2 diabetic case subjects enriched for diabetic nephropathy and in 1,054 African American control subjects. Characteristics of the study population are shown in Table 1. Within this cohort, we observed a greater percentage of female subjects in the case (63%) compared with the control subjects (55%). Control subjects were younger than case subjects but older than the mean age at which type 2 diabetes was diagnosed. The ages of 26% of the control subjects were unavailable. The mean age of end-stage renal disease diagnosis was 58.4 ± 10.5 years. In the case subjects, the estimated mean proportion of African ancestry was 0.821, whereas in the control subjects it was 0.795.

All SNPs were consistent with HWE proportions in the entire population (supplementary Table 1 [available in an online appendix at http://dx.doi.org/10.2337/db07-1319]). rs9300039, which is located in an intragenic region of chromosome 11p12, was inconsistent with HWE in the case population ($P = 0.028$) because of an excess of homozygotes. All SNPs examined were in HWE in the control population.

High levels of linkage disequilibrium were observed between the two CDKAL1 SNPs rs10946398 and rs7754840 ($D' = 1.000$; $r^2 = 0.996$). The three SNPs within the IDE/KIF11/HHEX region were in high-to-moderate linkage disequilibrium with pairwise $D'$ values of 0.679 ($r^2 = 0.244$) between rs1111875 and rs5015480, 0.945 ($r^2 = 0.140$) between rs5015480 and rs7923837, and 0.894 ($r^2 = 0.236$) between rs1111875 and rs7923837. Likewise, high linkage disequilibrium was also observed within the three SNPs in the EXT2/ALX4 region, with pairwise $D'$ values of 1.000 ($r^2 = 0.569$) between rs1113132 and rs11037909, 0.988 ($r^2 = 0.601$) between rs11037909 and rs3740878, and 1.000 ($r^2 = 0.935$) between rs1113132 and rs3740878.

Results of the single-SNP association analyses are shown in Table 2. Genotype frequencies and counts for each SNP are provided in supplementary Table 1. Evidence of association with type 2 diabetes was observed with rs10946398 (OR 1.15; additive $P = 0.029$) and rs7754840 (OR 1.14; $P = 0.039$), both of which are located in intron five of CDKAL1. However, after adjusting for admixture, neither SNP remained nominally significant. A significant association with type 2 diabetes was also seen with LOC387761 SNP rs7480010 (OR 1.33; $P = 0.002$), but this marker also did not show evidence of association after adjusting for admixture ($P = 0.084$). rs9300039, located in an intragenic region of chromosome 11p12, was also associated under the admixture-adjusted dominant model ($P = 0.029$) but deviated from HWE proportions in the case population ($P = 0.028$). In addition, the minor allele homozygote count for rs9300039 is small (21 in the case and 9 in the control subjects, respectively [supplementary Table 1]), so association values for this marker should be interpreted with caution. The most significant
### Table 2

