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Admixture mapping and fine-mapping of birth weight loci in the Black Women's Health Study

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Abstract

Several genome-wide association studies (GWAS) have identified genetic variants associated with birth weight. To date, however, most GWAS of birth weight have focused primarily on European ancestry samples even though prevalence of low birth weight is higher among African Americans. We conducted admixture mapping using 2,918 ancestral informative markers in 2,596 participants of the Black Women's Health Study, with the goal of identifying novel genomic regions where local African ancestry is associated with birth weight. In addition, we performed a replication analysis of 11 previously identified index single nucleotide polymorphisms (SNPs), and fine-mapped those genetic loci to identify better or new genetic variants associated with birth weight in African Americans. We found that high African ancestry at 12q14 was associated with low birth weight, and we identified multiple independent birth weight-lowering variants in this genomic region. We replicated the association of a previous GWAS SNP in *ADRB1* and our fine-mapping efforts suggested the presence of new birth weight-associated variants in *ADRB1*, *HMGA2*, and *SLC2A4*. Further studies are needed to determine whether birth weight-associated loci can in part explain race-associated birth weight disparities.

Keywords

Birth weight; African Americans; genetics; admixture mapping; fine-mapping

INTRODUCTION

Genome-wide association studies (GWAS) have identified genetic polymorphisms involved in human birth weight (Beaumont et al. 2018; Freathy et al. 2010; Horikoshi et al. 2016; Horikoshi et al. 2013; Urbanek et al. 2013). Most of these previous GWAS have primarily

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included individuals of European ancestry. Little is known about the genetic basis of birth weight in African Americans, even though this population group has twice the prevalence (13.1%) of low birth weight (<2,500 g) compared to white (7.0%) and Hispanic Americans (7.1%) (Hamilton et al. 2015). Low birth weight continues to be a significant public health problem in the United States and is associated with a range of short and long-term adverse health consequences (Hack et al. 1995; Risnes et al. 2011; Whincup et al. 2008).

Using data from the Black Women's Health Study (BWHS) we examined whether African ancestry is associated with birth weight, and carried out genome-wide admixture mapping to identify genomic loci with local African ancestry associated with birth weight. In addition, we conducted a genetic replication study of the associations between ten GWAS-identified index single nucleotide polymorphisms (SNPs) for birth weight, as well as fine-mapping of these loci to further refine these purported genetic associations in an African American sample and shed light onto the genetics of birth weight disparities.

METHODS

Study Population

The BWHS is an ongoing prospective cohort that enrolled 59,000 African American women aged 21–69 years starting in 1995 (Rosenberg et al. 1995). Study participants filled out health questionnaires that included demographics, medical and reproductive history, body weight, height, diet, smoking, physical activity, education, and other factors. The current study was approved by the Institutional Review Boards of Boston University and the University at Buffalo.

We studied BWHS participants who were selected as controls for a nested case-control study of genes and environment in relation to type 2 diabetes and obesity risk. The participants must have provided a DNA sample, completed the birth weight questions on the 1997 questionnaire, and never reported a diagnosis of type 2 diabetes. Information on DNA collection and processing has been previously published (Cozier et al. 2004).

Birth weight measurement

Study participants were asked to report their own birth weight in pounds and ounces on the 1997 BWHS questionnaire. We conducted a birth weight validation study among 637 BWHS participants born in Massachusetts using birth registry data from the Massachusetts Department of Public Health to corroborate self-reported data on birth weight (Ruiz-Narvaez et al. 2014). The Pearson correlation coefficient was 0.88 between self-reported birth weight and birth registry data. In addition, the reproducibility of self-reported birth weight in a subset of 776 BWHS participants who completed the 1997 questionnaire two times showed a Pearson correlation coefficient of 0.96 for duplicate self-reported birth weight (Ruiz-Narvaez et al. 2014). These results are in agreement with previous studies (Michels et al. 1996; Troy et al. 1996) demonstrating the validity of retrospectively collected self-reported birth weight.

