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Genome-wide admixture and association study of serum iron, ferritin, transferrin saturation and total iron binding capacity in African Americans

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Iron is an essential component of many important proteins and enzymes, including hemoglobin, which is responsible for carrying oxygen to the cells. African Americans (AAs) have a greater prevalence of iron deficiency compared with European Americans. We conducted genome-wide admixture-mapping and association studies for serum iron, serum ferritin, transferrin saturation (SAT) and total iron binding capacity (TIBC) in 2347 AAs participating in the Jackson Heart Study (JHS). Follow-up replication analyses for JHS iron-trait associated SNPs were conducted in 329 AA participants in the Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS). Higher estimated proportions of global African ancestry were significantly associated with lower levels of iron ($P = 2.4 \times 10^{-5}$), SAT ($P = 0.0019$) and TIBC ($P = 0.042$). We observed significant associations ($P < 5 \times 10^{-8}$) between serum TIBC levels and two independent SNPs around *TF* on chromosome 3*,* the first report of a genome-wide significant second independent signal in this region, and SNPs near two novel genes: *HDGFL1* on chromosome 6 and *MAF* on chromosome 16. We also observed significant associations between ferritin levels and SNPs near *GAB3* on chromosome X. We replicated our two independent associations at *TF* and our association at *GAB3* in HANDLS. Our study provides evidence for both shared and unique genetic risk factors that are associated with iron-related measures in AAs. The top two variants in *TF* explain 11.2% of the total variation in TIBC levels in AAs after accounting for age, gender, body mass index and background ancestry.

INTRODUCTION

Iron is critical to an array of metabolic functions, such as oxygen transport and oxidative phosphorylation. Normally, small daily losses of iron in the feces and through menstruation are balanced by its regulated intestinal absorption and its recovery from heme after phagocytosis of senescent red blood cells (RBCs) (1). Iron deficiency can cause anemia, while iron overload may lead to increased risk for cardiovascular disease, including cardiomyopathy, diabetes mellitus, arthritis and liver disease (2). Laboratory tests typically used to assess iron transport and storage include serum iron, total iron binding capacity (TIBC), transferrin saturation (SAT) and serum ferritin. Ferritin, the predominant iron storage protein, reflects the cumulative iron stores in the bone marrow and tissues. Transferrin functions in iron transport, and the concentration of transferrin is proportional to the TIBC in serum. Transferrin SAT, calculated as (serum iron/TIBC) × 100, is affected by the rate of iron absorption in

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the small bowel as well as the sufficiency of tissue iron stores. Genetic factors could affect iron metabolism through gastrointestinal absorption, transport, tissue uptake, storage or remobilization from tissue stores, and thus could have a large impact on the variation of these iron-related measures (2,3).

Genome-wide association studies (GWAS) have identified seven loci associated with these measures in subjects of European descent ($P < 5 \times 10^{-8}$) (4–7), including variants in or near *TF-SRPRB, SLC17A1, HFE, HIST1H2BJ, SIK3, PCSK7* and *TMPRSS6*. Here, we present a genome-wide admixture and association study of serum iron, TIBC, SAT and ferritin among African Americans (AAs) enrolled in the Jackson Heart Study (JHS) and Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) cohorts.

RESULTS

Descriptive statistics for the JHS and HANDLS participants included in this study are detailed in Table 1. The correlations between these four phenotypes in JHS are shown in Supplementary Material, Table S1.

Admixture analyses

A higher level of estimated overall average African ancestry was significantly associated ($P < 0.05$) with lower levels of TIBC, iron and SAT (Table 2). No individual region had local ancestry significantly associated with the iron measures. Three regions (*DZIP1L* on chr 3, *TRDN* on chr 6 and *TMCO5B-RYR3* on chr 15) had a LOD score >3 for TIBC and one region (*DEFB129-DEFB132* on chr 20) had a LOD score >3 for iron. The plots of the LOD scores across the whole genome are shown in Supplementary Material, Figure S1a–d.

Summary GWAS results in JHS

One-hundred-fifty-seven SNPs reached genome-wide significance ($P < 5 \times 10^{-8}$) for TIBC (153 SNPs on chromosome 3, 3 SNPs on chromosome 6 and 1 SNP on chromosome 16); five SNPs were significant for ferritin (all on chromosome X) (Supplementary Material, Table S2). No SNPs reached genome-wide significance for serum iron or SAT. Top results for all four traits are listed in Supplementary Material, Tables S3–S6. Manhattan plots and quantile–quantile (Q–Q) plots for the four traits are shown in Supplementary Material, Figures S2–S5. Q–Q plots revealed no substantial evidence for inflated results, due to population stratification, residual relatedness among subjects or experimental outliers.

TIBC GWAS results on chromosome 3

All top SNPs on chromosome 3 clustered within a region spanning <150 kb containing three genes: *TOPBP1*, *TF* and *SRPRB* (Fig. 1A). The strongest signal [rs8177253, $P = 1.8 \times 10^{-47}$, minor allele frequency (MAF) = 0.24] mapped to the *TF* gene, which encodes transferrin (Table 3). Rs8177253 was also nominally (defined as unadjusted $P < 0.05$) associated with SAT ($P = 3.0 \times 10^{-7}$). Thirty-six *TF* region SNPs were genome-wide significant for TIBC levels after multi-SNP analyses, including rs8177253 as a covariate (Supplementary Material, Table S7). The top SNP in the conditional analysis was rs9872999 ($P = 5.4 \times 10^{-20}$, MAF = 0.38), which was not significant ($P = 1.0 \times 10^{-6}$) prior to the adjustment for rs8177253 (Table 3 and Fig. 1B). There was no evidence of an interaction between rs8177253 and rs9872999 ($P = 0.11$). No SNPs remained genome-wide significant after covariate adjustment for both rs8177253 and rs9872999, although a large number of SNPs remained nominally significant (Supplementary Material, Table S8). SNPs rs8177253 and rs9872999 together explained an estimated 11.2% of the total variance of TIBC after accounting for age, gender, BMI and the first 10 PCs.

Higher local African ancestry at rs8177253 in the *TF* region was nominally associated with lower TIBC levels ($P = 0.0012$). The association between TIBC and rs8177253 remained robust after the adjustment for local African ancestry at rs8177253. When stratified by the estimated local number of European versus African chromosomes, the rs8177253–TIBC association was present among 1579 AA who were predicted to carry

Table 2. Association between global African ancestry estimate and phenotypes

Phenotypes	β[a]	SE	*P*-value
TIBC	−13.90	6.80	0.04
log_ferritin	0.13	0.13	0.32
log_iron	−0.20	0.05	2.4E-05
log_SAT	−0.15	0.05	0.0019

[a] The predicted change in the iron measure for each one-percentage point increase in estimated global African ancestry.

Table 1. Descriptive statistics of JHS and HANDLS participants

	JHS Total	Male	Female	HANDLS Total	Male	Female
Sample size	2347	1012	1335	329	189	140
Age (years)	54.5 ± 12.6	53.0 ± 12.8	55.7 ± 12.4	49.4 ± 8.3	49.0 ± 8.7	49.9 ± 7.7
BMI (kg/m^2)	31.5 ± 6.9	29.9 ± 6.1	32.8 ± 7.3	28.8 ± 7.6	27.1 ± 5.4	31.2 ± 9.3
Ferritin (ng/ml)	134.0 (74.0, 232.0)	177.5 (110.8, 286.0)	105 (58.0, 185.5)	107.5 (54.0, 201.0)	137.0 (76.0, 257.0)	71.0 (35.0, 113.0)
Iron (μg/dl)	81.0 (67.0, 98.0)	86.0 (70.0, 104.0)	78.0 (64.0, 94.0)	83.0 (66.2, 103.8)	86.0 (70.0, 109.0)	81.0 (64.0, 98.0)
SAT (%)	28.0 (23.0, 35.0)	30.0 (25.0, 37.0)	27.0 (22.0, 33.0)	25.0 (20.2, 31.1)	26.4 (20.8, 33.5)	23.7 (19.3, 27.3)
TIBC (μg/dl)	284 (260.0, 314.0)	280.0 (256.0, 307.0)	288.0 (263.0, 319.0)	332.0 (306.0, 372.0)	326.0 (300.0, 368.0)	342.5 (316.8, 379.0)

Note: data are mean ± SE, median (25th, 75th percentiles).
SAT, transferrin saturation; TIBC, total iron binding capacity.

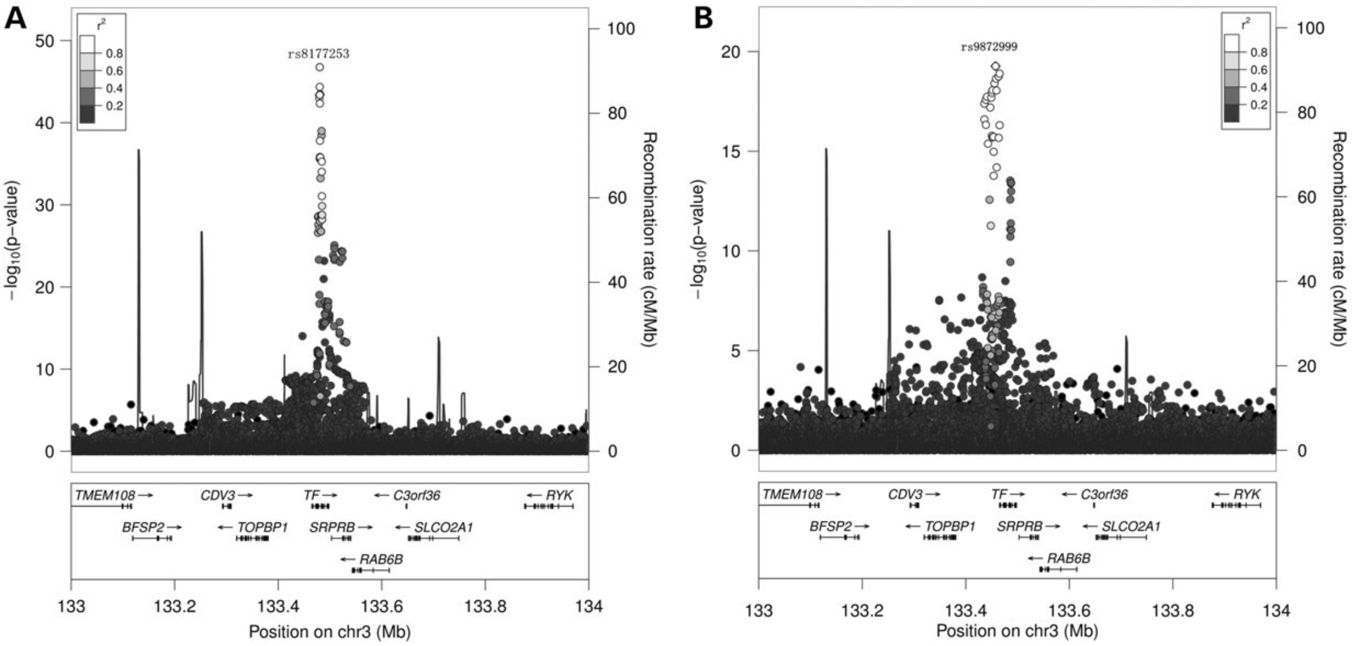

Figure 1. (**A**) Regional plot of the $-\log_{10}(P)$ values for the SNPs in the *TF* region for TIBC. The *X*-axis shows the human genome build 19 coordinates (Mb) and the genes in the region. The *Y*-axis shows the $-\log_{10}$ transformed association *P*-values of SNPs on the left, and recombination rates in cM per Mb on the right. Different colors of shading indicate the strength of linkage disequilibrium (LD) (r^2) between the top SNP and the other SNPs tested in the region. (**B**) Regional plot of the $-\log_{10}(P)$ values for the SNPs in the *TF* region for TIBC after adjusting for the top SNP rs8177253 in this region. The top SNP was rs9872999 after adjusting for rs8177253.

two African chromosomes ($\beta = 19.64 \pm 1.70$; $P = 8.5 \times 10^{-30}$) as well as the 768 AA who were predicted to carry at least one European chromosome ($\beta = 19.68 \pm 2.26$; $P = 1.8 \times 10^{-17}$). The rs9872999–TIBC association also remained significant after adjustment for both rs8177253 and local African ancestry at the genotyped marker nearest its location (data not shown).

TIBC GWAS results on chromosome 6

The three genome-wide significant SNPs on chromosome 6 mapped near the *HDGFL1* gene (Supplementary Material, Fig. S6). The strongest signal (rs115923437, $P = 1.1 \times 10^{-8}$) mapped ∼100 Kb distal to *HDGFL1*, which is a gene that encodes hepatoma-derived growth factor-like 1 and is associated with glycosylated hemoglobin level, and ∼3.5 Mb proximal to the known iron gene *HFE*. After conditioning on rs115923437, the remaining SNPs within 1 Mb of the SNP no longer showed strong evidence for association (all $P > 1 \times 10^{-4}$). SNP rs115923437 explained 1.3% of the total variance of TIBC after accounting for the covariates.

Local African ancestry near rs115923437 was also nominally associated with TIBC, although this time higher local African ancestry was associated with higher TIBC levels ($P = 0.0083$). The associations between TIBC and rs115923437 remained significant after the adjustment for local African ancestry at the genotyped marker nearest its location. When stratified by the estimated local number of European versus African chromosomes, the rs115923437–TIBC association was present among the 1569 AA who were predicted to carry two African chromosomes ($\beta = -14.11 \pm 2.95$; $P = 2.0 \times 10^{-6}$), as well as the 778 AA who were predicted to carry at least one European chromosome ($\beta = -15.42 \pm 5.78$; $P = 0.0070$).

TIBC GWAS results on chromosome 16

A single SNP (rs16951289, $P = 2.0 \times 10^{-8}$) on chromosome 16, an intronic variant in uncharacterized gene *LOC102467146* that is ∼150 Kb distal to the *MAF* gene (Supplementary Material, Fig. S7), reached genome-wide significance. *MAF* encodes v-maf musculoaponeurotic fibrosarcoma oncogene homolog. Local African ancestry in this region was not associated with TIBC ($P = 0.97$) and did not modify the evidence for association with rs16951289. Rs16951289 explained 1.2% of the total variance of TIBC.

Ferritin GWAS results on chromosome X

Five SNPs on chromosome X near the *GAB3* gene reached genome-wide significance for association with ferritin levels (Fig. 2). The strongest signal (rs141555380, $P = 1.1 \times 10^{-8}$) mapped to the UTR-3 region of the *GAB3* gene. *GAB3* encodes GRB2-associated binding protein 3, which is involved in several growth factor and cytokine signaling pathways. After conditioning on rs141555380, the remaining SNPs within 1 Mb of rs141555380 no longer showed significant evidence for association (all $P > 1 \times 10^{-4}$). The effect estimates for carriers of the rs141555380 minor allele in stratified analysis were similar for hemizygous males and homozygous females (hemizygous males: $\beta = 0.17 \pm 0.04$, $P = 5.05 \times 10^{-6}$; homozygous females: $\beta = 0.14 \pm 0.05$, $P = 0.002$). SNP rs141555380

Table 3. Top SNPs that reached genome-wide significance ($P < 5 \times 10^{-8}$) in JHS and replication results from HANDLS

Trait	Chr	Nearest gene	SNP	Pos(hg19)	EA	JHS EAF	N	R^2	β	SE	*P*	HANDLS EAF	N	R^2	β	SE	*P*
TIBC	3	*TF*	rs8177253	133480192	T	0.24	2347	NA	19.86	1.34	1.8E−47	0.23	329	0.98	26.72	4.91	1.1E−07
TIBC	3	*TF*	rs9872999	133457514	T	0.62	2347	0.80	−6.55	1.34	1.1E−06	0.60	329	0.93	−14.19	4.33	0.0012
TIBC	3	*TF*	rs9872999*	133457514	T	0.62	2347	0.80	−11.72	1.28	5.4E−20	0.60	329	0.93	−19.11	4.16	6.2E−06
TIBC	6	*HDGFL1*	rs115923437	22678302	C	0.06	2347	0.91	14.84	2.6	1.1E−08	0.05	329	0.96	−5.28	9.93	0.60
TIBC	16	*MAF-DYNLRB2*	rs16951289	79790621	T	0.07	2347	0.91	13.38	2.38	2.0E−08	0.08	329	0.97	−15.95	7.92	0.04
Log_ferritin	X	*GAB3*	rs141555380	153906012	T	0.14	2347	0.94	0.17	0.03	1.1E−08	0.13	329	0.98	0.24	0.08	0.0057

*: β, SE, and *P* were reported for rs9872999 after adjusting for rs8177253.
Chr, chromosome; Pos(hg19), physical position of the SNP according to human genome build version 19; EA, effect allele; EAF, effect allele frequency; β, β coefficients representing the estimated change in the raw or transformed trait value associated with each additional copy of the effect allele; SE, standard error; R^2, R^2 represents the imputation quality provided. "NA" indicates that the actual genotype data from the Affy 6.0 array were used in the analyses.

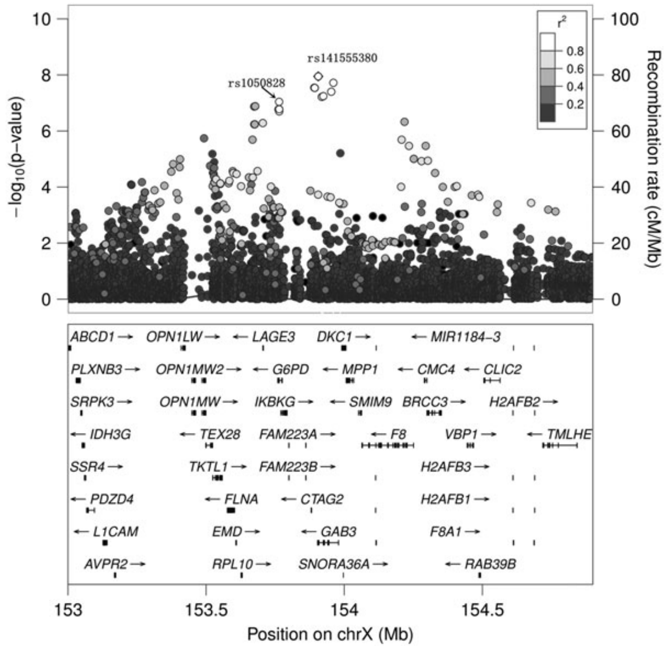

Figure 2. Regional plot of the $-\log_{10}(P)$ values for the SNPs in the *GAB3* region for log_ferritin.

explained 1.2% of the total variance of ferritin after accounting for age, gender, BMI and the first 10 PCs.