Single-SNP tests of association with type 2 diabetes–end-stage renal disease

| Gene                  | SNP                  | Reported European subject data | Reported African American subject data | Power to detect association in African Americans |
|-----------------------|----------------------|-------------------------------|---------------------------------------|-------------------------------------------------|
|                       | European SNP         | Risk frequency in control subjects | Risk frequency in case subjects | Additive $P$ | Additive-adjusted $P$ | Additive-adjusted OR (95% CI) | Reported risk frequency in control subjects | Reported risk frequency in case subjects | Reported OR (95% CI) | $\alpha = \alpha =$ |
| PKN2                  | rs6698181             | T                             | 0.153                                 | 0.156                   | 0.829               | 0.388               | 1.08 (0.91–1.29) | 0.290               | 0.320               | 1.11 (1.05–1.16) | 0.237               | 0.345               |
| IGF2BP2               | rs4402960             | T                             | 0.525                                 | 0.528                   | 0.865               | 0.803               | 0.98 (0.87–1.11) | 0.304               | 0.341               | 1.18 (1.08–1.28) | 0.555               | 0.675               |
| FLJ39370              | rs17044137            | A                             | 0.329                                 | 0.326                   | 0.854               | 0.747               | 0.98 (0.86–1.12) | 0.230               | 0.270               | 1.13 (1.06–1.19) | 0.060               | 0.115               |
| CDKAL1                | rs10946398            | C                             | 0.582                                 | 0.615                   | **0.029**           | 0.110               | 1.11 (0.98–1.26) | 0.319               | 0.361               | 1.16 (1.10–1.22) | 0.427               | 0.522               |
| CDKAL1                | rs7754840             | C                             | 0.585                                 | 0.616                   | **0.039**           | 0.136               | 1.10 (0.97–1.25) | 0.300               | 0.387               | 1.12 (1.03–1.22) | 0.427               | 0.552               |
| SLC30A8               | rs13266634            | C                             | 0.914                                 | 0.916                   | 0.861               | 0.543               | 1.46 (0.43–4.89) | 0.600               | 0.649               | 1.18 (1.09–1.29) | 0.169               | 0.263               |
| CDKN2B/CDKN2A         | rs564398              | T                             | 0.934                                 | 0.943                   | 0.196               | 0.320               | 2.99 (0.34–25.98) | 0.558               | 0.505               | 1.13 (1.08–1.19) | 0.140               | 0.225               |
| CDKN2B/CDKN2A         | rs10811661            | T                             | 0.933                                 | 0.927                   | 0.412               | 0.128               | 0.18 (0.02–1.64) | 0.850               | 0.872               | 1.20 (1.07–1.36) | 0.304               | 0.422               |
| IDE/KIF11/HHEX        | rs1111875             | C                             | 0.766                                 | 0.774                   | 0.547               | 0.767               | 1.02 (0.88–1.19) | 0.522               | 0.546               | 1.10 (1.01–1.19) | 0.371               | 0.495               |
| IDE/KIF11/HHEX        | rs5015480             | C                             | 0.633                                 | 0.621                   | 0.412               | 0.400               | 0.95 (0.83–1.08) | 0.425               | 0.379               | 1.13 (1.08–1.17) | 0.470               | 0.595               |
| IDE/KIF11/HHEX        | rs7923837             | G                             | 0.917                                 | 0.929                   | 0.143               | 0.303               | 1.87 (0.57–6.12) | 0.597               | 0.622               | 1.11 (1.02–1.20) | 0.143               | 0.229               |
| Intragenic            | rs9300060             | C                             | 0.889                                 | 0.884                   | 0.618               | **0.029**           | **0.42 (0.19–0.91)** | 0.892               | 0.924               | 1.48 (1.28–1.71) | 0.584               | 0.701               |
| LOC357761             | rs7480010             | G                             | 0.858                                 | 0.890                   | **0.002**           | 0.084               | 1.18 (0.98–1.44) | 0.301               | 0.336               | 1.14 (1.01–1.27) | 0.062               | 0.117               |
| EXT2/ALX4             | rs1113132             | C                             | 0.915                                 | 0.920                   | 0.579               | **0.221**           | 0.47 (0.14–1.57) | 0.733               | 0.703               | 1.15 (0.88–1.42) | 0.475               | 0.600               |
| EXT2/ALX4             | rs11037909            | T                             | 0.862                                 | 0.859                   | 0.768               | 0.511               | 0.94 (0.79–1.13) | 0.729               | 0.760               | 1.27 (0.97–1.57) | 0.913               | 0.935               |
| EXT2/ALX4             | rs3740878             | A                             | 0.907                                 | 0.914                   | 0.415               | **0.129**           | 0.46 (0.17–1.26) | 0.728               | 0.760               | 1.26 (0.97–1.55) | 0.760               | 0.846               |
| FTO                   | rs8050136             | A                             | 0.446                                 | 0.452                   | 0.686               | 0.783               | 1.02 (0.90–1.15) | 0.398               | 0.455               | 1.23 (1.18–1.32) | 0.711               | 0.808               |
| TCF7L2*               | rs7939146             | T                             | 0.284                                 | 0.354                   | **1.73 \times 10^{-6}** | **1.59 \times 10^{-6}** | **1.39 (1.21–1.60)** | 0.181               | 0.227               | 1.37 (1.31–1.43) | 0.997               | 0.999               |

*Power analysis for TCF7L2 was calculated using a population of 960 case and 1,000 control subjects. **SNPs have minor allele homozygote counts <10 in the case or control population, and dominant model $P$ values and ORs are reported. Data in bold are $P$ values <0.05 and corresponding ORs. European risk allele frequencies and ORs were obtained from recent WGA studies (refs. 1–6).
association with type 2 diabetes was observed with TCF7L2 SNP rs7903146 (OR 1.39; $P_a = 1.73 \times 10^{-6}$), and this SNP remained statistically significant after admixture adjustment ($P_a = 1.59 \times 10^{-6}$). All other SNPs examined failed to show evidence of association with type 2 diabetes in this African American cohort under an additive model (Table 2). Tests of association under the dominant and recessive genetic models are shown in supplementary Table 2. We also tested whether FTO SNP rs8050136 was associated with BMI as previously reported in European-derived populations (4,6). We found no evidence of association with this polymorphism and BMI ($P_a = 0.480$). Association with type 2 diabetes adjusted for age or sex was calculated for each SNP (data not shown) but did not meaningfully change the results of this study.