Birth weight-associated SNP selection

We searched for index SNPs for the present analysis by looking into the Early Growth Genetics (EGG) Consortium GWAS meta-analysis in primarily European-ancestry subjects (Horikoshi et al. 2013) and the GWAS catalog of the National Human Genome Research Institute (NHGRI) and European Bioinformatics Institute (EBI) (<https://www.ebi.ac.uk/gwas/>) queried in October 2013. We selected ten SNPs all reported by the EGG Consortium GWAS (Horikoshi et al. 2013): seven SNPs associated with birth weight at genome-wide level significance ($P < 5 \times 10^{-8}$), and three additional SNPs with $5 \times 10^{-8} < P < 5 \times 10^{-6}$. After our custom-genotyping array was designed and genotyping was carried out, the EGG Consortium published a larger GWAS that identified 60 loci (including the seven from the earlier EGG GWAS) associated with birth weight at $P < 5 \times 10^{-8}$ (Horikoshi et al. 2016). Two of these new SNPs are close to two of our selected ten loci (17p13 and 22q13). Then, we added an additional SNP at 17p13 to our analysis. The newly identified SNP at 22q13 is monomorphic in African ancestry populations and therefore, it was not included in our analysis. Supplementary Table 1 shows the final list of eleven SNPs in ten loci that were analyzed in the present work.

Tagging SNPs for fine-mapping were selected for each of these genomic regions (± 100 kb around each index SNP) in order to capture (at $r^2 \geq 0.9$) all SNPs with minor allele frequency (MAF) $\geq 5\%$, based on the African populations in 1000 Genomes Project.

Ancestral informative markers

2,918 autosomal ancestral informative markers (AIMs) from the Affymetrix Axiom Genomic Database were included in the SNP array. These AIMs have large frequency differences between African and European ancestry populations from the 1000 Genomes Project.

Genotyping and quality control

Samples were genotyped on an Affymetrix Axiom 45K custom array (Affymetrix, Santa Clara, CA, USA), designed to include genes and single nucleotide polymorphisms (SNPs) related to type 2 diabetes and obesity. The array also included ancestral informative markers. Genotyping was carried out at the Affymetrix laboratory (Santa Clara, CA, USA). The Axiom array data underwent extensive QC procedures carried out by Affymetrix and Slone Epidemiology Center. We removed about 13% of samples due to high missing call rates ($> 5\%$) and poor reproducibility. In addition, we excluded about 17% of SNPs because of poor cluster properties, high missing call rates ($> 10\%$), deviation of Hardy-Weinberg proportions ($p < 1 \times 10^{-5}$ in controls), or discordance between duplicate samples. After these exclusions, the final dataset included 2,596 individuals and 38,008 SNPs, including 4,738 selected for the current analysis.

After genotyping, we performed SNP imputation using the Michigan imputation server (<https://www.imputationserver.sph.umich.edu>) with the 1000 Genomes Project phase 3 African population reference panel. Imputation resulted in 10,897 SNPs with MAF $\geq 2\%$ and info score ≥ 0.5 for analysis at the birth weight loci.

Admixture mapping

We used ADMIXMAP software version 3.8.3103 (Hoggart et al. 2004) to estimate African locus-specific ancestry and identify genomic regions with differential ancestry associated with continuous birth weight in grams. The analysis was adjusted for global individual admixture, age, years of education (12, 13–15, 16), geographic region of residence (Northeast, South, Midwest, West), and genotyping batch. Statistical significance was assessed using Z statistics, with a threshold of $|Z| > 4.0$ considered genome-wide statistically significant. A positive Z-score indicates that African ancestry at a particular locus is associated with higher birth weight; a negative Z-score indicates that African ancestry is associated with low birth weight.

Replication of index SNPs and fine-mapping of birth weight loci

Analyses for both the replication study and fine-mapping were performed using SNPTest (Marchini et al. 2007). We used linear regression to estimate beta parameters (β , change of birth weight in grams per copy of effect allele) and 95% confidence intervals (CI) of the association between genetic variants and birth weight. β parameters were adjusted for same covariates as in the admixture mapping scan. Within each birth weight locus we corrected for multiple testing using the simpleM method (Gao et al. 2008), which estimates the effective number of independent tests using a principal component analysis approach.

RESULTS

Table 1 shows characteristics of the BWHS study participants in total and by tertiles of birth weight categories. Mean birth weight was 3,157 g and mean African ancestry was 77.8%. Tertiles of birth weight were similar with respect to baseline characteristics.