Menopause status-adjusted analyses of association with ferritin

Association analysis for serum ferritin was conducted by including menopausal status as an additional covariate. Menopausal status was significantly associated with serum ferritin levels $P = 5.3 \times 10^{-17}$; however, the effect size and significance of SNP-ferritin associations did not change considerably after adjusting for menopausal status. The top SNP rs141555380 ($P = 1.1 \times 10^{-8}$) continued to be the most significant SNP after adjusting for menopause status ($P = 1.4 \times 10^{-8}$). The effect sizes and *P*-values of top SNPs ($P < 10^{-7}$) before and after adjusting for menopause status are shown in Supplementary Material, Table S9. This result is consistent with previous findings that the effects of variation in menstrual blood loss, although significant, were small when compared with the genetic effects that influence the iron reserves (8).

Replication results in HANDLS

Four regions contained SNPs that reached genome-wide significance in JHS, including one region, the chromosome 3 *TF* region, which contained a second significant SNP (rs9872999) after covariate adjustment for the top SNP (rs8177253). Five SNPs (rs8177253, rs9872999, chromosome 6 top SNP rs115923437 and chromosome 16 top SNP rs16951289 for TIBC; chromosome X top SNP rs141555380 for ferritin) were selected and tested for association in HANDLS to determine whether the associations could be replicated (Table 3). Rs9872999 was tested before and after adjustment for rs8177253. Both associations in the *TF* region with TIBC were replicated ($P = 1.1 \times 10^{-7}$ for rs8177253; $P = 0.0012$ for rs9872999 before adjusting for rs8177253). As with JHS, the association between rs9872999 and TIBC became more significant after adjusting for the primary signal at rs8177253 ($P = 6.2 \times 10^{-6}$). The association between the *GAB3* region SNP rs141555380 and ferritin also replicated ($P = 5.7 \times 10^{-3}$). The associations between TIBC and SNPs rs115923437 and rs16951289 did not replicate in HANDLS; rs16951289 was nominally significant ($P = 0.04$), but the direction of the effect went in the opposite direction to that observed in JHS.

Prior European GWAS-established signals at $P < 5 \times 10^{-8}$ that are replicated in JHS at $P < 0.05$

GWAS have reported five regions to contain SNPs to be significantly associated ($P < 5 \times 10^{-8}$) with at least one of the following iron-related traits: iron, ferritin, SAT and transferrin, including *TF-SRPRB* (rs3811647*,* rs1830084)*, SLC17A1* (rs17342717), *HFE* (rs1799945 [H63D] and rs1800562 [C282Y]), *HIST1H2BJ* (rs13194491) and *TMPRSS6* (rs855791 [V736A] and rs4820268) in subjects of European descent (Table 4). Iron, ferritin and SAT are directly reported in the current study, while TIBC is proportional to transferrin [TIBC (μmol/L) = 25.1 × transferrin (g/L)]. All five regions contained a SNP, either the index SNP in the prior report or a SNP in strong linkage disequilibrium (defined as a SNP with estimated $r^2 > 0.8$ with the index SNP based on CEU 1000 Genomes subjects) with the index SNP, that was nominally associated with at least one corresponding iron measure in JHS at $P < 0.05$. For *HFE* rs1800562, only the associations with ferritin and transferrin were replicated, but not the associations with iron and SAT. For *HIST1H2BJ* rs13194491 and *TMPRSS6* rs855791, the associations with the index SNPs were not replicated, but nearby SNPs, which are estimated to be in high LD with the index SNPs in European populations, did reach nominal significance in JHS, suggesting a narrowing of the candidate regions for the causal variants if the causal variants are the same for the two populations.

DISCUSSION

We conducted genome-wide admixture and association studies for iron-related phenotypes, including serum iron, serum ferritin, SAT and TIBC in 2347 AAs participating in the JHS. We observed significant associations between SNPs around *TF,* a well-established region on chromosome 3, and two novel regions: near *HDGFL1* on chromosome 6 and *MAF* on chromosome 16, and TIBC levels. Conditional analyses revealed a second significant SNP associated with TIBC in the *TF* region that was independent of the top SNP from the unconditional analyses. We also observed significant associations between SNPs around *GAB3*, a novel region on chromosome X, and ferritin levels. The two independent associations for TIBC at *TF* and the association for ferritin at *GAB3* were successfully replicated in HANDLS. The associations between the JHS index SNPs near *HDGFL1* and *MAF* were not replicated. The available sample size in HANDLS ($N = 329$) was considerably smaller than for JHS. If we assume the index variants at *HDGFL1* and *MAF*

Table 4. Replication of signals established in prior GWAS including subjects of European descent

Trait	Chr	Index SNP result in JHS[a]							Most significant SNP in JHS[b]								Nearest gene
		Index SNP	Pos(hg19)	EA	EAF	β	SE	*P*	Most significant SNP	Pos(hg19)	EA	EAF	β	SE	*P*	LD r^2	
TIBC	3	rs3811647*(7)	133484029	A	0.22	17.55	1.43	9.7E−35	rs8177253	133480192	T	0.24	19.86	1.34	1.8E−47	1	*TF*
TIBC	3	rs1830084(7)	133508464	T	0.16	16.84	1.60	2.2E−25	rs1830084	133508464	T	0.16	16.84	1.60	2.2E−25	1	*TF*
log_ferritin	6	rs17342717*(4)	25821770	T	0.02	0.24	0.10	0.02	rs78273613*	25866075	G	0.02	0.26	0.10	0.01	0.88	*SLC17A1*
log_iron	6	rs1799945*(5)	26091179	G	0.04	0.08	0.03	7.8E−04	rs129128	26125342	C	0.03	0.09	0.02	1.0E−04	0.92	*HFE*
log_iron	6	rs1800562(7)	26093141	A	0.01	−0.03	0.04	0.37	rs1800562	26093141	A	0.01	−0.03	0.04	0.37	1	*HFE*
log_ferritin	6	rs1800562(4)	26093141	A	0.01	0.20	0.10	0.05	rs1800562	26093141	A	0.01	0.20	0.10	0.05	1	*HFE*
TIBC	6	rs1800562(7)	26093141	A	0.01	−24.63	5.13	1.7E−06	rs1800562	26093141	A	0.01	−24.63	5.13	1.7E−06	1	*HFE*
log_sat	6	rs1800562(7)	26093141	A	0.01	0.05	0.04	0.14	rs1800562	26093141	A	0.01	0.05	0.04	0.14	1	*HFE*
log_sat	6	rs13194491*(7)	27037080	T	0.02	0.02	0.05	0.75	rs35657082*	27067657	T	0.01	0.25	0.11	0.02	0.91	*HIST1H2BJ*
log_iron	22	rs855791*(11)	37462936	G	0.83	0.03	0.01	0.08	rs2072860*	37470604	A	0.73	0.03	0.01	7.7E−03	0.90	*TMPRSS6*
log_sat	22	rs855791*(11)	37462936	G	0.83	0.02	0.01	0.15	rs4820268*	37469591	A	0.73	0.02	0.01	0.03	0.90	*TMPRSS6*
log_iron	22	rs4820268*(5)	37469591	A	0.73	0.03	0.01	8.4E−03	rs9610638*	35775614	C	0.80	0.05	0.02	3.5E−03	0.83	*TMPRSS6*

*Imputed.

() besides "Index SNP" contains the citation to the initial association study for each individual variant.

[a] Index SNP: Index SNP that was reported to be significantly ($P < 5 \times 10^{-8}$) associated with iron traits in prior GWAS in subjects of European descent.

[b] Most significant SNP: the proxy for index SNP (LD $r^2 > 0.8$ in CEU 1000G with the index SNP) with the smallest association *P*-value in JHS.

LD r^2: r^2 with index SNP in CEU 1000G subjects.

each explain an estimated 1.3% of the total variance of TIBC, then we only had power of 0.34 to observe these associations at $P < 0.01$ in HANDLS. Thus, larger replication studies will be necessary to make more decisive statements regarding the overall evidence of these other regions. We did not observe any significant SNP associations for the other iron measures, although we were able to replicate associations from previous studies based on subjects of European descent using a less stringent significance threshold ($P < 0.05$).

The estimated average ("global") proportion of African ancestry was significantly associated with lower levels of TIBC, serum iron and SAT—which are entirely consistent with previous findings reporting lower levels of these same measures, on average, in AAs compared with European Americans (9,10). Subjects with higher levels of global African ancestry were observed to have higher levels of ferritin, also consistent with prior reported differences between individuals of European and African ancestry (9,10), although this result was not statistically significant. These results implicate novel genetic risk factors in AAs and underscore the importance of studying this population for genetic risk factors that uniquely/disproportionately impact them. Local ancestry was not significantly associated with any iron measures, although a couple of regions containing our GWAS top results were nominally significant.

Variants in and around *TF* have been observed to be associated with serum ferritin levels (7), transferrin levels (5–7), serum transferrin saturation (11) and serum levels of carbohydrate-deficient transferrin (12) in subjects of European descent. In JHS, the top SNP at *TF*, rs8177253, was associated with TIBC ($P = 1.8 \times 10^{-47}$) and nominally associated with SAT ($P = 3.0 \times 10^{-7}$). SNP rs8177253 is located in an intronic region of *TF* and is in high LD ($r^2 = 1$, $D' = 1$ in 1000 Genomes CEU) with GWAS index SNP rs3811647 previously reported to be associated with transferrin in subjects of European and Australian descent (7,9) [rs3811647 is also associated with TIBC ($P = 9.7 \times 10^{-35}$) and nominally associated with SAT ($P = 2.2 \times 10^{-6}$) in JHS]. After conditioning on rs8177253, all SNPs, including rs3811647, reported to be significantly associated with TIBC in previous studies became non-significant in JHS.

Our study is the first study to report a second significant independently associated SNP in the *TF* region for TIBC. Interestingly, this second signal (index SNP rs9872999 which maps to an intergenic region ~10 Kb proximal to *TF*) only became significant at the genome-wide level after conditioning on our top *TF* region SNP rs8177253. Rs8177253 and rs9872999 are in modest LD in 1000 Genomes YRI subjects ($r^2 = 0.07$, $D' = 0.58$) and in stronger LD in 1000 Genomes CEU subjects ($r^2 = 0.27$, $D' = 0.71$). The allele associated with an increase in TIBC for rs8177253 is preferentially on the same haplotype with the allele associated with a decrease in TIBC for rs9872999. Thus, the mean effects for rs9872999 are shrunk toward the null when not factoring in genotype for rs8177253. There is no evidence for an interaction between these SNPs on TIBC levels; thus the results indicate a second independent signal in the *TF* region. The MAF for rs9872999 is 0.39 in 1000 Genomes YRI subjects and 0.50 in 1000 Genomes CEU subjects. It is unclear if this second signal is specific to AAs, as results from conditional analyses in other populations have not been reported. Conditional analyses would likely be especially important for detecting significant mean effects for rs9872999 in populations of European descent given the stronger LD between the two SNPs in this population.

Variants in *HDGFL1* have been reported previously to be associated with glycosylated hemoglobin levels ($P = 2.4 \times 10^{-5}$) in European type 1 diabetic subjects (13) and nominally associated ($P < 0.05$) with levels of VLDL, LDL, Apolipoprotein C, HDL and carotid artery disease (14–16). In recent years, there has been considerable interest in the possibility that excessive tissue iron stores may contribute to the pathogenesis of both diabetes and ischemic heart disease (3). *MAF*, which encodes v-maf musculoaponeurotic fibrosarcoma oncogene homolog, appears to be important in early development. Mutations in *MAF* have been reported to co-segregate with cerulean congenital cataracts (17) and juvenile-onset pulverulent cataract (18) in human pedigrees. We can find no evidence in the literature suggesting a direct connection between *MAF* and iron metabolism. However, there is some evidence of pleiotropy for iron metabolism and cataracts, namely hereditary hyperferritinemia cataract syndrome, which is an inherited syndrome caused by a mutation within the L-ferritin gene and characterized by early-onset cataracts and elevated serum ferritin (19).

A cluster of SNPs near *GAB3* on chromosome X were significantly associated with ferritin (top SNP rs141555380, MAF = 0.14, $P = 1.1 \times 10^{-8}$) and nominally associated with SAT (rs141555380, $P = 0.037$). Although no prior studies observed any connection between this gene and iron metabolism, another gene ~0.2 Mb upstream of *GAB3*, *G6PD,* plays a critical role in iron metabolism. *G6PD* deficiency may cause acute hemolysis or severe chronic non-spherocytic hemolytic anemia. Increases in serum ferritin levels have been observed in *G6PD*-deficient patients (20,21), which is possibly due to both a shortened life span and increased break down of erythrocytes in *G6PD*-deficient patients. A functional missense variant in *G6PD*, rs1050828 (MAF = 0.13, leading to a Val68Met amino acid substitution), was also associated with ferritin but narrowly missed genome-wide significance ($P = 9.1 \times 10^{-8}$). Strong LD exists between this functional variant at *G6PD* and rs141555380 ($R^2 = 0.91$, $D' = 1$ in 1000 Genomes Project participants of African descent), and the association between rs141555380 and ferritin disappears after adjustment for rs1050828 ($P = 0.55$). Rs1050828 and nearby rs762516 (two SNPs in LD: $R^2 = 0.68$, $D' = 1.0$ in HapMap YRI) have been shown to be significantly associated with multiple erythrocyte traits in AAs, including hematocrit, hemoglobin, RBC count, mean corpuscular volume (MCV) and red cell distribution width (RDW) in previous GWAS or candidate gene studies (22,23). In JHS, rs1050828 is significantly associated with MCV ($P = 1.7 \times 10^{-8}$), RBC count ($P = 9.9 \times 10^{-16}$) and RDW ($P = 8.9 \times 10^{-21}$) and nominally associated with hematocrit ($P = 8.7 \times 10^{-7}$) and hemoglobin (7.1×10^{-8}). Ferritin levels are correlated with levels of hematocrit ($r = 0.25$), hemoglobin ($r = 0.27$), MCV ($r = 0.089$), RBC ($r = 0.15$) and RDW ($r = -0.13$). The associations for both hematocrit ($P = 2.9 \times 10^{-8}$) and hemoglobin ($P = 4.3 \times 10^{-10}$) both became genome-wide significant after additional covariate adjustment for ferritin. Similarly, the association between rs1050828 and ferritin also became genome-wide significant after adjustment for hematocrit (7.2×10^{-9}) and hemoglobin (1.3×10^{-9}), but evidence for association with ferritin decreased after covariate adjustment for MCV (1.1×10^{-4}), RBC (5.2×10^{-6}) and RDW (7.2×10^{-3}). Since *G6DP* has been reported to play an important role in hemolysis and affects the levels of erythrocyte traits, the signal we observed at this region may help explain the relationship between hemolysis and iron metabolism. This variant is also implicated in malaria resistance, and the A-form of G6PD deficiency in Africa is under strong natural selection from the preferential protection it provides to hemizygous males and homozygous females against life-threatening malaria (24). This natural selection of G6PD deficiency in African descent may help explain some of the marked differences in iron measures among ethnic groups.

In summary, we report that global genetic admixture is an important predictor of iron measures in AAs, further implicating the importance of unique genetic effect alleles in the AA population. We observed SNPs in or near three genes, *TF*, *HDGFL1* and *MAF,* which were significantly associated with TIBC in JHS, and SNPs near *GAB3* that were significantly associated with ferritin. We identified a novel second independently associated SNP in the *TF* region for TIBC that was only identified after conditioning on the top SNP in the region. The two *TF* signals and the *GAB3* signal were replicated in a small independent AA sample from HANDLS. Larger replication samples will be necessary to draw firm conclusions regarding the associations for the other loci. The *TF* region is known to be associated with various serum iron-related measures in subjects of European descent; we now show similar associations in AA. While the *G6DP-GAB3* region is known to be associated with multiple erythrocyte traits in AA, this is the first time it has been reported to be significantly associated with ferritin, a specific iron-related measure. We have also nominally replicated four other established loci from other populations in our AA samples. Future fine-mapping studies, including rare and uncommon variants, and functional studies should be undertaken to better characterize these and other loci and to identify the functional variants directly influencing iron levels in AA.

MATERIALS AND METHODS

Study subjects

Discovery stage

The JHS is a longitudinal, population-based cohort designed to identify risk factors for the development of cardiovascular disease, diabetes, obesity, chronic kidney disease and stroke in more than 5000 AAs from the Jackson, metropolitan area (25). The design, recruitment and initial characterization of this study have been described previously (26). The JHS participants for the current study included 1012 AA males and 1335 AA females with available iron-related measures and genome-wide genotype data.

Replication stage

The HANDLS is a community-based, longitudinal epidemiological study that aims to examine the influences of race and socioeconomic status on the development of age-related diseases in African and European Americans from the city of Baltimore. The study consists of 2200 AAs and 1522 European Americans aged 30–64 years. The design, recruitment and initial characterization of this study have been described previously (27). The HANDLS participants for the current study included 329 AAs with iron measures and genome-wide genotype data.

JHS and HANDLS participants provided written informed consent. The study protocols and consent forms for these studies were approved by the responsible research ethics committees and institutional research boards.