It is interesting to note that 5 of the 18 SNPs had ORs in the opposite direction, inconsistent with the previously reported OR. In fact, the 95\% CI for 7 of the 18 SNPs did not include the previously reported OR from the European-American samples.

With this very limited evidence of association in our African American population, the question arises whether adequate power was available in this sample to detect association. This has been addressed by calculating the power to detect association for each SNP based on the estimated effect size from studies in European-derived populations and the observed allele frequency of the risk allele in the African American population. Power was calculated for $\alpha = 0.05$ (nominal evidence of association) and $\alpha = 0.10$ (for the ability to detect loci that are trending toward association). The power estimates using an intermediate measure of effect size (between the highest and lowest reported in European-derived populations) under the additive model are shown in Table 2. More extensive power estimates are shown in supplementary Table 3, which also provides estimates for high and low observed effect sizes. For some SNPs, the power is quite low (e.g., rs7480010) but for other SNPs (rs5740878, rs11037909, and rs8050136) power is 70\% for $\alpha = 0.05$.

All three SNPs examined in the EXT2/ALX4 region reside in a single linkage disequilibrium block but showed no haplotypic association with type 2 diabetes (data not shown). Of the three SNPs genotyped in the IDE/KIF11/\(HHEX\) region, two (rs5015480 and rs7923837) were located in an linkage disequilibrium block but also showed no evidence of association. Haplotype analysis of the two CDKAL1 SNPs (rs10946398 and rs7754840) show significant association with type 2 diabetes (global empirical $P = 0.036$; data not shown) but provides little information beyond that obtained with single-SNP analysis as a result of high measures of linkage disequilibrium ($D' = 1.000$; $r^2 = 0.996$).

**DISCUSSION**

We examined 18 SNPs in 12 loci identified in recent genome-wide association studies in European-derived populations that were associated with type 2 diabetes or BMI (FTO) for association with type 2 diabetes in a large African American population. There is very limited evidence that any of these European-derived genome-wide association studies SNPs contribute to diabetes in African Americans. In contrast, significant association with type 2 diabetes was observed with the previously described TCF7L2 SNP rs7903146. TCF7L2 has been the focus of multiple investigations and is one of the most highly replicated type 2 diabetes candidate genes in several populations (1–5). Few publications have examined the influence of TCF7L2 on type 2 diabetes risk in African Americans. In this study, we expand on the previous investigation from our center by Sale et al. (8), which described compelling evidence of association with type 2 diabetes for polymorphisms in this gene. From the results of these studies and the convincing replication of association with type 2 diabetes in European-derived populations, a more comprehensive study of TCF7L2 polymorphisms in African Americans is warranted. Paraphetically, this observation of strong association gives us confidence that the ascertainment and diagnoses used to recruit these African American subjects are accurate and the analyses of the European-derived type 2 diabetes loci presented here are valid.

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**TABLE 3**

Minor allele frequencies for African American, YRI, and CEU populations

| SNP          | Alleles | Reported risk allele | Reported risk allele frequency |
|--------------|---------|----------------------|-------------------------------|
|              |         |                      | African American frequency  |
|              |         |                      | HAPMAP frequency (YRI)       |
|              |         |                      | HAPMAP frequency (CEU)       |
| rs6698181    | C/T     | T                    | 0.155                         |
| rs4402960    | T/G     | T                    | 0.527                         |
| rs17044137   | T/A     | A                    | 0.327                         |
| rs10946398   | C/A     | C                    | 0.598                         |
| rs7754840    | C/G     | C                    | 0.600                         |
| rs13266634   | C/T     | C                    | 0.915                         |
| rs564398     | T/C     | T                    | 0.939                         |
| rs10811661   | T/C     | T                    | 0.930                         |
| rs111875     | C/T     | C                    | 0.770                         |
| rs5015480    | C/T     | C                    | 0.627                         |
| rs7923837    | G/A     | G                    | 0.923                         |
| rs9300039    | C/A     | C                    | 0.886                         |
| rs7480010    | G/A     | G                    | 0.873                         |
| rs1113132    | C/G     | C                    | 0.918                         |
| rs11037909   | T/C     | T                    | 0.860                         |
| rs3740878    | A/G     | A                    | 0.911                         |
| rs8050136    | C/A     | A                    | 0.449                         |
| rs7903146    | C/T     | T                    | 0.319                         |