Global African ancestry was not associated with birth weight; β (95% CI) per 10% increase of African ancestry was equal to -1 g (-23 g, 20 g) $p = 0.91$. However, admixture mapping identified a genome-wide significant locus at 12q14 with high local African ancestry associated with low birth weight (Figure 1; $Z = -4.7$, $p = 2.4 \times 10^{-6}$). The admixture signal ($|Z| \geq 4.0$) extended over a region of 7.4 Mb (Supplementary Table 2). Fine-mapping of the identified admixture region identified two independent SNPs, rs9739580 and rs10878313 ($r^2 < 0.01$ in African ancestry populations from 1000 Genomes Project), associated with birth weight (Table 2). Effect alleles at rs9739580 and rs10878313 were associated with 116 g and 128 g lower birth weight, respectively. These birth weight-lowering alleles were more frequent in African (AFR) ancestry populations compared to European (EUR) ancestry populations (Table 2). To elucidate whether rs9739580 and rs10878313 explain the admixture signal at 12q14, we performed the admixture mapping scan adjusting for these two SNPs. The admixture peak disappeared after adjustment for rs9739580 and rs10878313 ($Z = -1.0$, $p = 0.30$).

Table 3 shows the results from the replication analysis of the 11 index SNPs. Only three SNPs showed associations with birth weight in this study. The first one, rs1801253 in *ADRB1* at 10q25, had the same direction of association with birth weight as previously reported GWAS. The β coefficient for each copy of the effect G-allele was -40 g (vs -20 g

from GWAS). The second SNP, rs1042725 in *HMGA2* at 12q14, showed an opposite direction of association with birth weight as previous GWAS. The β coefficient for each copy of the effect T-allele was 36 g (vs -23 g from GWAS). The third SNP, rs113086489 in *SLC2A4/CLDN7* at 17p13, also had an opposite direction of association compared to the reported GWAS. The β coefficient for each copy of the effect C-allele was 42 g (vs -15 g from GWAS).

We identified new locus-wide significant associations at three birth weight loci (Table 4 and Supplementary Figure 1). At 10q25, we identified a low frequency allele (G) at rs145063088 associated with higher birth weight ($\beta=260$ g, $p=2.9\times10^{-5}$). At 12q14, we found rs6581664 to be associated with birth weight. The effect T-allele was associated with lower birth weight ($\beta=-83$ g, $p=1.1\times10^{-4}$). Lastly, a deletion at rs145481098 on 17p13 was associated with lower birth weight ($\beta=-218$ g, $p=5.2\times10^{-5}$). Using summary statistics downloaded from the NHGRI-EBI GWAS catalog (<https://www.ebi.ac.uk/gwas/>), we found that the fetal rs6581664 was not associated with birth weight in European ancestry populations (β of the T-allele = 2 g, $p = 0.61$, $N = 67,786$) (Horikoshi et al. 2016), but the maternal rs6581664 was associated with higher birth weight of the offspring (β of the T-allele = 10 g, $p = 0.023$, $N = 48,632$) (Beaumont et al. 2018). The other two new SNPs, rs145063088 at 10q25 and rs145481098 at 17p13, are monomorphic in European ancestry populations.

DISCUSSION

In the present study, we conducted whole-genome admixture mapping and fine-mapping of 11 previously GWAS-identified birth weight loci in 2,596 African American women, who are participants in the Black Women's Health Study.

Admixture mapping

To our knowledge, ours is the first birth weight whole-genome admixture mapping scan. Although global African ancestry was not associated with birth weight, we found that higher local African ancestry at 12q14 was associated with lower birth weight. This admixture signal at 12q14 seems to be explained by the two SNPs (rs9739580 and rs10878313) identified by us in the present work. This region includes the *HMGA2* gene, which belongs to the High Mobility Group A (HMGA) chromatin architectural factors that are highly expressed during development of the embryo (Sgarra et al. 2018). *HMGA2* carries GWAS-identified SNPs associated with phenotypes from different stages of life such as birth weight (Horikoshi et al. 2016; Horikoshi et al. 2013), birth and infant length (van der Valk et al. 2015), childhood height (Weedon et al. 2007), and type 2 diabetes (Mahajan et al. 2014; Morris et al. 2012; Ng et al. 2014; Voight et al. 2010; Zhao et al. 2017) and anthropometric traits (Carty et al. 2012; He et al. 2015; Justice et al. 2017; N'Diaye et al. 2011; Shungin et al. 2015; Soranzo et al. 2009; Weedon et al. 2007) in adulthood. It is noteworthy that SNPs associated with risk of type 2 diabetes (Ng et al. 2014) and adult height (N'Diaye et al. 2011) in African Americans were also associated with birth weight in our population. For example, the rs343092 T-allele associated with higher risk of type 2 diabetes (Ng et al. 2014) was associated with a decrease of 78 g in birth weight ($p=1.2\times10^{-3}$), and the rs7979673 T-allele associated with low adult height (N'Diaye et al. 2011) was associated with a decrease