Phenotypes

All phenotype measures came from blood samples that were collected from fasting blood during the baseline examination, which occurred during 2000–2004 for JHS and 2004–2009 for HANDLS. Iron measures included total levels of serum iron (μg/dl), serum ferritin (ng/ml), TIBC (μg/dl) and SAT (%). Serum iron in JHS participants was measured by the FerroZine colorimetric assay (Roche), standardized to NIST traceable iron standards and calibrated against control sera from the manufacturer. TIBC was determined by colorimetric (FerroZine) measurement of iron that remains unbound after addition of a known amount of iron to the serum. The assay was standardized and calibrated as for serum iron. Ferritin was measured by an immunoturbidimetric assay (Roche) based on agglutination of anti-ferritin-latex conjugates, standardized with human spleen ferritin and calibrated against a standard protein solution provided by the manufacturer. For HANDLS, serum iron and TIBC were measured using standard clinical laboratory spectrophotometric assays. Serum ferritin was measured using chemiluminescence assays. For both studies, SAT was calculated as: (serum iron/TIBC)*100%.

Participants were excluded if they were taking iron supplements, or not fasting at time of blood draw or if they had known chronic infectious or inflammatory disease, or residual cancer. Additional exclusions included hematocrit <35%, hemoglobin <11 g/dl, mean red cell volume >100 fl, white blood cell count >11 000 per mm^3, platelet count >400 000 per mm^3, C-reactive protein >3 standard deviations above the mean or transferrin saturation <15% (indicates iron deficiency likely due to blood loss).

Genotyping and imputation

A total of 3030 JHS participants were genotyped using the Affymetrix Genome-Wide Human SNP Array 6.0. 874 712 SNPs, with a call rate >0.95, MAF >0.01 and genotype distributions consistent with the Hardy–Weinberg equilibrium (HWE, $P > 1 \times 10^{-5}$) were included for further analysis. Following pre-phasing using MACH 1.0.18 software (28), 38 million SNPs, excluding SNPs monomorphic in CEU/YRI, were imputed using minimac (29) based on 1000 Genome Project phase I reference samples (November 2010, Version 3). Analyses were limited to the ∼17 million imputed SNPs with estimated imputation quality of $r^2 > 0.3$.

A total of 1024 HANDLS participants were genotyped using the Illumina 1 M SNP array, including 329 AAs with iron measures. SNPs with HWE $P > 1 \times 10^{-7}$, MAF > 0.01 and call rate > 95% were included for further analysis. 2 939 993 SNPs were imputed using MACH (28) and Minimac (29) software based on combined reference haplotype data from HapMap Phase 2 CEU + YRI samples that includes monomorphic SNPs in either of the two constituent populations (release 22, build 36.3). Chromosome X variants were imputed based on 1000 Genomes Project EUR + AFR + AMR + ASN reference samples. Only index variants demonstrating significant evidence for association in JHS ($P < 5 \times 10^{-8}$) were subsequently analyzed for the relevant iron phenotype in HANDLS.

Statistical analyses

To assess the impact of genetic admixture on iron measures within the AA population, we first estimated the genome-wide average of African ancestry for each JHS participant ("global ancestry"). We used the software ADMIXTURE (30) with $K = 2$ clusters and tested, using linear models implemented in R, whether this estimated global ancestry proportion was associated with each of our iron measures after covariate adjustment for age, sex and BMI. Values of serum ferritin, total iron and SAT were natural log-transformed to achieve approximate normality of residuals.

ANCESTRYMAP (31) was used to estimate local ancestry (probabilities of whether an individual has 0, 1 or 2 alleles of European ancestry) at 738 831 autosomal SNPs across the genome, for each participant in JHS, as previously described (32). In brief, local ancestry was inferred using a hidden Markov model based on the genotypes from a panel of densely spaced markers differentiated in frequency between African and European populations. To assess whether there were any regions where local ancestry was associated with iron-related measures, we performed admixture mapping across the whole genome by regressing each of our iron measures on the local ancestry estimates at each SNP location, including covariate adjustment for age, sex, BMI and estimated global ancestry. The conventionally reported LOD score, defined as the log, base 10, ratio of the maximum likelihood of the data under a local-ancestry-associated model divided by the likelihood of the data under the null model (with no local ancestry predictor), was computed at each SNP location. For regions showing association of increased African ancestry with higher levels of iron measures, the LOD scores were assigned positive values, and for regions showing association of increased African ancestry with lower level of iron measures, the LOD scores were assigned negative values. The LOD scores were plotted across the genome, and a LOD score of 5 was assumed to be the threshold of statistical significance (31).

Individual genotyped and imputed SNPs were tested for association using multivariable linear regression models in PLINK (33) and MACH2QTL v.1.08 (28), respectively; adjusted for age, sex, BMI and 10 principal components that we constructed using the software EIGENSOFT (34) to model background ancestry. A second level of covariate adjustment for log-ferritin additionally included self-reported menopausal status, which was available on a large subset of JHS subjects and has been shown previously to be a strong predictor of serum ferritin levels (8,35). We assumed an additive mode of inheritance and reported β coefficients representing the estimated change in the raw or transformed trait value associated with each additional copy of the effect allele. For chromosome X SNPs, hemizygous males were modeled so that males with the minor allele had the same value as females homozygous for the minor allele. We used a significance threshold of $P = 5 \times 10^{-8}$ to maintain an overall type 1 error rate of ∼5% for each phenotype.

Manhattan plots were made to illustrate the association results across the genome and Q–Q plots were made to assess any systematic inflation of the regression test statistics across the genome. In regions demonstrating significant evidence for association, we examined multivariable regression models that included the genotype data of the most strongly associated SNP as a covariate to assess whether there was any evidence for multiple independently associated SNPs in a particular region. If a second signal also reached genome-wide significance after conditioning on the top variant, multivariable regression models were repeated to include the genotypes of both SNPs as covariates. The relevant SNP–SNP interactions were also tested. Region-specific ("locus-zoom") plots were made to show the magnitude of association between all SNPs and the relevant iron phenotype as well as the LD between each SNP in the region and the most strongly associated SNP (36). Finally, to control for possible confounding between SNP genotype and local ancestry in any observed iron trait-SNP associations, we identified the genetic position of the most strongly associated SNP, selected the local ancestry estimate at the location closest to that SNP (either the SNP itself if genotyped or the closest genotyped SNP) and examined multivariable regression models as described above, but now including estimated local ancestry proportion as an additional covariate.

SNPs that reached genome-wide significance in JHS were selected for testing in the replication study of HANDLS. At each associated region, only the single SNP with the most significant *P*-value (index SNP) was selected to avoid over adjustment for multiple testing. For the *TF* region, where conditional analyses revealed a second independently associated SNP with TIBC, the second independent SNP was also included in the replication analyses. A GWAS result was considered replicated if the effect in the replication was in the same direction as in the discovery stage, and if the association in the replication stage was statistically significant after Bonferroni correction adjusting for the number of SNPs tested.

Ethnic differences in iron-related measures have also been observed between subjects of European and African descent (9). Thus, we compared our association results in JHS with established variants from GWASs in populations of European descent in order to assess the importance of these same variants in an AA population. For each prior GWAS-established SNP, we identified and tested all genotyped or imputed proxy SNPs in JHS that were estimated to be in high LD ($r^2 > 0.8$ in CEU based on 1000 Genomes data) with the GWAS index SNPs for association with the reported iron phenotype.

SUPPLEMENTARY MATERIAL

Supplementary Material is available at *HMG* online.

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Conflict of Interest statement. None declared.

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Supplementary Table 1. Correlation between phenotypes

	TIBC	log_ferritin	log_iron	log_sat
TIBC	1.00	-0.32	0.20	-0.29
log_ferritin		1.00	0.08	0.23
log_iron			1.00	0.88
log_sat				1.00

Supplementary Table 2. SNPs associated with any iron trait at P<5x10^{-8}

Chr	Nearest Gene	MARKER	Pos(hg19)	Trait	EA	EAF	β	SE	*P*	Imputed(Y/N)	R^2	Function
3	*TOPBP1-TF*	rs113549909	133414194	TIBC	T	0.19	-10.13	1.69	2.15E-09	Y	0.75	intergenic
3	*TOPBP1-TF*	rs72972269	133414687	TIBC	T	0.18	-10.09	1.69	2.37E-09	Y	0.76	intergenic
3	*TOPBP1-TF*	rs113656013	133415112	TIBC	T	0.18	-10.04	1.69	2.55E-09	Y	0.77	intergenic
3	*TOPBP1-TF*	rs16840652	133419849	TIBC	T	0.18	-9.59	1.61	2.34E-09	Y	0.84	intergenic
3	*TOPBP1-TF*	rs4437139	133421781	TIBC	T	0.66	7.40	1.26	4.35E-09	Y	0.95	intergenic
3	*TOPBP1-TF*	rs6769437	133422504	TIBC	G	0.66	7.34	1.25	4.45E-09	Y	0.96	intergenic
3	*TOPBP1-TF*	3:133422542:AC_A	133422542	TIBC	A	0.65	7.01	1.26	2.89E-08	Y	0.93	intergenic
3	*TOPBP1-TF*	rs4419374	133423473	TIBC	T	0.35	-7.37	1.23	2.67E-09	N	NA	intergenic
3	*TOPBP1-TF*	rs4854745	133423975	TIBC	G	0.66	7.70	1.26	1.09E-09	Y	0.94	intergenic
3	*TOPBP1-TF*	rs4854746	133424325	TIBC	C	0.66	7.37	1.27	5.85E-09	Y	0.93	intergenic
3	*TOPBP1-TF*	rs9830153	133426570	TIBC	G	0.66	7.58	1.32	8.55E-09	Y	0.86	intergenic
3	*TOPBP1-TF*	rs58448410	133426694	TIBC	C	0.18	-9.22	1.60	7.88E-09	Y	0.85	intergenic
3	*TOPBP1-TF*	rs58327809	133427871	TIBC	G	0.18	-9.26	1.60	7.26E-09	Y	0.84	intergenic
3	*TOPBP1-TF*	rs3935228	133428824	TIBC	C	0.66	7.85	1.35	6.60E-09	Y	0.81	intergenic
3	*TOPBP1-TF*	rs9830001	133433470	TIBC	G	0.31	7.05	1.28	4.34E-08	N	NA	intergenic
3	*TOPBP1-TF*	rs74639761	133433523	TIBC	G	0.10	-12.91	2.16	2.24E-09	Y	0.84	intergenic
3	*TOPBP1-TF*	rs79799101	133433773	TIBC	T	0.10	-13.90	2.25	6.35E-10	Y	0.81	intergenic
3	*TOPBP1-TF*	rs16840692	133433900	TIBC	A	0.10	-12.76	2.10	1.13E-09	Y	0.89	intergenic
3	*TOPBP1-TF*	rs16840699	133437601	TIBC	T	0.13	-9.69	1.76	3.79E-08	Y	1.00	intergenic
3	*TOPBP1-TF*	rs4582061	133438026	TIBC	A	0.10	-11.87	2.01	4.19E-09	N	NA	intergenic
3	*TOPBP1-TF*	rs11717407	133438264	TIBC	G	0.10	-11.90	2.02	4.08E-09	Y	0.99	intergenic
3	*TOPBP1-TF*	3:133440155:GA_G	133440155	TIBC	G	0.14	-10.02	1.76	1.25E-08	Y	0.90	intergenic
3	*TOPBP1-TF*	3:133440157:AT_A	133440157	TIBC	A	0.13	-10.78	1.85	5.32E-09	Y	0.87	intergenic
3	*TOPBP1-TF*	rs145713832	133445820	TIBC	C	0.51	-8.14	1.49	4.63E-08	Y	0.62	intergenic
3	*TOPBP1-TF*	rs192259748	133445956	TIBC	A	0.14	-10.54	1.79	4.19E-09	Y	0.88	intergenic
3	*TOPBP1-TF*	rs4854748	133446881	TIBC	T	0.19	-12.38	1.60	9.50E-15	Y	0.88	intergenic
3	*TOPBP1-TF*	rs4854749	133447397	TIBC	A	0.14	-10.44	1.78	4.03E-09	Y	0.88	intergenic
3	*TOPBP1-TF*	rs4854750	133447489	TIBC	G	0.14	-10.14	1.76	8.77E-09	Y	0.89	intergenic
3	*TOPBP1-TF*	rs4854752	133447571	TIBC	G	0.14	-10.74	1.79	2.07E-09	Y	0.87	intergenic
3	*TOPBP1-TF*	rs142438877	133448336	TIBC	A	0.14	-10.90	1.81	1.68E-09	Y	0.87	intergenic
3	*TOPBP1-TF*	rs150209289	133448351	TIBC	T	0.15	-9.80	1.74	1.72E-08	Y	0.87	intergenic
3	*TOPBP1-TF*	rs10935081	133451352	TIBC	T	0.14	-9.98	1.70	4.15E-09	Y	0.96	intergenic
3	*TOPBP1-TF*	3:133452109:A_AG	133452109	TIBC	AG	0.14	-10.18	1.69	1.70E-09	Y	0.97	intergenic
3	*TOPBP1-TF*	rs4241356	133452444	TIBC	G	0.14	-9.77	1.68	5.57E-09	Y	0.98	intergenic

3	*TOPBP1-TF*	rs4854755	133452671	TIBC	A	0.15	-9.47	1.68	1.59E-08	Y	0.95	intergenic
3	*TOPBP1-TF*	rs10935083	133453827	TIBC	C	0.10	-12.40	2.02	7.63E-10	Y	0.94	intergenic
3	*TOPBP1-TF*	rs4854595	133454182	TIBC	T	0.14	-9.95	1.71	5.56E-09	Y	0.94	intergenic
3	*TOPBP1-TF*	rs6801244	133454847	TIBC	A	0.14	-10.05	1.71	4.00E-09	Y	0.94	intergenic
3	*TOPBP1-TF*	rs148959957	133456056	TIBC	T	0.14	-10.18	1.74	4.51E-09	Y	0.91	intergenic
3	*TOPBP1-TF*	rs139374172	133458144	TIBC	G	0.15	-10.22	1.74	4.55E-09	Y	0.89	intergenic
3	*TOPBP1-TF*	rs147634092	133458182	TIBC	G	0.14	-10.33	1.75	3.75E-09	Y	0.89	intergenic
3	*TF*	rs8177185	133464618	TIBC	A	0.10	-12.67	2.07	9.42E-10	Y	0.88	upstream
3	*TF*	rs8177186	133465201	TIBC	T	0.10	-12.64	2.07	1.06E-09	Y	0.88	UTR5
3	*TF*	rs4428180	133466374	TIBC	G	0.13	-9.97	1.83	4.71E-08	Y	0.89	intronic
3	*TF*	rs4532136	133466885	TIBC	A	0.10	-12.70	2.07	9.16E-10	Y	0.88	intronic
3	*TF*	rs76351673	133468306	TIBC	G	0.04	17.72	3.16	2.07E-08	Y	0.88	intronic
3	*TF*	rs8177224	133474003	TIBC	G	0.18	9.60	1.51	2.62E-10	N	NA	intronic
3	*TF*	rs12769	133474328	TIBC	A	0.14	9.47	1.71	3.19E-08	Y	0.98	exonic
3	*TF*	rs6797713	133474832	TIBC	C	0.19	9.39	1.52	5.96E-10	Y	0.97	intronic
3	*TF*	rs1799852	133475722	TIBC	T	0.06	-16.43	2.43	1.80E-11	N	NA	exonic
3	*TF*	rs8177232	133475787	TIBC	C	0.20	-9.17	1.47	5.91E-10	N	NA	exonic
3	*TF*	rs8177232	133475787	TIBC	C	0.20	-9.09	1.47	5.96E-10	Y	1.00	exonic
3	*TF*	rs8177235	133476083	TIBC	A	0.06	-17.69	2.48	1.37E-12	N	NA	intronic
3	*TF*	rs3811658	133476852	TIBC	T	0.17	17.26	1.59	2.55E-27	Y	0.94	intronic
3	*TF*	rs8177240	133477701	TIBC	G	0.17	17.36	1.57	2.64E-28	Y	0.95	intronic
3	*TF*	rs8177241	133477961	TIBC	T	0.05	19.12	2.69	1.45E-12	N	NA	intronic
3	*TF*	rs41295782	133478388	TIBC	A	0.02	27.61	4.76	6.74E-09	Y	1.00	intronic
3	*TF*	rs6762415	133478557	TIBC	G	0.41	12.33	1.22	4.72E-24	Y	0.91	intronic
3	*TF*	rs8177243	133478578	TIBC	C	0.02	27.61	4.76	6.74E-09	Y	1.00	intronic
3	*TF*	rs8177245	133479230	TIBC	G	0.17	17.12	1.57	9.84E-28	Y	0.99	intronic
3	*TF*	rs8177247	133479499	TIBC	G	0.22	19.62	1.42	1.04E-43	Y	0.99	intronic
3	*TF*	rs8177248	133479626	TIBC	T	0.13	15.84	1.73	9.24E-20	N	NA	intronic
3	*TF*	rs8177249	133479643	TIBC	T	0.05	19.17	2.70	1.20E-12	Y	0.98	intronic
3	*TF*	rs8177250	133479737	TIBC	C	0.05	19.14	2.70	1.32E-12	Y	0.98	intronic
3	*TF*	rs8177252	133480174	TIBC	A	0.24	19.16	1.38	4.18E-44	Y	1.00	intronic
3	*TF*	rs8177253	133480192	TIBC	T	0.24	19.86	1.34	1.76E-47	N	NA	intronic
3	*TF*	rs8177256	133480276	TIBC	T	0.22	17.77	1.41	2.47E-36	Y	1.00	intronic
3	*TF*	rs8177257	133480337	TIBC	T	0.03	-26.19	3.76	3.33E-12	Y	0.82	intronic
3	*TF*	rs8177258	133480387	TIBC	A	0.17	17.26	1.55	1.01E-28	Y	0.99	intronic
3	*TF*	rs8177259	133480388	TIBC	C	0.22	17.77	1.41	2.29E-36	Y	1.00	intronic
3	*TF*	rs8177260	133480458	TIBC	A	0.25	18.90	1.37	4.62E-43	Y	0.97	intronic