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**DISCUSSION**

We examined 18 SNPs in 12 loci identified in recent genome-wide association studies in European-derived populations that were associated with type 2 diabetes or BMI (FTO) for association with type 2 diabetes in a large African American population. There is very limited evidence that any of these European-derived genome-wide association studies SNPs contribute to diabetes in African Americans. In contrast, significant association with type 2 diabetes was observed with the previously described TCF7L2 SNP rs7903146. TCF7L2 has been the focus of multiple investigations and is one of the most highly replicated type 2 diabetes candidate genes in several populations (1–5). Few publications have examined the influence of TCF7L2 on type 2 diabetes risk in African Americans. In this study, we expand on the previous investigation from our center by Sale et al. (8), which described compelling evidence of association with type 2 diabetes for polymorphisms in this gene. From the results of these studies and the convincing replication of association with type 2 diabetes in European-derived populations, a more comprehensive study of TCF7L2 polymorphisms in African Americans is warranted. Paraphetically, this observation of strong association gives us confidence that the ascertainment and diagnoses used to recruit these African American subjects are accurate and the analyses of the European-derived type 2 diabetes loci presented here are valid.
Of all the other loci examined, the only nominally significant association with type 2 diabetes in African Americans before admixture adjustment was observed with the SNPs located in \textit{CDKAL1} and \textit{LOC387761}. If one takes into consideration that multiple SNPs were genotyped, any standard multiple-comparisons correction suggests that the evidence for association is very modest. Both rs10946398 and rs7754840 have been previously associated with type 2 diabetes in European-derived populations (3,4,6). In addition, other publications have also reported evidence of association in this region, making \textit{CDKAL1} one of the most highly replicated genes identified from recent WGA studies (2,5). Measures of linkage disequilibrium between rs10946398 and rs7754840 in African Americans (D’ = 1.00; r² = 0.996) were similar to those reported in European Americans (6). In contrast, the frequencies of rs10946398 and rs7754840 risk allele (C for both) differed substantially between African American (0.60, 0.60), Yoruba in Ibaden, Nigeria (YRI) (0.67, 0.67), and Utah residents with ancestry from northern and western Europe (CEU) (0.31, 031) populations. In addition, \textit{FTO} SNP rs8050136 was previously associated with BMI (7); however, we found no evidence of association with this trait in any genetic model.

The genotyping data have been evaluated for association with type 2 diabetes taking into consideration the European-African admixture of African Americans. We have adjusted association statistics using estimates of individual proportions of European and African ancestry for each subject. This approach may under- or overestimate the true association at each locus because the difference in allele frequencies between the ancestral populations might vary at each marker, and, thus, the adjustment for an individual genome may overestimate or underestimate admixture at a specific site. Thus, it is possible in this dataset that stronger evidence of association might be revealed by a locus-specific analysis. Given the magnitude of the great majority of the P values observed here (Table 2), this influence would have to be very substantial to adjust the P values into the range suggesting association.

Even though all of the SNPs examined in this study showed highly significant association with type 2 diabetes in European-derived populations, we found limited evidence of association with these markers in African Americans. For some of these SNPs, we have limited power to detect evidence of association given the sample sizes, allele frequencies, and effect sizes (Table 2) (supplementary Table 3). There is, however, reasonable power to detect association for a number of the SNPs. It is important to note that these conventional power analyses reflect the power to detect association at a single locus. If one takes into consideration the overall study, we would have expected to see evidence of association with four to five loci at \( \alpha = 0.05 \).

Another caveat to this study is that we have tested only one to three SNPs per gene that were highly associated in European-derived populations. Ongoing extensive analyses of individual genes, a pending genome-wide association study in these samples, and genotyping in additional samples of case and control subjects will further clarify the role of these loci in the African American diabetic population. The absence of association that was observed in this study may, however, be attributable to differences in genetic risk factors that exist between African and European-derived populations. Moreover, multiple other type 2 diabetes susceptibility genes reported in populations with European descent fail to show association in African-derived samples (9).

Disparities in allele frequencies between different ethnic groups may impair our ability to observe true associations if they exist in African Americans. For example, the type 2 diabetes risk allele reported by recent WGA studies for \textit{CDKNA2A/CDKNA2B} SNPs rs10811661 and rs564398, \textit{ID1/ KIF11/HHEX} SNP rs7923837, and \textit{LOC387761} SNP rs7480010 have frequencies of 1.00, i.e., are monomorphic, in the YRI population of the HAPMAP project (20) (Table 3). This observation presumes that Yoruba subjects are representative of all African populations. We have compared these sequences with chimpanzee and other available primate sequences, but no common pattern of sequence variation is apparent. Presumably, the non-African alleles for these loci are the result of European admixture, which is not great enough to provide an observable level of protection from type 2 diabetes. The observation that these loci are nonpolymorphic in Africans and that solely Africans have the risk allele suggests that these loci may, in part, contribute to the increased overall prevalence of type 2 diabetes in African-derived populations compared with that in European-derived populations. Thus, the appropriate conclusion from this study is that these European type 2 diabetes susceptibility loci do not measurably contribute to differential susceptibility in the African-American population.

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