of 69 g in birth weight ($p=8.1\times 10^{-4}$). Although both SNP associations did not survive correction for multiple testing, they highlight the genetic link between growth and type 2 diabetes. Both birth weight-lowering alleles are more frequent in African ancestry populations compared to European ancestry populations (rs343092 T-allele frequency in AFR = 0.94 vs EUR = 0.17; and rs7979673 T-allele frequency in AFR = 0.35 vs EUR = 0.04), as well as the birth weight-lowering alleles of SNPs rs10878313 and rs6581664 (see Tables 2 and 4). The fact that these four SNPs are uncorrelated in African ancestry populations ($r^2 < 0.1$ for any pair of SNPs), suggests that multiple independent birth weight-lowering variants in or near the *HMGA2* gene may explain in part the higher prevalence of low birth weight in African Americans relative to European-ancestry Americans.

In addition to variants in *HMGA2*, our admixture mapping approach identified intronic SNP rs9739580 in the *TBC1D30* gene, which codes for a small G protein and is highly expressed in fetal and adult brain (Nagase et al. 1999). A single GWAS has found evidence of association of SNP rs939876 ($r^2=0.03$ with our identified birth weight SNP rs9739580) with cognitive performance (Cirulli et al. 2010). Ours is the first study to report the presence of a birth weight-associated SNP in the *TBC1D30* gene.

Replication and fine-mapping

We were able to replicate the association of the index SNP rs1801253 with birth weight in the *ADRB1* gene, which codes for the $\beta 1$ -adrenergic receptor protein that is highly expressed in lungs, heart, and brain, and mediates the action of catecholamines in the sympathetic nervous system (Mottet et al. 2016). The birth weight-lowering minor G-allele has higher frequency in African ancestry populations compared to European ancestry populations (0.43 vs 0.32, respectively). The magnitude of our effect estimate was twice the effect reported in GWAS (40 g vs 20 g lower birth weight, respectively) (Horikoshi et al. 2013). We also found evidence of an independent signal tagged by SNP rs145063088. The minor G-allele, which has a frequency of 2% in African ancestry populations and is absent in European populations (i.e. the SNP is monomorphic), was associated with higher birth weight.

The association of rs1801253 (a nonsynonymous Arg389Gly variation) with birth weight links prenatal growth with blood pressure in adulthood since the same SNP has been widely found associated with blood pressure and hypertension. In particular, the minor Gly-allele (G-allele in the DNA sequence) has been associated with low systolic and diastolic blood pressure as well as low risk of hypertension (Johnson et al. 2011; Wang et al. 2013). Epidemiological associations between birth weight and blood pressure make up some of the strongest evidence supporting the fetal origins of adult disease. Most studies report a linear inverse association throughout the birth weight distribution, whereby lower birth weight is associated with higher adult blood pressure (Mu et al. 2012). There is also evidence that birth weights at the high end of the distribution are associated with higher blood pressure (Gamborg et al. 2007). Based on these studies, one might expect the blood pressure-raising Arg-allele to be associated with lower birth weight. However, we found the Gly instead of the Arg allele to be associated with lower birth weight. The same results as ours were reported by the GWAS of the EGG Consortium (Horikoshi et al. 2016; Horikoshi et al.

2013). Evidence from the EGG consortium suggests that effects of maternal genotype during fetal development may explain in part the *ADRB1* genetic association between low birth weight and low blood pressure (Horikoshi et al. 2016). Unfortunately, we did not have maternal genotype data to test this hypothesis in our study.

We found GWAS index SNP rs1042725 in the *HMGA2* gene to be associated with birth weight in the opposite direction as previously reported (Horikoshi et al. 2013).