3	*TF*	rs8177261	133480588	TIBC	C	0.22	17.78	1.41	2.25E-36	Y	1.00	intronic
3	*TF*	rs8177262	133480652	TIBC	A	0.22	18.19	1.38	1.61E-38	N	NA	intronic
3	*TF*	rs8177263	133480754	TIBC	G	0.02	27.74	4.79	7.10E-09	Y	0.99	intronic
3	*TF*	rs6762719	133480817	TIBC	G	0.24	19.19	1.38	3.42E-44	Y	1.00	intronic
3	*TF*	rs8177266	133481255	TIBC	T	0.02	27.75	4.80	7.58E-09	Y	0.99	intronic
3	*TF*	rs6439439	133481498	TIBC	T	0.22	17.85	1.42	1.72E-36	Y	0.99	intronic
3	*TF*	rs1405022	133481718	TIBC	T	0.31	15.48	1.27	5.78E-34	Y	0.98	intronic
3	*TF*	rs8177268	133481751	TIBC	A	0.02	27.74	4.81	8.03E-09	Y	0.98	intronic
3	*TF*	rs8177271	133482230	TIBC	A	0.17	16.97	1.56	1.68E-27	Y	1.00	intronic
3	*TF*	rs8177272	133482870	TIBC	A	0.16	17.69	1.56	3.56E-29	N	NA	intronic
3	*TF*	rs1880669	133483696	TIBC	C	0.35	16.33	1.25	3.63E-39	Y	0.97	intronic
3	*TF*	rs3811647	133484029	TIBC	A	0.22	17.55	1.43	9.67E-35	Y	0.98	intronic
3	*TF*	rs8177275	133484066	TIBC	C	0.02	26.81	4.77	1.89E-08	Y	0.89	intronic
3	*TF*	rs1358023	133484393	TIBC	C	0.27	15.76	1.34	8.84E-32	Y	0.97	intronic
3	*TF*	rs1525892	133484712	TIBC	A	0.27	14.80	1.29	1.65E-29	N	NA	intronic
3	*TF*	rs2692695	133485454	TIBC	G	0.51	9.57	1.19	6.63E-16	Y	0.96	intronic
3	*TF*	rs8177280	133485664	TIBC	G	0.02	27.74	4.85	1.04E-08	Y	0.96	intronic
3	*TF*	rs2715634	133487807	TIBC	C	0.54	11.33	1.18	1.05E-21	Y	0.96	intronic
3	*TF*	rs1358021	133488877	TIBC	C	0.54	12.21	1.21	6.62E-24	Y	0.90	intronic
3	*TF*	rs1525889	133490033	TIBC	C	0.20	12.62	1.48	1.73E-17	Y	0.93	intronic
3	*TF*	rs6794361	133490310	TIBC	G	0.41	9.12	1.21	5.53E-14	Y	0.94	intronic
3	*TF*	rs6794370	133490334	TIBC	C	0.88	16.05	1.96	2.43E-16	Y	0.78	intronic
3	*TF*	rs181412842	133490453	TIBC	T	0.03	29.32	4.90	2.10E-09	Y	0.62	intronic
3	*TF*	rs8177295	133490513	TIBC	A	0.20	13.17	1.55	2.31E-17	Y	0.88	intronic
3	*TF*	rs34252038	133490621	TIBC	T	0.20	12.39	1.51	2.41E-16	Y	0.90	intronic
3	*TF*	3:133491569:TTGAA	133491569	TIBC	T	0.93	17.48	2.55	6.95E-12	Y	0.78	intronic
3	*TF*	3:133491570:TGAAA	133491570	TIBC	T	0.94	19.33	2.67	4.11E-13	Y	0.76	intronic
3	*TF*	rs2718798	133492088	TIBC	C	0.42	10.58	1.21	2.46E-18	Y	0.94	intronic
3	*TF*	rs7638018	133495461	TIBC	G	0.19	13.19	1.48	8.06E-19	N	NA	intronic
3	*TF*	rs12595	133496553	TIBC	C	0.19	12.97	1.48	2.32E-18	Y	0.98	intronic
3	*TF*	rs4854760	133498741	TIBC	G	0.36	8.69	1.21	7.39E-13	N	NA	downstream
3	*TF*	rs4854761	133498789	TIBC	A	0.30	10.68	1.26	3.99E-17	N	NA	downstream
3	*TF-SRPRB*	rs4854762	133499063	TIBC	A	0.25	8.90	1.33	2.56E-11	N	NA	intergenic
3	*TF-SRPRB*	rs13326361	133500294	TIBC	G	0.09	-14.13	2.14	3.69E-11	Y	0.87	intergenic
3	*TF-SRPRB*	rs9843728	133501407	TIBC	T	0.43	8.46	1.23	5.26E-12	Y	0.91	intergenic
3	*TF-SRPRB*	rs9844205	133501529	TIBC	A	0.09	-12.44	2.17	1.02E-08	Y	0.86	intergenic
3	*SRPRB*	rs9882812	133506127	TIBC	G	0.16	16.57	1.62	1.49E-24	Y	0.96	intronic

3	*SRPRB*	3:133507482:TC_T	133507482	TIBC	T	0.10	13.44	2.01	2.06E-11	Y	0.91	intronic
3	*SRPRB*	rs9871148	133507509	TIBC	C	0.11	13.11	1.95	1.79E-11	Y	0.94	intronic
3	*SRPRB*	rs77478723	133507903	TIBC	C	0.05	22.64	2.80	6.15E-16	Y	0.92	intronic
3	*SRPRB*	rs1830084	133508464	TIBC	T	0.16	16.84	1.60	2.16E-25	N	NA	intronic
3	*SRPRB*	rs1830083	133508551	TIBC	A	0.16	16.21	1.60	3.31E-24	Y	1.00	intronic
3	*SRPRB*	rs76160422	133508942	TIBC	T	0.04	20.97	3.24	1.02E-10	Y	0.90	intronic
3	*SRPRB*	rs138605336	133512479	TIBC	C	0.04	20.59	3.20	1.29E-10	Y	0.87	intronic
3	*SRPRB*	rs115984495	133512982	TIBC	A	0.04	20.55	3.22	1.66E-10	Y	0.88	intronic
3	*SRPRB*	rs111783714	133513076	TIBC	A	0.04	21.14	3.28	1.12E-10	Y	0.87	intronic
3	*SRPRB*	rs9813689	133514822	TIBC	T	0.10	13.74	2.00	5.78E-12	Y	0.92	intronic
3	*SRPRB*	rs74324191	133515820	TIBC	A	0.04	20.96	3.31	2.52E-10	Y	0.86	intronic
3	*SRPRB*	rs6794945	133518463	TIBC	T	0.13	14.41	1.83	5.40E-15	N	NA	intronic
3	*SRPRB*	rs111440472	133518464	TIBC	A	0.04	21.19	3.33	1.90E-10	Y	0.85	intronic
3	*SRPRB*	rs111285664	133518816	TIBC	T	0.04	21.07	3.33	2.47E-10	Y	0.85	intronic
3	*SRPRB*	rs35332919	133519002	TIBC	A	0.16	16.39	1.63	8.84E-24	Y	0.95	intronic
3	*SRPRB*	rs112117383	133522190	TIBC	C	0.04	20.77	3.32	4.12E-10	Y	0.84	intronic
3	*SRPRB*	rs13079426	133522334	TIBC	G	0.16	17.34	1.68	4.35E-25	Y	0.89	intronic
3	*SRPRB*	rs12490148	133523973	TIBC	T	0.16	16.98	1.67	3.06E-24	Y	0.89	intronic
3	*SRPRB*	rs113009116	133525691	TIBC	G	0.04	20.87	3.31	2.85E-10	Y	0.84	intronic
3	*SRPRB*	rs113644535	133526326	TIBC	A	0.06	21.10	2.79	3.97E-14	Y	0.85	intronic
3	*SRPRB*	rs113862503	133526563	TIBC	C	0.04	20.77	3.30	3.13E-10	Y	0.84	intronic
3	*SRPRB*	rs112398870	133526655	TIBC	T	0.04	20.75	3.30	3.26E-10	Y	0.84	exonic
3	*SRPRB*	rs112671459	133526833	TIBC	C	0.04	20.73	3.30	3.32E-10	Y	0.84	intronic
3	*SRPRB*	3:133530813:TACTG	133530813	TIBC	T	0.06	20.93	2.78	5.20E-14	Y	0.85	intronic
3	*SRPRB*	rs76977536	133530861	TIBC	G	0.06	20.94	2.78	5.04E-14	Y	0.85	intronic
3	*SRPRB*	rs75509322	133530961	TIBC	G	0.06	20.92	2.78	5.33E-14	Y	0.85	intronic
3	*SRPRB*	rs78229685	133531569	TIBC	A	0.06	20.88	2.78	5.63E-14	Y	0.85	intronic
3	*SRPRB*	rs6806081	133532054	TIBC	A	0.23	-8.53	1.43	2.20E-09	Y	0.91	intronic
3	*SRPRB*	rs113324170	133532415	TIBC	G	0.04	19.90	3.23	6.83E-10	Y	0.84	intronic
3	*SRPRB*	rs112140815	133532695	TIBC	C	0.04	20.33	3.27	5.05E-10	Y	0.84	intronic
3	*SRPRB*	rs182426351	133533256	TIBC	C	0.05	18.78	3.17	3.29E-09	Y	0.83	intronic
3	*SRPRB*	rs113115303	133533276	TIBC	T	0.04	20.11	3.26	6.79E-10	Y	0.84	intronic
3	*SRPRB*	rs112613578	133533741	TIBC	A	0.04	19.85	3.24	9.30E-10	Y	0.84	intronic
3	*SRPRB*	rs79071659	133533986	TIBC	C	0.04	19.74	3.24	1.10E-09	Y	0.84	intronic
3	*SRPRB*	rs113405105	133534289	TIBC	G	0.04	19.60	3.23	1.36E-09	Y	0.85	intronic
3	*SRPRB*	rs112110148	133537129	TIBC	G	0.04	19.13	3.22	2.88E-09	Y	0.85	intronic
3	*SRPRB*	rs113943912	133539175	TIBC	G	0.05	18.04	3.17	1.20E-08	Y	0.83	UTR3

3	*SRPRB*	3:133539541:GTCT_	133539541	TIBC	G	0.05	16.44	2.95	2.53E-08	Y	0.91	UTR3
3	*SRPRB-RAB6B*	rs6773354	133541774	TIBC	T	0.04	17.14	2.96	7.66E-09	N	NA	intergenic
3	*RAB6B*	rs12637730	133546297	TIBC	T	0.05	16.01	2.88	2.78E-08	Y	0.95	UTR3
3	*RAB6B*	rs181361454	133552284	TIBC	A	0.02	-31.84	5.78	3.68E-08	Y	0.55	intronic
3	*RAB6B*	rs79533570	133554873	TIBC	T	0.04	19.75	3.45	1.08E-08	Y	0.74	intronic
3	*RAB6B*	rs113924363	133561383	TIBC	C	0.05	23.64	4.15	1.19E-08	Y	0.49	intronic
3	*RAB6B*	rs113625677	133564224	TIBC	A	0.05	24.22	4.25	1.15E-08	Y	0.46	intronic
3	*RAB6B*	rs77232880	133566878	TIBC	G	0.05	23.76	4.29	3.10E-08	Y	0.45	intronic
6	*HDGFL1-NRSN1*	rs115923437	22678302	TIBC	C	0.06	14.84	2.60	1.13E-08	Y	0.91	intergenic
6	*HDGFL1-NRSN1*	rs9466438	22682102	TIBC	C	0.06	13.25	2.42	4.09E-08	Y	1.00	intergenic
6	*HDGFL1-NRSN1*	rs9466442	22687627	TIBC	G	0.06	13.79	2.52	4.42E-08	Y	0.92	intergenic
16	*MAF-DYNLRB2*	rs16951289	79790621	TIBC	T	0.07	13.38	2.38	2.03E-08	Y	0.91	intergenic
X	*GAB3*	rs7063597	153891601	log_ferritin	T	0.14	0.17	0.03	2.85E-08	Y	0.94	intergenic
X	*GAB3*	rs146474788	153893403	log_ferritin	A	0.14	0.17	0.03	2.90E-08	Y	0.94	intergenic
X	*GAB3*	rs141555380	153906012	log_ferritin	T	0.14	0.17	0.03	1.13E-08	Y	0.94	UTR3
X	*GAB3*	rs149621038	153953125	log_ferritin	T	0.16	0.16	0.03	3.98E-08	Y	0.94	intronic
X	*GAB3*	rs7885619	153960717	log_ferritin	G	0.15	0.17	0.03	1.91E-08	Y	0.94	intronic

Supplementary Table 3. Top SNPs associated with TIBC at $P<10^{-6}$

Chr	Nearest Gene	# of SNPs	Most Significant SNP	Pos(hg19)	EA	EAF	β	SE	*P*	Imputed (Y/N)	R^2	Function
1	*BAI2*	1	rs182815963	32219928	T	0.00	-93.66	18.51	4.2E-07	Y	0.44	intronic
2	*SERTAD2-LOC400958*	7	rs185183332	64967342	A	0.03	-20.46	4.01	3.3E-07	Y	0.69	intergenic
2	*RPRM-GALNT13*	2	rs189855038	154428028	C	0.00	-90.97	17.96	4.1E-07	Y	0.31	intergenic
3	*LOC440970*	1	3:84190898:A_AT	84190898	AT	0.02	37.67	7.59	6.9E-07	Y	0.36	intergenic
3	***TF***	221	rs8177253	133480192	T	0.24	19.86	1.34	**1.8E-47**	N	NA	intronic
4	*DCK-SLC4A4*	1	rs147549040	72028308	G	0.00	85.49	17.17	6.4E-07	Y	0.39	intergenic
6	***HDGFL1-NRSN1***	10	rs115923437	22678302	C	0.06	14.84	2.60	**1.1E-08**	Y	0.91	intergenic
6	*MIR5695*	1	rs112647290	126435741	T	0.03	23.52	4.67	4.7E-07	Y	0.58	intronic
10	*FRMD4A-MIR1265*	1	rs59376103	14442418	T	0.04	-17.36	3.37	2.6E-07	Y	0.78	intergenic
10	*KCNMA1*	2	rs71475649	79082679	C	0.01	70.63	13.65	2.3E-07	Y	0.33	intronic
11	*LUZP2*	1	rs61877888	24602715	G	0.15	9.36	1.87	5.3E-07	Y	0.80	intronic
13	*SLITRK1*	2	rs192989741	83958956	G	0.00	-76.76	15.20	4.4E-07	Y	0.38	intergenic
13	*ATP11A-MCF2L-AS1*	1	rs114067519	113547283	C	0.04	22.38	4.48	5.9E-07	Y	0.41	intergenic
16	*IGFALS-HAGH*	1	rs2256923	1844781	G	0.72	-9.98	2.04	9.9E-07	Y	0.41	intergenic
16	*SLX4-DNASE1*	1	rs60860998	3690092	C	0.03	32.70	6.47	4.3E-07	Y	0.33	intergenic
16	***MAF-DYNLRB2***	2	rs16951289	79790621	T	0.07	13.38	2.38	**2.0E-08**	Y	0.91	intergenic
18	*PTPN2-SEH1L*	1	rs73407743	12943299	A	0.10	11.06	2.25	9.0E-07	Y	0.73	intergenic
21	*ADAMTS5-MIR5009*	1	rs13052896	28481882	G	0.08	11.04	2.25	9.8E-07	Y	0.83	intergenic
21	*HUNK*	1	21:33316076:CCTT_	33316076	C	0.04	18.04	3.63	6.5E-07	Y	0.74	intronic

Supplementary Table 4. Top SNPs associated with log_ferritin at $P<10^{-6}$

Chr	Nearest Gene	# of SNPs	Most Significant SNP	Pos(hg19)	EA	EAF	β	SE	*P*	Imputed (Y/N)	R^2	Function
1	*RCC2-ARHGEF10L*	1	rs2477740	17831605	A	0.82	0.19	0.04	3.9E-07	Y	0.65	intergenic
3	*FHIT*	1	rs13074132	60321082	C	0.18	0.16	0.03	3.0E-07	Y	0.92	intronic
10	*RSU1*	1	rs76969309	16824397	A	0.05	0.33	0.06	8.3E-08	Y	0.72	intronic
10	*ADRA2A-GPAM*	1	rs17129425	113727270	G	0.19	-0.16	0.03	3.9E-07	Y	0.87	intergenic
18	*CEP192*	1	rs1787009	13063889	A	0.13	-0.20	0.04	7.6E-07	Y	0.76	intronic
19	*C19orf18*	4	rs192471137	58469524	A	0.00	1.72	0.32	1.2E-07	Y	0.40	intergenic
X	***G6PD-GAB3***	21	rs141555380	153906012	T	0.14	0.17	0.03	**1.1E-08**	Y	0.94	UTR-3

Supplementary Table 5. Top SNPs associated with log_iron at $P<10^{-6}$

Chr	Nearest Gene	# of SNPs	Most Significant SNP	Pos(hg19)	EA	EAF	β	SE	*P*	Imputed (Y/N)	R^2	Function
2	*ERBB4*	5	rs139713297	212423072	A	0.00	0.74	0.14	1.6E-07	Y	0.33	intronic
2	*SPHKAP-PID1*	1	rs1727563	229669613	T	0.31	-0.06	0.01	6.1E-07	Y	0.59	intergenic
4	*CC2D2A*	1	rs188125026	15490175	C	0.00	1.61	0.32	5.2E-07	Y	0.37	intronic
4	*SLIT2*	3	rs143034438	20560387	A	0.01	0.28	0.05	8.7E-08	Y	0.48	intronic
4	*HSP90AB3P-SPP1*	1	rs143957415	88837386	T	0.03	0.15	0.03	2.1E-07	Y	0.65	intergenic
8	*EPHX2-CLU*	5	rs79882106	27414335	C	0.00	0.80	0.15	8.0E-08	Y	0.32	intergenic
8	*EYA1-MSC*	1	rs191222090	72718862	G	0.00	0.49	0.10	6.2E-07	Y	0.44	intergenic
15	*SPRED1*	1	rs1522782	38544590	G	0.88	-0.08	0.02	3.8E-07	Y	0.63	intergenic
15	*LINC00052-NTRK3*	1	rs139196658	88173631	T	0.00	1.50	0.31	8.6E-07	Y	0.36	intergenic
16	*RBFOX1*	1	rs2109459	6440752	T	0.47	0.05	0.01	6.2E-07	Y	0.64	intronic
16	*ZCCHC14*	1	16:87446849	87446849	C	0.00	0.82	0.16	2.3E-07	Y	0.37	intronic
X	*HTATFS1-VGLL1*	1	rs184017266	135612099	A	0.00	31.47	6.26	4.9E-07	Y	0.35	intergenic
X	*SETP8*	2	rs190571075	116387808	T	0.00	2.86	0.58	8.0E-07	Y	0.32	intergenic
X	*HTR2C-IL13RA2*	1	rs140631409	114166154	T	0.00	0.95	0.19	8.6E-07	Y	0.53	intergenic

Supplementary Table 6. Top SNPs associated with log_SAT at $P<10^{-6}$

Chr	Nearest Gene	# of SNPs	Most significant SNP	Pos(hg19)	EA	EAF	β	SE	*P*	Imputed (Y/N)	R^2	Function
1	*LOC100129138-PRMT6*	1	rs113982601	106475276	A	0.10	0.09	0.02	9.4E-07	Y	0.56	intergenic
2	*SPHKAP-PID1*	1	rs6756903	229646101	C	0.31	-0.06	0.01	6.5E-07	Y	0.64	intergenic
2	*NGEF*	1	rs938575	233768788	A	0.10	-0.07	0.02	3.9E-07	Y	0.88	intronic
3	*TF*	4	rs6762719	133480817	G	0.24	-0.05	0.01	5.1E-07	Y	1.00	intronic
5	*LSM11*	1	rs145829393	157176316	T	0.02	0.25	0.05	7.8E-07	Y	0.44	intronic
8	*CSMD1-LOC100287015*	1	rs140656346	5682652	G	0.00	0.55	0.11	6.1E-07	Y	0.34	intergenic
8	*MFHAS1-ERI1*	1	rs115730735	8820986	T	0.05	0.13	0.03	8.7E-07	Y	0.60	intergenic
10	*RHOBTB1*	9	rs112298642	62634356	T	0.00	0.39	0.07	2.1E-07	Y	0.60	intronic
13	*KLF12-LINC00381*	1	rs67180317	74869018	G	0.27	0.06	0.01	2.9E-07	Y	0.67	intergenic
14	*ESRRB-VASH1*	1	rs75838009	77065324	T	0.02	0.21	0.04	1.1E-07	Y	0.75	intergenic
15	*SPRED1*	1	rs1522782	38544590	G	0.88	-0.08	0.02	4.8E-07	Y	0.63	intergenic
15	*CKMT1A-CATSPER2P1*	1	rs150805357	44016403	C	0.01	-0.30	0.06	6.3E-07	Y	0.53	intergenic
16	*ZCCHC14*	1	16:87446849	87446849	C	0.00	0.86	0.16	1.2E-07	Y	0.37	intronic
17	*ASIC2-CCL2*	1	rs142195977	32540548	T	0.03	-0.18	0.04	6.1E-07	Y	0.46	intergenic
19	*SMARCA4*	1	rs116337692	11107134	A	0.07	-0.10	0.02	6.2E-07	Y	0.63	intronic

Supplementary Table 7. SNPs on Chromosome 3 that reached genome-wide significance ($P<5x10^{-8}$) after adjusting for the top variant rs8177253

					Before adjusting for rs8177253			After adjusting for rs8177253					
Nearest Gene	MARKER	Pos(hg19)	EA	EAF	β	SE	*P*	β	SE	*P*	Imputed(Y/N)	R^2	Function
TOPBP1	rs112327474	133348668	A	0.03	23.15	4.87	1.96E-06	25.74	4.65	3.13E-08	Y	0.48	intronic
TOPBP1	rs113969369	133348677	A	0.03	23.17	4.86	1.87E-06	25.78	4.65	2.90E-08	Y	0.48	intronic
TOPBP1-TF	rs79213250	133391145	A	0.03	22.77	4.75	1.62E-06	25.41	4.54	2.16E-08	Y	0.55	intergenic
TOPBP1-TF	rs6806769	133431627	A	0.10	9.56	2.31	3.58E-05	13.24	2.21	2.12E-09	Y	0.69	intergenic
TOPBP1-TF	rs9830001	133433470	G	0.31	7.05	1.28	4.34E-08	7.04	1.23	1.06E-08	N	NA	intergenic
TOPBP1-TF	rs4078166	133435979	A	0.66	-6.73	1.33	4.23E-07	-11.03	1.27	4.11E-18	Y	0.86	intergenic
TOPBP1-TF	rs6782434	133438834	G	0.66	-6.76	1.33	3.46E-07	-11.06	1.27	2.65E-18	Y	0.87	intergenic
TOPBP1-TF	rs4443173	133439378	G	0.74	-4.65	1.39	8.19E-04	-7.37	1.33	2.75E-08	Y	0.90	intergenic
TOPBP1-TF	rs9843635	133440977	T	0.65	-6.71	1.35	6.42E-07	-11.29	1.29	1.85E-18	Y	0.83	intergenic
TOPBP1-TF	rs11921527	133441167	A	0.52	-0.84	1.26	5.06E-01	-6.81	1.20	1.51E-08	Y	0.85	intergenic
TOPBP1-TF	rs13066859	133442939	G	0.58	-6.65	1.41	2.43E-06	-10.97	1.35	4.20E-16	Y	0.71	intergenic
TOPBP1-TF	rs145713832	133445820	C	0.51	-8.14	1.49	4.63E-08	-10.40	1.42	2.72E-13	Y	0.62	intergenic
TOPBP1-TF	rs6804904	133447231	G	0.62	-6.30	1.34	2.83E-06	-11.08	1.29	6.41E-18	Y	0.80	intergenic
TOPBP1-TF	rs6439432	133448242	A	0.56	-5.51	1.39	7.54E-05	-9.17	1.33	5.44E-12	Y	0.72	intergenic
TOPBP1-TF	rs9820225	133449189	G	0.66	-6.77	1.31	2.26E-07	-10.94	1.25	2.08E-18	Y	0.89	intergenic
TOPBP1-TF	rs6439434	133450371	G	0.66	-6.45	1.28	5.00E-07	-10.81	1.23	1.18E-18	Y	0.93	intergenic
TOPBP1-TF	rs9869311	133451613	T	0.66	-6.48	1.28	3.75E-07	-10.79	1.22	8.74E-19	Y	0.94	intergenic
TOPBP1-TF	rs6439436	133453779	T	0.36	4.67	1.23	1.57E-04	9.75	1.21	1.07E-15	N	NA	intergenic
TOPBP1-TF	rs150431546	133455441	G	0.66	-6.69	1.29	2.05E-07	-11.01	1.23	3.96E-19	Y	0.92	intergenic
TOPBP1-TF	rs9872999	133457514	T	0.62	-6.55	1.34	9.97E-07	-11.72	1.28	5.44E-20	Y	0.80	intergenic
TOPBP1-TF	rs79354095	133458401	A	0.66	-6.82	1.31	1.99E-07	-11.29	1.25	2.30E-19	Y	0.89	intergenic
TOPBP1-TF	rs4854596	133459260	C	0.66	-6.81	1.31	2.02E-07	-11.08	1.25	9.02E-19	Y	0.89	intergenic
TOPBP1-TF	rs10935085	133459735	T	0.64	-4.86	1.28	1.51E-04	-9.54	1.23	6.50E-15	Y	0.91	intergenic
TOPBP1-TF	rs8177177	133463195	C	0.49	-0.21	1.18	8.61E-01	-6.74	1.20	1.95E-08	N	NA	intergenic
TOPBP1-TF	rs8177179	133463457	A	0.66	-6.88	1.29	9.62E-08	-11.12	1.23	1.78E-19	Y	0.92	intergenic
TOPBP1-TF	rs8177182	133464314	A	0.10	4.93	2.18	2.37E-02	11.54	2.09	3.19E-08	Y	0.80	intergenic
TF	rs1130459	133465283	G	0.66	-7.00	1.30	7.43E-08	-11.27	1.24	1.27E-19	Y	0.90	UTR-5

TF	rs148600419	133467945	T	0.10	5.11	2.23	2.21E-02	11.67	2.13	4.47E-08	Y	0.78	intronic
TF	rs8177235	133476083	A	0.06	-17.69	2.48	1.37E-12	-13.35	2.40	3.10E-08	N	NA	intronic
TF	rs8177237	133476421	G	0.35	0.62	1.32	6.41E-01	-7.49	1.27	3.28E-09	Y	0.86	intronic
TF	rs8177257	133480337	T	0.03	-26.19	3.76	3.33E-12	-19.73	3.60	4.06E-08	Y	0.82	intronic
TF	rs2715632	133485830	T	0.31	1.34	1.26	2.87E-01	9.48	1.29	2.64E-13	N	NA	intronic
TF	rs2718806	133486093	A	0.40	3.49	1.19	3.43E-03	7.15	1.14	3.59E-10	Y	0.97	intronic
TF	rs8649	133486958	C	0.31	1.57	1.25	2.10E-01	8.27	1.19	4.15E-12	Y	0.99	exonic
TF	rs1358022	133487621	G	0.31	1.51	1.26	2.31E-01	9.61	1.28	1.02E-13	N	NA	intronic
TF	rs1358021	133488877	C	0.54	12.21	1.21	6.62E-24	6.32	1.16	5.05E-08	Y	0.90	intronic

Supplementary Table 8. SNPs in the *TOPBP1-TF-RAB6B* region that reached nominal significance (P<0.05) after adjusting for rs8177253 and rs9872999

						Before adjusting			After adjusting for rs8177253			After adjusting for rs8177253 and rs9872999			
Nearest Gene	MARKER	Pos(hg19)	EA	EAF	R^2	β	SE	*P*	β	SE	*P*	β	SE	*P*	Function
TOPBP1	rs7645330	133320827	A	0.05	0.99	12.85	2.77	3.58E-06	6.74	2.65	1.10E-02	6.49	2.60	1.24E-02	intronic
TOPBP1	3:133321487:AGACA	133321487	A	0.06	0.55	-12.71	3.31	1.22E-04	-8.21	3.16	9.41E-03	-7.46	3.10	1.61E-02	intronic
TOPBP1	rs138973031	133322687	T	0.01	0.32	43.18	10.37	3.11E-05	14.89	9.94	1.34E-01	20.35	9.75	3.68E-02	intronic
TOPBP1	rs115587350	133323915	T	0.07	0.62	7.39	2.79	8.10E-03	12.24	2.67	4.57E-06	5.32	2.62	4.20E-02	intronic
TOPBP1	rs145840422	133325556	G	0.00	0.33	27.45	17.07	1.08E-01	40.88	16.32	1.22E-02	46.10	15.99	3.95E-03	intronic
TOPBP1	rs4241354	133325868	T	0.89	0.74	-0.17	2.20	9.40E-01	-3.40	2.10	1.07E-01	-6.19	2.06	2.72E-03	intronic
TOPBP1	rs6780074	133328713	C	0.05	0.71	15.68	3.37	3.17E-06	7.48	3.22	2.00E-02	7.23	3.15	2.19E-02	intronic
TOPBP1	rs71317417	133331230	T	0.08	0.81	-5.85	2.34	1.25E-02	-6.40	2.24	4.28E-03	-4.55	2.20	3.83E-02	intronic
TOPBP1	3:133331601:AAAGT	133331601	A	0.08	0.80	-5.69	2.34	1.52E-02	-6.25	2.24	5.29E-03	-4.43	2.20	4.35E-02	intronic
TOPBP1	rs7651295	133331626	A	0.05	0.71	14.89	3.25	4.62E-06	7.76	3.11	1.26E-02	7.51	3.05	1.37E-02	intronic
TOPBP1	rs184914692	133331631	G	0.00	0.60	-33.67	10.33	1.11E-03	-26.70	9.87	6.84E-03	-22.84	9.68	1.83E-02	intronic
TOPBP1	rs148249876	133331763	A	0.02	0.33	4.83	7.41	5.14E-01	13.69	7.08	5.33E-02	22.57	6.94	1.15E-03	intronic
TOPBP1	rs2017361	133335248	A	0.05	0.67	15.01	3.30	5.32E-06	7.83	3.15	1.30E-02	7.51	3.09	1.51E-02	intronic
TOPBP1	rs73861160	133336486	A	0.05	0.68	15.09	3.31	5.07E-06	7.81	3.16	1.36E-02	7.51	3.10	1.54E-02	intronic
TOPBP1	rs138004807	133337712	C	0.00	0.60	-33.23	10.33	1.29E-03	-26.34	9.87	7.63E-03	-22.61	9.68	1.95E-02	intronic
TOPBP1	rs73861163	133338273	T	0.05	0.67	15.12	3.34	5.94E-06	7.70	3.19	1.59E-02	7.40	3.13	1.81E-02	intronic
TOPBP1	rs4854588	133338862	C	0.90	1.00	-0.02	1.94	9.92E-01	-2.67	1.85	1.49E-01	-5.34	1.82	3.27E-03	intronic
TOPBP1	rs2887747	133339340	G	0.90	0.98	-0.12	1.98	9.53E-01	-3.14	1.90	9.73E-02	-5.81	1.86	1.76E-03	intronic
TOPBP1	3:133340657:CAG_C	133340657	C	0.08	0.61	8.19	2.76	2.97E-03	13.10	2.64	6.87E-07	5.89	2.59	2.29E-02	intronic
TOPBP1	rs149898537	133340772	G	0.00	0.38	-41.37	14.76	5.06E-03	-34.75	14.11	1.38E-02	-33.03	13.83	1.69E-02	intronic
TOPBP1	rs9818392	133343308	G	0.04	0.66	-13.14	3.77	4.96E-04	-12.47	3.61	5.45E-04	-9.68	3.53	6.17E-03	intronic
TOPBP1	rs114824478	133343795	T	0.01	0.32	14.63	13.35	2.73E-01	19.92	12.76	1.19E-01	29.79	12.51	1.72E-02	intronic
TOPBP1	rs75001273	133348173	G	0.04	0.64	18.81	4.10	4.47E-06	7.52	3.92	5.51E-02	8.64	3.84	2.45E-02	intronic
TOPBP1	rs78996709	133348343	A	0.02	0.37	3.16	7.06	6.55E-01	12.02	6.75	7.49E-02	20.42	6.61	2.02E-03	intronic
TOPBP1	rs34664124	133348373	T	0.04	0.67	-12.54	3.77	8.78E-04	-12.05	3.60	8.29E-04	-9.35	3.53	8.12E-03	intronic
TOPBP1	rs112327474	133348668	A	0.03	0.48	23.15	4.87	1.96E-06	25.74	4.65	3.13E-08	18.28	4.56	6.08E-05	intronic
TOPBP1	rs113969369	133348677	A	0.03	0.48	23.17	4.86	1.87E-06	25.78	4.65	2.90E-08	18.31	4.56	5.84E-05	intronic