A deletion in the *SLC2A4* gene was associated with a large reduction in birth weight (about 217 g). The deletion, which has a frequency of 3% in African ancestry populations and is absent in European populations (i.e. the SNP is monomorphic), may play a role in the higher prevalence of low birth weight in African Americans. *SLC2A4* codes for an insulin-regulated glucose transporter, and it is expressed in a wide range of tissues including adipose and skeletal muscle. Genetic variants in or near *SLC2A4* have been associated with serum metabolite levels (Kettunen et al. 2012) and blood pressure (Warren et al. 2017).

Our study sheds light on the genetic basis of birth weight in African Americans, as GWAS of birth weight have been based mostly in European ancestry subjects (Beaumont et al. 2018; Freathy et al. 2010; Horikoshi et al. 2016; Horikoshi et al. 2013; Urbanek et al. 2013). Although a recent GWAS from the EGG consortium analyzed data from about 153,781 subjects including 6,635 African American individuals, results from African Americans were not separately reported (Horikoshi et al. 2016). The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study performed GWAS in 4,281 newborns from four ethnic groups including 1,095 Afro-Caribbean babies (Urbanek et al. 2013). The HAPO GWAS found a genome-wide significant result at 3q25 in the combined sample, although there was no evidence of association in the Afro-Caribbean group alone. We also did not find any suggestion of association with birth weight in the 3q25 locus.

One limitation of our study is that our sample size restricts power to identify small genetic associations with birth weight using a purely agnostic GWAS approach. Power limitations were circumvented to some extent by using admixture mapping and fine-mapping approaches, which have a lower multiple testing burden compared to GWAS. Because of our relatively small sample size, we must also interpret with caution our positive associations. Another limitation is the use of self-reported birth weight many years after the fact. However, our validation study showed high correlations between self-reported birth weight and birth registry data (Ruiz-Narvaez et al. 2014). We also did not have data on maternal metabolic status during pregnancy or maternal genotypes, and therefore we were unable to control for those unmeasured variables. Finally, the present study did not include novel recent birth weight loci identified in the two most recent GWAS (Beaumont et al. 2018; Horikoshi et al. 2016) because our custom genotyping array was designed before publication of these GWAS.

In summary, our genome-wide admixture mapping identified multiple birth weight-lowering variants at the 12q14 genomic region via both admixture mapping and fine-mapping of GWAS loci. All of these alleles were more frequent in African ancestry populations relative to European ancestry populations, and they may explain in part the genetic basis of the high

prevalence of low birth weight in African Americans. We replicated the association of the index SNP in the *ADRB1* gene, and found evidence of independent new birth weight-associated variants in the *ADRB1*, *HMGA2*, and *SLC2A4* genes. Future research should expand our findings to further uncover the genetic basis of birth weight in African American populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Admixture mapping results of birth weight in the Black Women's Health Study. The X-axis indicates the chromosome number, and the Y-axis shows P-values in logarithmic scale. Positive values in the Y-axis denote local African ancestry associated with high birth weight, and negative values mean local African ancestry associated with low birth weight. We identified a genome-wide significant association between local African ancestry at 12q14 and low birth weight (arrow).

Table 1

Baseline characteristics (1995) of BWHS participants, by birth weight.

Characteristic	Overall	Tertiles of birth weight		
		T1	T2	T3
No. of women	2,596	835	838	923
Birth weight g, mean (SD)	3,157 (666)	2,453 (455)	3,129 (158)	3,820 (388)
Age years, mean (SD)	40.0 (10.0)	40.0 (9.7)	39.3 (10.0)	40.5 (10.1)
Education >12 years, n (%)	2,277 (87.7)	730 (87.4)	743 (88.7)	804 (87.1)
African ancestry %, mean (SD)	77.8 (12.0)	78.0 (12.0)	77.8 (11.9)	77.5 (12.3)
Region of residence, n (%)				
Northeast	662 (25.5)	221 (26.5)	213 (25.4)	228 (24.7)
South	862 (33.2)	279 (33.4)	282 (33.7)	301 (32.6)
Midwest	631 (24.3)	203 (24.3)	196 (23.4)	232 (25.1)
West	441 (17.0)	132 (15.8)	147 (17.5)	162 (17.6)

Table 2
Associations of independent SNPs with birth weight at the admixture peak at 12q14.