TOPBP1	3:133349445:A_AT	133349445	AT	0.07	0.96	-3.92	2.41	1.04E-01	-1.90	2.31	4.10E-01	-4.73	2.26	3.68E-02	intronic
TOPBP1	rs6767770	133350222	C	0.91	1.00	0.62	1.96	7.50E-01	-2.34	1.87	2.12E-01	-5.01	1.84	6.33E-03	intronic
TOPBP1	rs9871504	133351675	A	0.09	0.78	-4.95	2.31	3.19E-02	-6.13	2.21	5.40E-03	-4.96	2.16	2.19E-02	intronic
TOPBP1	rs140878201	133351695	T	0.01	0.46	32.85	7.99	3.97E-05	29.78	7.64	9.72E-05	20.64	7.49	5.86E-03	intronic
TOPBP1	rs77263689	133351696	A	0.05	0.65	16.04	3.40	2.32E-06	8.29	3.25	1.07E-02	7.88	3.18	1.33E-02	intronic
TOPBP1	rs78032154	133353071	T	0.05	0.65	17.10	3.58	1.81E-06	8.14	3.43	1.75E-02	7.88	3.36	1.89E-02	intronic
TOPBP1	rs9881110	133353198	T	0.09	0.79	-5.29	2.30	2.13E-02	-6.35	2.20	3.87E-03	-5.16	2.15	1.66E-02	intronic
TOPBP1	rs62282420	133356383	C	0.07	0.95	-3.85	2.41	1.11E-01	-1.81	2.31	4.34E-01	-4.60	2.26	4.21E-02	intronic
TOPBP1	rs7623155	133358118	C	0.96	0.55	-4.30	3.84	2.63E-01	-8.49	3.67	2.08E-02	-13.52	3.60	1.75E-04	intronic
TOPBP1	rs79417893	133359114	C	0.08	0.62	8.78	2.73	1.28E-03	13.41	2.61	2.72E-07	6.07	2.56	1.76E-02	intronic
TOPBP1	rs62282421	133359293	C	0.07	0.95	-3.98	2.42	1.00E-01	-1.92	2.32	4.06E-01	-4.70	2.27	3.85E-02	intronic
TOPBP1	rs56289481	133360888	C	0.05	0.63	15.94	3.46	3.96E-06	8.12	3.30	1.39E-02	7.90	3.24	1.48E-02	intronic
TOPBP1	rs78279593	133361350	A	0.02	0.38	31.74	7.26	1.21E-05	11.81	6.94	8.86E-02	14.67	6.80	3.10E-02	intronic
TOPBP1	rs4854739	133361561	A	0.91	0.75	0.43	2.29	8.51E-01	-3.09	2.18	1.58E-01	-6.28	2.14	3.35E-03	intronic
TOPBP1	rs11708197	133361643	T	0.07	0.85	-4.21	2.53	9.54E-02	-2.15	2.42	3.75E-01	-5.08	2.37	3.20E-02	intronic
TOPBP1	rs17301889	133362154	G	0.08	0.87	-4.26	2.39	7.48E-02	-2.13	2.29	3.53E-01	-4.59	2.25	4.08E-02	exonic
TOPBP1	rs34736000	133364032	T	0.04	0.77	-11.73	3.56	9.88E-04	-11.11	3.40	1.09E-03	-8.60	3.34	9.96E-03	intronic
TOPBP1	rs9836356	133364444	T	0.09	0.98	-4.54	2.09	2.95E-02	-5.50	2.00	5.83E-03	-4.47	1.96	2.24E-02	intronic
TOPBP1	rs57367367	133364721	A	0.01	0.51	15.18	6.97	2.94E-02	18.84	6.66	4.71E-03	13.32	6.53	4.15E-02	intronic
TOPBP1	rs56394911	133364947	T	0.05	0.63	16.03	3.46	3.63E-06	8.08	3.31	1.45E-02	7.86	3.24	1.54E-02	intronic
TOPBP1	rs1373551	133365966	T	0.91	0.73	0.50	2.33	8.31E-01	-3.07	2.23	1.69E-01	-6.28	2.18	4.06E-03	intronic
TOPBP1	rs13315841	133366665	A	0.04	0.75	-11.67	3.58	1.11E-03	-11.01	3.42	1.29E-03	-8.49	3.35	1.14E-02	intronic
TOPBP1	3:133367784:C_CT	133367784	CT	0.08	0.71	-5.11	2.49	3.97E-02	-2.60	2.38	2.74E-01	-4.63	2.33	4.70E-02	intronic
TOPBP1	rs7644419	133370427	A	0.08	0.63	8.07	2.71	2.88E-03	12.76	2.59	8.51E-07	5.45	2.54	3.20E-02	intronic
TOPBP1	rs76048243	133370487	T	0.00	0.32	-43.93	14.29	2.10E-03	-38.98	13.66	4.32E-03	-39.40	13.39	3.25E-03	intronic
TOPBP1	rs6779063	133372919	G	0.09	0.87	-5.18	2.12	1.44E-02	-6.15	2.02	2.37E-03	-5.01	1.98	1.16E-02	intronic
TOPBP1	rs7639941	133374030	C	0.94	0.49	15.19	3.50	1.43E-05	12.46	3.35	1.96E-04	8.04	3.28	1.43E-02	intronic
TOPBP1	rs1348574	133375081	C	0.09	0.93	-4.77	2.15	2.64E-02	-5.61	2.05	6.24E-03	-4.50	2.01	2.52E-02	intronic
TOPBP1	3:133376340:C_CT	133376340	CT	0.09	0.89	-4.87	2.19	2.64E-02	-5.76	2.10	6.01E-03	-4.62	2.05	2.44E-02	intronic
TOPBP1	rs9810823	133376850	G	0.09	0.87	-4.51	2.20	4.02E-02	-5.52	2.10	8.70E-03	-4.43	2.06	3.18E-02	intronic

TOPBP1	rs2718803	133377075	T	0.67	0.68	1.18	1.49	4.29E-01	3.66	1.43	1.03E-02	3.15	1.40	2.44E-02	intronic
TOPBP1	rs146189271	133377506	G	0.01	0.55	28.35	8.18	5.28E-04	31.24	7.82	6.46E-05	20.74	7.66	6.80E-03	intronic
TOPBP1	rs80311995	133377568	C	0.05	0.63	17.80	3.66	1.17E-06	8.67	3.50	1.33E-02	8.54	3.43	1.28E-02	intronic
TOPBP1	rs2718804	133377782	A	0.09	0.69	-0.49	2.39	8.38E-01	3.17	2.28	1.65E-01	6.47	2.24	3.80E-03	intronic
TOPBP1	rs7618605	133378053	G	0.05	0.61	16.56	3.48	1.92E-06	8.73	3.33	8.65E-03	8.52	3.26	8.98E-03	intronic
TOPBP1	rs77009352	133378156	T	0.02	0.32	2.53	7.85	7.47E-01	11.84	7.50	1.15E-01	20.97	7.36	4.36E-03	intronic
TOPBP1	rs9827019	133380128	G	0.09	0.81	-5.05	2.28	2.68E-02	-6.00	2.18	5.93E-03	-4.88	2.14	2.23E-02	intronic
TOPBP1	rs9865536	133380436	C	0.09	0.81	-5.00	2.28	2.84E-02	-5.95	2.18	6.36E-03	-4.83	2.14	2.39E-02	intronic
TOPBP1-TF	rs148239185	133383456	A	0.01	0.36	43.92	8.78	5.68E-07	15.68	8.39	6.18E-02	20.80	8.23	1.15E-02	intergenic
TOPBP1-TF	rs6798570	133383729	T	0.09	0.77	-4.84	2.31	3.62E-02	-5.78	2.21	8.98E-03	-4.72	2.17	2.95E-02	intergenic
TOPBP1-TF	rs6774104	133383854	G	0.09	0.78	-4.78	2.31	3.85E-02	-5.70	2.21	9.89E-03	-4.66	2.17	3.14E-02	intergenic
TOPBP1-TF	rs2589271	133384252	A	0.67	0.67	1.24	1.50	4.08E-01	3.66	1.44	1.10E-02	3.21	1.41	2.28E-02	intergenic
TOPBP1-TF	rs180807578	133384759	T	0.08	0.63	7.93	2.67	3.02E-03	12.55	2.56	9.33E-07	5.31	2.51	3.41E-02	intergenic
TOPBP1-TF	rs9863253	133384936	C	0.10	0.68	-0.94	2.38	6.93E-01	2.79	2.28	2.21E-01	6.19	2.23	5.57E-03	intergenic
TOPBP1-TF	rs139529901	133385251	C	0.01	0.37	-21.83	10.51	3.77E-02	-14.06	10.04	1.61E-01	-21.22	9.84	3.11E-02	intergenic
TOPBP1-TF	rs56296963	133385676	T	0.05	0.61	15.40	3.47	9.25E-06	7.63	3.32	2.15E-02	7.46	3.25	2.18E-02	intergenic
TOPBP1-TF	rs147969084	133385790	G	0.07	0.70	-4.93	2.75	7.26E-02	-2.61	2.63	3.22E-01	-5.29	2.58	4.02E-02	intergenic
TOPBP1-TF	rs145382136	133386481	T	0.01	0.46	-25.68	10.03	1.04E-02	-22.82	9.59	1.73E-02	-18.52	9.40	4.88E-02	intergenic
TOPBP1-TF	rs75891599	133389763	A	0.10	0.91	-7.49	2.01	2.01E-04	-5.21	1.93	6.83E-03	-5.95	1.89	1.63E-03	intergenic
TOPBP1-TF	3:133390336:AG_A	133390336	A	0.03	0.37	-14.65	5.31	5.84E-03	-11.32	5.08	2.58E-02	-13.48	4.98	6.76E-03	intergenic
TOPBP1-TF	rs2370410	133390337	A	0.10	0.92	-7.51	2.00	1.76E-04	-5.30	1.92	5.63E-03	-6.03	1.88	1.32E-03	intergenic
TOPBP1-TF	rs9852403	133390340	T	0.09	0.73	-4.65	2.33	4.62E-02	-5.55	2.23	1.29E-02	-4.60	2.19	3.55E-02	intergenic
TOPBP1-TF	rs79213250	133391145	A	0.03	0.55	22.77	4.75	1.62E-06	25.41	4.54	2.16E-08	18.06	4.45	4.90E-05	intergenic
TOPBP1-TF	3:133391661:AAAAG	133391661	A	0.10	0.98	-7.10	1.94	2.62E-04	-4.96	1.86	7.62E-03	-5.73	1.82	1.68E-03	intergenic
TOPBP1-TF	rs7628914	133391687	G	0.17	0.86	-6.39	1.66	1.14E-04	-5.48	1.59	5.45E-04	-6.04	1.55	1.01E-04	intergenic
TOPBP1-TF	rs11713248	133392191	C	0.10	1.00	-7.08	1.93	2.50E-04	-4.97	1.85	7.17E-03	-5.73	1.81	1.57E-03	intergenic
TOPBP1-TF	rs11709132	133392210	T	0.10	1.00	-7.09	1.93	2.46E-04	-4.98	1.85	7.10E-03	-5.74	1.81	1.55E-03	intergenic
TOPBP1-TF	3:133392557:CTTTG	133392557	C	0.06	0.87	-4.02	2.55	1.15E-01	-2.04	2.44	4.03E-01	-4.99	2.39	3.71E-02	intergenic
TOPBP1-TF	rs11718050	133393323	T	0.10	0.96	-7.13	1.97	2.87E-04	-5.01	1.88	7.78E-03	-5.76	1.84	1.79E-03	intergenic
TOPBP1-TF	3:133393568:G_GGT	133393568	GGT	0.10	0.88	-7.61	2.07	2.44E-04	-4.95	1.98	1.26E-02	-5.48	1.94	4.83E-03	intergenic

TOPBP1-TF	3:133393583:CT_C	133393583	C	0.10	0.90	-7.88	2.07	1.45E-04	-5.84	1.98	3.22E-03	-6.39	1.94	1.00E-03	intergenic
TOPBP1-TF	rs75271466	133394302	A	0.03	0.60	19.07	4.22	6.24E-06	6.76	4.03	9.36E-02	8.27	3.95	3.64E-02	intergenic
TOPBP1-TF	rs11706586	133394930	A	0.13	0.82	-9.24	1.92	1.55E-06	-6.54	1.84	3.80E-04	-6.59	1.80	2.58E-04	intergenic
TOPBP1-TF	rs185092464	133395171	C	0.01	0.55	28.83	7.69	1.78E-04	31.96	7.35	1.39E-05	21.68	7.21	2.64E-03	intergenic
TOPBP1-TF	rs11714392	133395366	T	0.10	0.89	-7.23	2.02	3.43E-04	-5.05	1.93	8.91E-03	-5.83	1.89	2.07E-03	intergenic
TOPBP1-TF	rs2589276	133395690	T	0.89	0.71	5.50	2.17	1.13E-02	6.40	2.08	2.04E-03	5.03	2.03	1.34E-02	intergenic
TOPBP1-TF	rs2718817	133396671	A	0.04	0.50	2.46	4.08	5.46E-01	6.51	3.90	9.52E-02	11.98	3.82	1.72E-03	intergenic
TOPBP1-TF	rs139635005	133397050	T	0.04	0.70	-15.78	3.63	1.40E-05	-12.66	3.47	2.65E-04	-9.30	3.40	6.30E-03	intergenic
TOPBP1-TF	rs2099985	133398690	T	0.09	0.74	-5.00	2.33	3.16E-02	-5.78	2.23	9.38E-03	-4.81	2.18	2.74E-02	intergenic
TOPBP1-TF	rs2589274	133399105	C	0.36	0.73	-0.96	1.44	5.02E-01	1.27	1.37	3.57E-01	3.21	1.35	1.71E-02	intergenic
TOPBP1-TF	rs2718814	133399205	G	0.36	0.73	-0.96	1.44	5.05E-01	1.27	1.37	3.56E-01	3.22	1.35	1.67E-02	intergenic
TOPBP1-TF	rs76969652	133399346	T	0.08	0.66	7.94	2.57	1.99E-03	12.47	2.46	3.88E-07	5.26	2.41	2.88E-02	intergenic
TOPBP1-TF	rs34672862	133400121	T	0.09	0.74	-4.95	2.32	3.29E-02	-5.72	2.22	9.94E-03	-4.70	2.17	3.08E-02	intergenic
TOPBP1-TF	rs145278211	133400422	C	0.04	0.68	-16.15	3.65	9.66E-06	-12.88	3.49	2.22E-04	-9.55	3.42	5.24E-03	intergenic
TOPBP1-TF	rs138476353	133401521	T	0.03	0.60	20.81	4.42	2.43E-06	6.79	4.22	1.08E-01	8.98	4.14	3.00E-02	intergenic
TOPBP1-TF	rs4854741	133402380	C	0.36	0.76	-0.77	1.42	5.89E-01	1.49	1.36	2.73E-01	3.42	1.33	1.01E-02	intergenic
TOPBP1-TF	rs146996388	133403296	G	0.43	0.74	0.43	1.39	7.55E-01	1.06	1.33	4.26E-01	3.18	1.30	1.46E-02	intergenic
TOPBP1-TF	rs28846461	133405398	A	0.11	0.76	-7.65	2.15	3.70E-04	-5.19	2.06	1.15E-02	-6.16	2.01	2.24E-03	intergenic
TOPBP1-TF	3:133405662:CA_C	133405662	C	0.36	0.81	-1.06	1.36	4.36E-01	1.13	1.30	3.86E-01	3.00	1.28	1.87E-02	intergenic
TOPBP1-TF	rs146609703	133408033	T	0.04	0.67	-15.80	3.59	1.09E-05	-12.59	3.43	2.46E-04	-9.33	3.37	5.61E-03	intergenic
TOPBP1-TF	rs9847690	133408058	A	0.09	0.85	-4.58	2.16	3.43E-02	-5.31	2.07	1.03E-02	-4.37	2.03	3.12E-02	intergenic
TOPBP1-TF	rs115330090	133408155	A	0.02	0.61	-9.03	5.68	1.12E-01	-5.17	5.43	3.41E-01	-10.74	5.32	4.35E-02	intergenic
TOPBP1-TF	rs78178708	133408761	A	0.09	0.73	7.51	2.42	1.87E-03	11.70	2.31	4.12E-07	4.80	2.27	3.42E-02	intergenic
TOPBP1-TF	rs113977484	133408966	G	0.03	0.58	19.23	5.09	1.59E-04	22.36	4.87	4.34E-06	15.58	4.77	1.09E-03	intergenic
TOPBP1-TF	rs13325440	133409403	G	0.12	1.00	-3.54	1.78	4.70E-02	-4.36	1.70	1.04E-02	-3.71	1.67	2.63E-02	intergenic
TOPBP1-TF	rs2589267	133409669	A	0.36	1.00	-0.75	1.24	5.43E-01	1.13	1.18	3.40E-01	2.81	1.16	1.54E-02	intergenic
TOPBP1-TF	rs34519945	133409835	T	0.12	0.99	-3.53	1.78	4.73E-02	-4.31	1.70	1.13E-02	-3.63	1.67	2.95E-02	intergenic
TOPBP1-TF	3:133409877:TTG_T	133409877	T	0.35	0.94	-1.30	1.29	3.12E-01	0.65	1.23	5.96E-01	2.70	1.21	2.54E-02	intergenic
TOPBP1-TF	rs2718808	133409878	A	0.34	0.93	-1.21	1.29	3.49E-01	0.73	1.24	5.53E-01	2.77	1.21	2.21E-02	intergenic
TOPBP1-TF	rs77497127	133409879	T	0.34	0.92	-1.29	1.30	3.21E-01	0.64	1.25	6.06E-01	2.71	1.22	2.65E-02	intergenic

TOPBP1-TF	rs36033747	133409910	A	0.12	1.00	-3.53	1.78	4.74E-02	-4.28	1.70	1.18E-02	-3.60	1.67	3.07E-02	intergenic
TOPBP1-TF	rs34375330	133409953	A	0.12	1.00	-3.52	1.78	4.76E-02	-4.27	1.70	1.20E-02	-3.59	1.66	3.12E-02	intergenic
TOPBP1-TF	rs16840601	133410173	C	0.12	1.00	-3.55	1.78	4.54E-02	-4.29	1.70	1.14E-02	-3.61	1.66	3.00E-02	intergenic
TOPBP1-TF	rs9863830	133411224	C	0.12	1.00	-3.53	1.78	4.78E-02	-4.29	1.71	1.19E-02	-3.58	1.67	3.20E-02	intergenic
TOPBP1-TF	rs78639373	133412135	G	0.03	0.49	23.40	5.26	8.48E-06	6.90	5.02	1.70E-01	10.28	4.93	3.69E-02	intergenic
TOPBP1-TF	rs13061966	133412277	A	0.36	0.92	3.52	1.25	4.93E-03	0.88	1.20	4.65E-01	2.55	1.17	3.02E-02	intergenic
TOPBP1-TF	rs16840612	133412360	A	0.34	0.99	4.22	1.22	5.48E-04	1.65	1.17	1.57E-01	2.64	1.14	2.10E-02	intergenic
TOPBP1-TF	rs11914965	133412629	G	0.37	0.93	4.14	1.24	8.74E-04	1.59	1.19	1.81E-01	3.01	1.17	9.82E-03	intergenic
TOPBP1-TF	rs9985395	133413119	T	0.38	0.95	4.12	1.22	7.22E-04	1.59	1.16	1.73E-01	3.26	1.14	4.25E-03	intergenic
TOPBP1-TF	3:133413727:TTTA_	133413727	T	0.43	0.55	4.99	1.58	1.58E-03	0.54	1.51	7.22E-01	2.95	1.48	4.63E-02	intergenic
TOPBP1-TF	3:133414103:T_TC	133414103	TC	0.04	0.61	-18.75	3.92	1.68E-06	-15.14	3.74	5.28E-05	-11.16	3.67	2.36E-03	intergenic
TOPBP1-TF	rs4854742	133415371	G	0.35	0.88	5.00	1.30	1.23E-04	2.08	1.25	9.45E-02	3.35	1.22	6.05E-03	intergenic
TOPBP1-TF	rs114088124	133417455	C	0.03	0.60	-13.81	4.46	1.98E-03	-11.98	4.27	4.99E-03	-9.49	4.18	2.33E-02	intergenic
TOPBP1-TF	rs16840641	133417657	A	0.04	0.63	-18.58	3.88	1.64E-06	-14.82	3.71	6.36E-05	-10.58	3.63	3.59E-03	intergenic
TOPBP1-TF	rs142793064	133417975	C	0.03	0.61	-13.91	4.47	1.85E-03	-12.14	4.27	4.46E-03	-9.66	4.19	2.10E-02	intergenic
TOPBP1-TF	rs143017285	133419146	A	0.03	0.61	-14.35	4.47	1.32E-03	-12.61	4.27	3.15E-03	-10.08	4.19	1.60E-02	intergenic
TOPBP1-TF	rs4420866	133421515	A	0.35	0.79	5.24	1.37	1.36E-04	1.97	1.31	1.33E-01	3.40	1.29	8.33E-03	intergenic
TOPBP1-TF	rs4437139	133421781	T	0.66	0.95	7.40	1.26	4.35E-09	5.20	1.21	1.58E-05	3.33	1.18	4.78E-03	intergenic
TOPBP1-TF	rs112764019	133422112	C	0.01	0.51	-29.03	9.03	1.30E-03	-20.07	8.63	2.01E-02	-19.61	8.46	2.04E-02	intergenic
TOPBP1-TF	rs76739644	133422350	C	0.03	0.62	-14.44	4.46	1.19E-03	-12.67	4.26	2.92E-03	-10.18	4.18	1.47E-02	intergenic
TOPBP1-TF	rs6769437	133422504	G	0.66	0.96	7.34	1.25	4.45E-09	5.15	1.20	1.67E-05	3.29	1.17	5.11E-03	intergenic
TOPBP1-TF	3:133422542:AC_A	133422542	A	0.65	0.93	7.01	1.26	2.89E-08	5.12	1.21	2.21E-05	3.47	1.18	3.37E-03	intergenic
TOPBP1-TF	rs78153150	133423359	C	0.04	0.66	-18.88	3.81	7.15E-07	-14.97	3.64	3.92E-05	-10.55	3.57	3.10E-03	intergenic
TOPBP1-TF	rs4419374	133423473	C	0.65	1.00	7.25	1.23	3.26E-09	5.09	1.17	1.39E-05	3.23	1.15	4.89E-03	intergenic
TOPBP1-TF	rs77108953	133423701	C	0.04	0.66	-18.84	3.81	7.65E-07	-14.95	3.64	4.08E-05	-10.58	3.57	3.04E-03	intergenic
TOPBP1-TF	rs146944707	133423937	T	0.01	0.55	-26.17	8.09	1.22E-03	-18.67	7.74	1.58E-02	-15.53	7.58	4.06E-02	intergenic
TOPBP1-TF	rs4854745	133423975	G	0.66	0.94	7.70	1.26	1.09E-09	5.48	1.21	5.78E-06	3.40	1.18	4.10E-03	intergenic
TOPBP1-TF	rs187394868	133424033	A	0.04	0.65	-18.73	3.84	1.06E-06	-14.80	3.67	5.49E-05	-10.42	3.60	3.76E-03	intergenic
TOPBP1-TF	rs4854746	133424325	C	0.66	0.93	7.37	1.27	5.85E-09	5.14	1.21	2.18E-05	3.19	1.19	7.15E-03	intergenic
TOPBP1-TF	rs9830153	133426570	G	0.66	0.86	7.58	1.32	8.55E-09	5.17	1.26	4.09E-05	3.13	1.23	1.12E-02	intergenic

TOPBP1-TF	rs4854592	133427192	C	0.52	0.74	5.57	1.35	3.49E-05	4.30	1.29	8.32E-04	3.42	1.26	6.61E-03	intergenic
TOPBP1-TF	rs16840672	133427212	C	0.04	0.63	-18.81	3.89	1.33E-06	-14.58	3.72	8.84E-05	-10.30	3.65	4.74E-03	intergenic
TOPBP1-TF	rs4854593	133427224	G	0.52	0.74	5.56	1.34	3.53E-05	4.30	1.29	8.32E-04	3.42	1.26	6.63E-03	intergenic
TOPBP1-TF	rs116175745	133427318	C	0.04	0.63	-18.73	3.89	1.47E-06	-14.53	3.72	9.29E-05	-10.26	3.65	4.89E-03	intergenic
TOPBP1-TF	rs3935228	133428824	C	0.66	0.81	7.85	1.35	6.60E-09	5.32	1.29	3.86E-05	3.22	1.27	1.11E-02	intergenic
TOPBP1-TF	rs9283586	133429740	C	0.86	0.71	1.08	1.99	5.87E-01	0.80	1.90	6.74E-01	3.68	1.86	4.81E-02	intergenic
TOPBP1-TF	rs77611807	133429754	A	0.03	0.57	23.39	4.59	3.52E-07	5.94	4.39	1.76E-01	9.10	4.30	3.44E-02	intergenic
TOPBP1-TF	rs13085923	133430043	C	0.31	0.66	3.54	1.54	2.18E-02	1.87	1.47	2.05E-01	3.57	1.44	1.33E-02	intergenic
TOPBP1-TF	rs192410596	133430785	A	0.01	0.50	-31.46	9.11	5.52E-04	-21.88	8.71	1.20E-02	-21.02	8.54	1.38E-02	intergenic
TOPBP1-TF	rs114132545	133431179	C	0.03	0.64	-18.43	3.93	2.68E-06	-13.71	3.75	2.59E-04	-9.44	3.68	1.03E-02	intergenic
TOPBP1-TF	rs6806769	133431627	A	0.10	0.69	9.56	2.31	3.58E-05	13.24	2.21	2.12E-09	4.40	2.17	4.23E-02	intergenic
TOPBP1-TF	rs145063290	133433774	C	0.06	0.82	-13.92	2.76	4.56E-07	-9.64	2.64	2.57E-04	-5.97	2.59	2.10E-02	intergenic
TOPBP1-TF	rs78796046	133435333	A	0.05	0.87	-12.81	2.90	1.01E-05	-8.87	2.77	1.39E-03	-5.99	2.72	2.78E-02	intergenic
TOPBP1-TF	rs75526026	133435334	A	0.05	0.87	-12.80	2.90	1.02E-05	-8.86	2.77	1.40E-03	-5.98	2.72	2.78E-02	intergenic
TOPBP1-TF	rs139440485	133435981	T	0.02	0.66	-22.73	4.82	2.36E-06	-17.61	4.60	1.31E-04	-12.74	4.51	4.77E-03	intergenic
TOPBP1-TF	rs75581091	133436577	T	0.06	0.90	-14.25	2.71	1.51E-07	-10.51	2.59	5.07E-05	-5.01	2.54	4.88E-02	intergenic
TOPBP1-TF	rs138064837	133438760	T	0.02	0.68	-22.68	4.78	2.04E-06	-17.56	4.57	1.19E-04	-12.73	4.48	4.45E-03	intergenic
TOPBP1-TF	rs74791200	133439449	T	0.05	0.91	-12.15	2.83	1.76E-05	-8.24	2.71	2.32E-03	-5.47	2.65	3.91E-02	intergenic
TOPBP1-TF	rs4441652	133439450	G	0.85	0.83	-4.18	1.76	1.76E-02	-6.14	1.68	2.64E-04	3.54	1.65	3.20E-02	intergenic
TOPBP1-TF	rs193215634	133439894	C	0.02	0.65	-24.13	5.35	6.40E-06	-18.63	5.11	2.67E-04	-13.54	5.01	6.86E-03	intergenic
TOPBP1-TF	rs183954521	133439951	A	0.02	0.67	-22.45	4.77	2.51E-06	-17.40	4.56	1.35E-04	-12.56	4.47	4.94E-03	intergenic
TOPBP1-TF	rs187859806	133440534	A	0.02	0.68	-22.07	4.74	3.20E-06	-17.04	4.53	1.69E-04	-12.24	4.44	5.85E-03	intergenic
TOPBP1-TF	rs138112191	133442633	C	0.04	0.82	-4.68	3.45	1.74E-01	-0.17	3.30	9.59E-01	6.46	3.23	4.54E-02	intergenic
TOPBP1-TF	rs147186394	133443344	C	0.04	0.81	-3.63	3.21	2.58E-01	-0.28	3.07	9.27E-01	6.02	3.01	4.52E-02	intergenic
TOPBP1-TF	rs138665349	133444086	C	0.04	0.78	-3.59	3.20	2.62E-01	-0.17	3.06	9.55E-01	6.29	3.00	3.61E-02	intergenic
TOPBP1-TF	rs148392763	133444356	T	0.05	0.92	-12.21	2.82	1.48E-05	-8.14	2.69	2.52E-03	-5.29	2.64	4.52E-02	intergenic
TOPBP1-TF	rs143985389	133444726	A	0.05	0.92	-12.19	2.82	1.57E-05	-8.11	2.70	2.64E-03	-5.26	2.64	4.65E-02	intergenic
TOPBP1-TF	rs182721564	133444902	G	0.02	0.70	-21.07	4.70	7.16E-06	-16.12	4.49	3.30E-04	-11.70	4.40	7.84E-03	intergenic
TOPBP1-TF	rs4854751	133447518	T	0.04	0.82	-4.91	3.44	1.54E-01	-0.26	3.29	9.38E-01	6.36	3.23	4.89E-02	intergenic
TOPBP1-TF	rs140165880	133448148	A	0.05	0.93	-12.17	2.80	1.43E-05	-8.07	2.68	2.63E-03	-5.18	2.63	4.88E-02	intergenic
TOPBP1-TF	rs6439433	133448335	C	0.82	0.73	-0.88	1.74	6.11E-01	-3.09	1.66	6.26E-02	5.09	1.63	1.77E-03	intergenic

TOPBP1-TF	rs148836292	133451716	C	0.02	0.72	-21.03	4.63	5.53E-06	-15.93	4.43	3.18E-04	-11.83	4.34	6.40E-03	intergenic
TOPBP1-TF	rs114127460	133451720	A	0.02	0.72	-21.02	4.63	5.62E-06	-15.95	4.43	3.12E-04	-11.88	4.34	6.17E-03	intergenic
TOPBP1-TF	rs141663013	133451872	C	0.02	0.72	-21.05	4.63	5.47E-06	-15.99	4.43	3.02E-04	-11.93	4.34	5.95E-03	intergenic
TOPBP1-TF	rs190298993	133452697	T	0.00	0.38	-58.71	39.62	1.38E-01	-53.11	37.87	1.61E-01	-73.98	37.12	4.63E-02	intergenic
TOPBP1-TF	rs141053059	133453676	T	0.02	0.72	-20.85	4.62	6.52E-06	-15.75	4.42	3.67E-04	-11.72	4.33	6.86E-03	intergenic
TOPBP1-TF	rs143371332	133453688	C	0.02	0.72	-20.84	4.62	6.60E-06	-15.73	4.42	3.71E-04	-11.71	4.33	6.90E-03	intergenic
TOPBP1-TF	rs183898243	133454058	A	0.02	0.72	-20.86	4.62	6.34E-06	-15.76	4.42	3.60E-04	-11.71	4.33	6.82E-03	intergenic
TOPBP1-TF	rs13317774	133454410	A	0.04	0.86	-4.93	3.38	1.45E-01	-0.34	3.23	9.16E-01	6.35	3.17	4.50E-02	intergenic
TOPBP1-TF	rs139232096	133455172	T	0.04	0.85	-4.83	3.38	1.53E-01	-0.26	3.23	9.35E-01	6.41	3.17	4.31E-02	intergenic
TOPBP1-TF	rs10049065	133455761	G	0.84	0.81	-4.91	1.76	5.30E-03	-6.68	1.69	7.40E-05	3.47	1.65	3.55E-02	intergenic
TOPBP1-TF	rs142393858	133456380	A	0.04	0.85	-4.88	3.41	1.52E-01	-0.34	3.26	9.16E-01	6.32	3.19	4.77E-02	intergenic
TOPBP1-TF	rs187012510	133456769	G	0.02	0.73	-20.97	4.59	4.93E-06	-15.84	4.39	3.07E-04	-11.66	4.30	6.71E-03	intergenic
TOPBP1-TF	rs141233467	133457122	T	0.02	0.73	-20.95	4.60	5.24E-06	-15.82	4.40	3.21E-04	-11.65	4.31	6.87E-03	intergenic
TOPBP1-TF	rs185839795	133458000	T	0.02	0.73	-20.96	4.61	5.54E-06	-15.72	4.41	3.63E-04	-11.48	4.32	7.90E-03	intergenic
TOPBP1-TF	rs190945904	133458057	A	0.02	0.73	-21.00	4.61	5.29E-06	-15.77	4.41	3.50E-04	-11.53	4.32	7.65E-03	intergenic
TOPBP1-TF	rs4637289	133458497	G	0.04	0.86	-3.54	3.12	2.56E-01	-0.32	2.98	9.15E-01	5.85	2.92	4.54E-02	intergenic
TOPBP1-TF	rs182704234	133458808	T	0.02	0.73	-21.02	4.61	5.12E-06	-15.78	4.41	3.41E-04	-11.52	4.32	7.67E-03	intergenic
TOPBP1-TF	rs182722776	133459125	G	0.00	0.40	138.69	79.54	8.12E-02	160.78	76.03	3.45E-02	182.49	74.53	1.44E-02	intergenic
TOPBP1-TF	rs140542915	133461124	A	0.02	0.73	-20.89	4.56	4.63E-06	-15.62	4.36	3.40E-04	-11.41	4.27	7.60E-03	intergenic
TOPBP1-TF	rs4640562	133462497	G	0.03	0.81	-14.84	3.57	3.22E-05	-10.71	3.41	1.70E-03	-6.59	3.34	4.89E-02	intergenic
TF	rs189667665	133465169	T	0.02	0.73	-20.63	4.53	5.31E-06	-15.29	4.33	4.17E-04	-11.11	4.25	8.91E-03	UTR5
TF	rs115845336	133466532	G	0.02	0.74	-20.31	4.51	6.68E-06	-14.92	4.31	5.36E-04	-10.76	4.23	1.09E-02	intronic
TF	rs8177189	133467517	A	0.01	0.70	-15.98	8.41	5.75E-02	-11.27	8.04	1.61E-01	-17.83	7.88	2.37E-02	intronic
TF	rs8177191	133468139	A	0.08	1.00	7.34	2.23	1.02E-03	10.87	2.13	3.54E-07	4.83	2.09	2.09E-02	intronic
TF	rs139227195	133470573	T	0.00	0.33	86.12	30.53	4.79E-03	66.34	29.18	2.30E-02	61.07	28.61	3.28E-02	intronic
TF	rs8177212	133472037	C	0.03	0.84	10.51	3.56	3.12E-03	14.22	3.40	2.91E-05	6.74	3.33	4.31E-02	intronic
TF	rs3811655	133472775	G	0.16	0.91	1.35	1.68	4.21E-01	4.57	1.60	4.30E-03	3.27	1.57	3.76E-02	intronic
TF	rs3828347	133472897	A	0.16	0.91	1.43	1.67	3.94E-01	4.64	1.60	3.75E-03	3.32	1.57	3.42E-02	intronic
TF	rs8177216	133472996	C	0.01	0.77	-24.41	5.30	4.08E-06	-18.53	5.06	2.53E-04	-13.13	4.96	8.18E-03	intronic
TF	rs8177217	133473105	A	0.08	0.96	6.80	2.27	2.71E-03	10.47	2.17	1.35E-06	4.78	2.12	2.43E-02	intronic
TF	rs8177221	133473643	A	0.08	0.95	5.02	2.19	2.21E-02	9.05	2.10	1.57E-05	4.18	2.06	4.18E-02	intronic