SNP	Position	Alleles ^a	EAF ^b			$\beta^{d,e}$ (95% CI)	P value
			BWHS	AFR ^c	EUR ^c		
rs9739580	65244114	C/T	0.52	0.69	0.02	-116 g (-166 g, -68 g)	2.7×10^{-6}
rs10878313	66058670	A/G	0.71	0.91	0.23	-128 g (-186 g, -69 g)	1.9×10^{-5}

^aEffect allele/reference allele

^bEffect allele frequency

^cAFR and EUR = African and European populations from 1000 Genomes Project, respectively

^dThe β value is the change in grams per effect allele

^e β adjusted for % African ancestry, age, years of education, geographic region of residence, and genotyping batch

Table 3

Associations of birth weight GWAS index SNPs in the Black Women's Health Study.

Gene	Chromosome	SNP	Alleles ^b	EAF ^c		BWHs results		
				BWHs	AFR ^d	EUR ^d	β^e (95% CI)	P value
<i>ADCY5</i>	3q21	rs9883204	C/T	0.68	0.65	0.81	1 g (-38 g, 40 g)	0.96
<i>CCNLI</i>	3q25	rs900400	C/T	0.26	0.24	0.39	3 g (-39 g, 45 g)	0.90
<i>LCORL</i>	4p15	rs724577	C/A	0.68	0.67	0.71	-2 g (-41 g, 37 g)	0.90
Unknown	5q11	rs4432842	C/T	0.72	0.81	0.27	-12 g (-53 g, 29 g)	0.57
<i>CDKALI</i>	6p22	rs6931514	G/A	0.24	0.26	0.28	7 g (-35 g, 50 g)	0.74
<i>CALCR</i>	7q21	rs7780752	T/C	0.87	0.93	0.66	26 g (-30 g, 82 g)	0.36
<i>ADRB1</i>	10q25	rs1801253	G/C	0.40	0.43	0.32	-40 g (-78 g, -3 g)	0.03
<i>HMG2</i>	12q14	rs1042725	T/C	0.39	0.34	0.54	36 g (-2 g, 74 g)	0.06
<i>SLC24A4/CLDN7</i>	17p13	rs5415	T/C	0.12	0.06	0.31	16 g (-43 g, 74 g)	0.60
<i>SLC24A4/CLDN7</i>	17p13	rs113086489	C/T	0.61	0.65	0.45	42 g (5 g, 80 g)	0.03
<i>CENPM</i>	22q13	rs758511	A/G	0.08	0.03	0.27	-13 g (-84 g, 59 g)	0.72

^aThe β value is the change in grams per effect allele^bEffect allele/reference allele^cEffect allele frequency^dAFR and EUR = African and European populations from 1000 Genomes Project, respectively^e β adjusted for % African ancestry, age, years of education, geographic region of residence, and genotyping batch

Table 4
Locus-wide significant SNPs associated with birth weight in the Black Women’s Health Study at GWAS-identified loci.

Gene	Chromosome	SNP	Alles ^a	EAf ^b			$\beta^{d,e}$ (95% CI)	r ² with index SNP ^f	Locus-wide alpha-level	P value
				BWHS	AFR ^c	EUR ^c				
<i>ADRB1</i>	10q25	rs145063088	G/A	0.02	0.02	0.0	260 g (138 g, 382 g)	NA, 0.01	1.0×10 ⁻⁴	2.9×10 ⁻⁵
<i>HMGGA2</i>	12q14	rs6581664	T/A	0.49	0.56	0.19	-83 g (-126 g, -41 g)	<0.01, <0.01	1.3×10 ⁻⁴	1.1×10 ⁻⁴
<i>SLC24A4</i>	17p13	rs145481098	Del/Ins	0.03	0.03	0.0	-218 g (-323 g, -112 g)	NA, <0.01	1.0×10 ⁻⁴	5.2×10 ⁻⁵

^aEffect allele/reference allele
^bEffect allele frequency
^cAFR and EUR = African and European populations from 1000 Genomes Project, respectively
^dThe β value is the change in grams per effect allele
^e β adjusted for % African ancestry, age, years of education, geographic region of residence, and genotyping batch
^fCorrelation with index SNP in European and African populations from 1000 Genomes Project, respectively