TF	rs144878001	133474518	G	0.00	0.60	78.77	31.20	1.16E-02	66.77	29.82	2.51E-02	57.33	29.23	4.99E-02	intronic
TF	rs3811657	133474607	A	0.06	1.00	7.41	2.48	2.80E-03	11.05	2.37	3.10E-06	5.92	2.32	1.09E-02	intronic
TF	rs41295764	133475529	A	0.02	0.89	-17.53	4.46	8.58E-05	-14.07	4.27	9.79E-04	-8.89	4.18	3.37E-02	intronic
TF	rs1799852	133475722	T	0.06	1.00	-16.22	2.44	3.05E-11	-12.16	2.33	1.88E-07	-7.87	2.29	5.85E-04	exonic
TF	rs1799899	133475812	A	0.01	0.88	-22.38	6.65	7.64E-04	-16.60	6.36	9.01E-03	-13.33	6.23	3.24E-02	exonic
TF	rs8177235	133476083	A	0.06	0.99	-18.00	2.51	7.10E-13	-13.26	2.40	3.20E-08	-8.76	2.35	1.95E-04	intronic
TF	rs7645538	133476327	C	0.92	1.00	-4.65	2.06	2.43E-02	-10.36	1.97	1.53E-07	-4.09	1.94	3.45E-02	intronic
TF	rs8177237	133476421	G	0.35	0.86	0.62	1.32	6.41E-01	-7.49	1.27	3.28E-09	-4.38	1.24	4.16E-04	intronic
TF	rs183495846	133476824	T	0.00	0.64	-50.64	10.35	9.93E-07	-42.32	9.89	1.88E-05	-34.95	9.70	3.13E-04	intronic
TF	rs8177244	133479190	A	0.04	0.91	-13.56	2.93	3.76E-06	-9.07	2.80	1.21E-03	-5.93	2.75	3.10E-02	intronic
TF	rs8177251	133480021	T	0.02	0.93	6.58	4.62	1.54E-01	-8.59	4.42	5.16E-02	-12.49	4.33	3.90E-03	intronic
TF	rs8177257	133480337	T	0.03	0.82	-26.19	3.76	3.33E-12	-19.73	3.60	4.06E-08	-15.06	3.52	1.91E-05	intronic
TF	rs1405023	133481128	C	0.61	0.91	-6.53	1.25	1.88E-07	6.01	1.20	5.10E-07	3.67	1.17	1.78E-03	intronic
TF	3:133481627:C_CA	133481627	CA	0.02	0.91	6.49	4.63	1.61E-01	-8.70	4.42	4.91E-02	-12.69	4.33	3.41E-03	intronic
TF	rs8177269	133482042	T	0.02	0.89	6.18	4.61	1.80E-01	-8.73	4.41	4.75E-02	-12.82	4.32	3.00E-03	intronic
TF	rs8177270	133482130	C	0.02	0.89	6.21	4.61	1.78E-01	-8.72	4.41	4.79E-02	-12.81	4.32	3.04E-03	intronic
TF	rs41295784	133482681	T	0.02	0.88	6.10	4.61	1.85E-01	-8.68	4.40	4.87E-02	-12.81	4.32	3.00E-03	intronic
TF	rs41295788	133482806	A	0.02	0.88	6.12	4.61	1.84E-01	-8.65	4.40	4.95E-02	-12.78	4.32	3.06E-03	intronic
TF	rs8177274	133483193	C	0.02	0.86	5.72	4.57	2.11E-01	-8.60	4.37	4.91E-02	-12.82	4.28	2.76E-03	intronic
TF	rs60832366	133483682	A	0.02	0.86	5.65	4.57	2.16E-01	-8.59	4.37	4.92E-02	-12.83	4.28	2.73E-03	intronic
TF	rs8177277	133484830	C	0.02	1.00	-0.14	4.50	9.76E-01	4.67	4.30	2.78E-01	10.44	4.22	1.34E-02	intronic
TF	rs8177278	133485359	T	0.02	0.84	4.63	4.65	3.20E-01	-9.29	4.45	3.68E-02	-13.77	4.36	1.59E-03	intronic
TF	rs2692695	133485454	G	0.51	0.96	9.57	1.19	6.63E-16	6.07	1.13	8.17E-08	3.36	1.11	2.47E-03	intronic
TF	rs2715632	133485830	T	0.31	1.00	1.48	1.25	2.36E-01	8.14	1.19	8.12E-12	3.94	1.17	7.39E-04	intronic
TF	rs2718806	133486093	A	0.40	0.97	3.49	1.19	3.43E-03	7.15	1.14	3.59E-10	3.19	1.12	4.34E-03	intronic
TF	rs8649	133486958	C	0.31	0.99	1.57	1.25	2.10E-01	8.27	1.19	4.15E-12	4.07	1.17	5.06E-04	exonic
TF	rs1358022	133487621	G	0.31	1.00	1.48	1.24	2.34E-01	8.10	1.19	9.11E-12	3.95	1.17	6.87E-04	intronic
TF	rs2715634	133487807	C	0.54	0.96	11.33	1.18	1.05E-21	5.93	1.13	1.64E-07	3.40	1.11	2.19E-03	intronic
TF	rs1358021	133488877	C	0.54	0.90	12.21	1.21	6.62E-24	6.32	1.16	5.05E-08	3.16	1.14	5.39E-03	intronic
TF	rs6794370	133490334	C	0.88	0.78	16.05	1.96	2.43E-16	9.59	1.87	3.00E-07	4.33	1.83	1.82E-02	intronic
TF	rs181412842	133490453	T	0.03	0.62	29.32	4.90	2.10E-09	20.82	4.68	8.60E-06	12.09	4.59	8.40E-03	intronic

TF	3:133491569:TTGAA	133491569	T	0.93	0.78	17.48	2.55	6.95E-12	11.10	2.44	5.26E-06	8.58	2.39	3.31E-04	intronic
TF-SRPRB	rs183505879	133500017	A	0.00	0.43	57.85	29.50	4.98E-02	59.14	28.19	3.60E-02	65.22	27.64	1.83E-02	intergenic
TF-SRPRB	rs13326361	133500294	G	0.09	0.87	-14.13	2.14	3.69E-11	-8.43	2.04	3.65E-05	-4.12	2.00	3.96E-02	intergenic
TF-SRPRB	rs185628354	133500486	T	0.00	0.41	50.59	29.27	8.39E-02	52.20	27.97	6.21E-02	59.00	27.42	3.14E-02	intergenic
SRPRB	rs1589901	133505886	T	0.03	0.72	9.39	3.79	1.33E-02	15.90	3.63	1.16E-05	8.90	3.56	1.23E-02	intronic
SRPRB	rs62280613	133506729	G	0.03	0.82	-14.02	4.03	5.05E-04	-8.84	3.85	2.18E-02	-7.71	3.78	4.12E-02	intronic
SRPRB	rs2718807	133507033	G	0.03	0.72	9.24	3.78	1.46E-02	15.71	3.62	1.41E-05	8.71	3.55	1.40E-02	intronic
SRPRB	rs13321671	133507062	C	0.04	0.86	-4.36	3.14	1.66E-01	0.93	3.01	7.57E-01	6.56	2.95	2.60E-02	intronic
SRPRB	rs77478723	133507903	C	0.05	0.92	22.64	2.80	6.15E-16	6.91	2.68	9.88E-03	6.59	2.62	1.21E-02	intronic
SRPRB	rs76160422	133508942	T	0.04	0.90	20.97	3.24	1.02E-10	4.53	3.10	1.44E-01	6.63	3.04	2.91E-02	intronic
SRPRB	rs116480382	133509570	A	0.04	0.77	-15.66	3.38	3.56E-06	-10.74	3.23	8.81E-04	-6.51	3.17	3.98E-02	intronic
SRPRB	rs114241201	133509904	A	0.04	0.79	-14.72	3.20	4.14E-06	-10.10	3.06	9.48E-04	-5.96	3.00	4.67E-02	intronic
SRPRB	rs115500269	133510390	C	0.01	0.38	-5.87	10.77	5.86E-01	-20.34	10.30	4.82E-02	-27.49	10.10	6.48E-03	intronic
SRPRB	rs142799596	133510635	C	0.00	0.43	-15.64	11.82	1.86E-01	-23.40	11.30	3.84E-02	-32.67	11.08	3.19E-03	intronic
SRPRB	rs180675164	133511441	T	0.00	0.78	-36.89	10.95	7.56E-04	-31.76	10.47	2.41E-03	-25.94	10.26	1.15E-02	intronic
SRPRB	rs138605336	133512479	C	0.04	0.87	20.59	3.20	1.29E-10	5.21	3.06	8.91E-02	7.49	3.00	1.26E-02	intronic
SRPRB	rs115984495	133512982	A	0.04	0.88	20.55	3.22	1.66E-10	4.76	3.08	1.22E-01	6.94	3.01	2.13E-02	intronic
SRPRB	rs111783714	133513076	A	0.04	0.87	21.14	3.28	1.12E-10	4.67	3.13	1.37E-01	6.87	3.07	2.54E-02	intronic
SRPRB	rs76456178	133513789	A	0.04	0.77	-14.89	3.21	3.58E-06	-10.23	3.07	8.64E-04	-6.11	3.01	4.26E-02	intronic
SRPRB	rs74324191	133515820	A	0.04	0.86	20.96	3.31	2.52E-10	4.36	3.17	1.69E-01	6.59	3.11	3.39E-02	intronic
SRPRB	rs111440472	133518464	A	0.04	0.85	21.19	3.33	1.90E-10	4.53	3.18	1.54E-01	6.72	3.12	3.12E-02	intronic
SRPRB	3:133518618:AC_A	133518618	A	0.03	0.72	8.91	3.76	1.77E-02	15.31	3.59	2.02E-05	8.54	3.52	1.53E-02	intronic
SRPRB	rs116336568	133518760	A	0.04	0.77	-15.54	3.30	2.50E-06	-10.50	3.16	8.76E-04	-6.34	3.09	4.03E-02	intronic
SRPRB	rs111285664	133518816	T	0.04	0.85	21.07	3.33	2.47E-10	4.47	3.18	1.60E-01	6.68	3.12	3.24E-02	intronic
SRPRB	rs147333002	133519331	A	0.00	0.79	-37.31	11.13	8.01E-04	-32.46	10.64	2.28E-03	-26.25	10.43	1.18E-02	intronic
SRPRB	rs151060476	133520813	T	0.01	0.61	6.88	9.93	4.88E-01	-10.24	9.49	2.80E-01	-21.40	9.30	2.14E-02	intronic
SRPRB	rs62280618	133521316	C	0.00	0.32	-37.17	23.33	1.11E-01	-29.21	22.30	1.90E-01	-46.89	21.86	3.19E-02	intronic
SRPRB	rs77653936	133521701	A	0.04	0.92	-3.49	3.06	2.53E-01	1.42	2.92	6.28E-01	6.74	2.86	1.85E-02	intronic
SRPRB	rs74515528	133521746	G	0.04	0.76	-15.87	3.32	1.72E-06	-10.91	3.17	5.83E-04	-6.68	3.11	3.18E-02	intronic
SRPRB	rs112117383	133522190	C	0.04	0.84	20.77	3.32	4.12E-10	4.30	3.18	1.76E-01	6.50	3.11	3.69E-02	intronic
SRPRB	rs113009116	133525691	G	0.04	0.84	20.87	3.31	2.85E-10	4.39	3.16	1.65E-01	6.54	3.10	3.51E-02	intronic

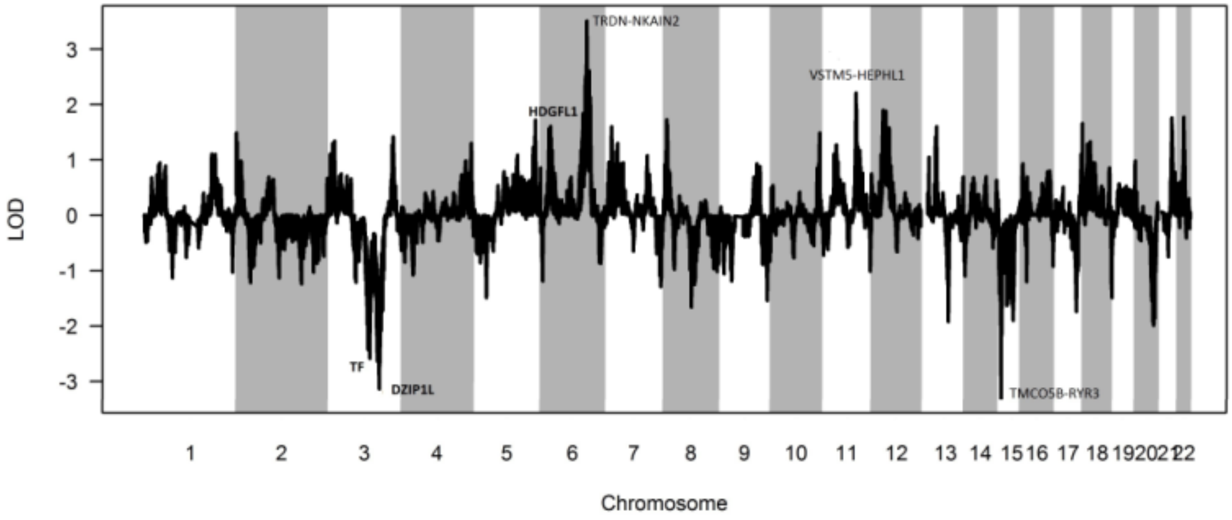
SRPRB	rs113644535	133526326	A	0.06	0.85	21.10	2.79	3.97E-14	6.39	2.67	1.66E-02	6.09	2.62	2.00E-02	intronic
SRPRB	rs113862503	133526563	C	0.04	0.84	20.77	3.30	3.13E-10	4.44	3.16	1.59E-01	6.58	3.09	3.34E-02	intronic
SRPRB	rs112398870	133526655	T	0.04	0.84	20.75	3.30	3.26E-10	4.45	3.16	1.59E-01	6.58	3.09	3.33E-02	exonic
SRPRB	rs112671459	133526833	C	0.04	0.84	20.73	3.30	3.32E-10	4.42	3.15	1.61E-01	6.55	3.09	3.41E-02	intronic
SRPRB	3:133530813:TACTG	133530813	T	0.06	0.85	20.93	2.78	5.20E-14	6.23	2.66	1.91E-02	5.98	2.61	2.17E-02	intronic
SRPRB	rs76977536	133530861	G	0.06	0.85	20.94	2.78	5.04E-14	6.25	2.66	1.87E-02	6.01	2.61	2.12E-02	intronic
SRPRB	rs75509322	133530961	G	0.06	0.85	20.92	2.78	5.33E-14	6.24	2.66	1.89E-02	6.00	2.61	2.13E-02	intronic
SRPRB	rs78229685	133531569	A	0.06	0.85	20.88	2.78	5.63E-14	6.22	2.66	1.91E-02	5.97	2.60	2.18E-02	intronic
SRPRB	rs142000559	133532048	G	0.01	0.64	6.55	9.97	5.11E-01	-10.25	9.53	2.83E-01	-21.30	9.35	2.27E-02	intronic
SRPRB	rs115282007	133532211	C	0.01	0.34	61.61	12.34	5.98E-07	23.62	11.80	4.53E-02	27.33	11.56	1.81E-02	intronic
SRPRB	rs113324170	133532415	G	0.04	0.84	19.90	3.23	6.83E-10	4.23	3.08	1.70E-01	6.34	3.02	3.59E-02	intronic
SRPRB	rs112140815	133532695	C	0.04	0.84	20.33	3.27	5.05E-10	4.15	3.13	1.85E-01	6.31	3.06	3.95E-02	intronic
SRPRB	rs9853123	133532782	G	0.04	0.91	-2.66	3.03	3.81E-01	1.86	2.90	5.22E-01	6.98	2.84	1.39E-02	intronic
SRPRB	rs113115303	133533276	T	0.04	0.84	20.11	3.26	6.79E-10	4.02	3.12	1.97E-01	6.19	3.05	4.28E-02	intronic
SRPRB	rs112613578	133533741	A	0.04	0.84	19.85	3.24	9.30E-10	3.87	3.10	2.12E-01	6.03	3.04	4.71E-02	intronic
SRPRB	rs79071659	133533986	C	0.04	0.84	19.74	3.24	1.10E-09	3.81	3.10	2.18E-01	5.99	3.04	4.87E-02	intronic
SRPRB	rs76497943	133536026	G	0.00	0.60	-54.38	12.71	1.88E-05	-43.66	12.15	3.25E-04	-36.65	11.91	2.09E-03	intronic
SRPRB	rs1534166	133537067	G	0.31	1.00	-1.24	1.26	3.27E-01	-0.27	1.21	8.21E-01	-2.65	1.18	2.50E-02	intronic
RAB6B	rs191098011	133542394	A	0.01	0.48	-53.98	10.24	1.33E-07	-44.26	9.78	6.08E-06	-37.52	9.59	9.15E-05	downstream
RAB6B	rs116393910	133550131	T	0.02	0.56	-2.32	5.22	6.57E-01	5.36	4.99	2.82E-01	10.08	4.89	3.93E-02	intronic
RAB6B	rs11921187	133551642	C	0.18	0.66	-4.24	1.87	2.34E-02	-4.87	1.79	6.53E-03	-4.24	1.76	1.57E-02	intronic
RAB6B	rs181361454	133552284	A	0.02	0.55	-31.84	5.78	3.68E-08	-25.40	5.53	4.34E-06	-18.73	5.42	5.48E-04	intronic
RAB6B	rs78798392	133552662	A	0.14	0.67	-9.25	2.08	8.37E-06	-7.53	1.99	1.50E-04	-4.10	1.95	3.51E-02	intronic
RAB6B	rs189705402	133553011	T	0.01	0.46	-57.39	10.86	1.25E-07	-47.70	10.38	4.32E-06	-40.02	10.17	8.35E-05	intronic
RAB6B	rs75883617	133553620	T	0.04	0.62	-12.92	3.56	2.78E-04	-11.24	3.40	9.42E-04	-7.53	3.33	2.38E-02	intronic
RAB6B	rs79533570	133554873	T	0.04	0.74	19.75	3.45	1.08E-08	3.95	3.30	2.31E-01	6.54	3.24	4.33E-02	intronic
RAB6B	rs17376530	133555155	T	0.13	0.63	-3.46	2.16	1.10E-01	-7.67	2.07	2.03E-04	-4.28	2.02	3.45E-02	intronic
RAB6B	rs78136918	133555265	A	0.05	0.45	-2.64	3.77	4.83E-01	-7.19	3.60	4.57E-02	-7.83	3.53	2.65E-02	intronic
RAB6B	rs143626136	133556503	G	0.02	0.54	-30.60	5.66	6.58E-08	-24.24	5.41	7.53E-06	-18.17	5.31	6.19E-04	intronic
RAB6B	rs115106219	133558619	A	0.04	0.55	-12.87	3.75	6.03E-04	-11.27	3.59	1.67E-03	-7.54	3.52	3.20E-02	intronic
RAB6B	rs75252591	133558967	C	0.00	0.64	-46.19	12.68	2.71E-04	-36.73	12.12	2.45E-03	-30.17	11.88	1.11E-02	intronic

RAB6B	rs142370912	133559739	A	0.00	0.54	-42.45	14.05	2.52E-03	-36.96	13.43	5.94E-03	-30.94	13.17	1.88E-02	intronic
RAB6B	rs79951982	133562303	C	0.00	0.33	16.94	19.88	3.94E-01	24.01	19.01	2.07E-01	39.60	18.63	3.35E-02	intronic
RAB6B	rs17310798	133562939	C	0.04	0.54	-9.87	3.99	1.34E-02	-8.24	3.82	3.08E-02	-10.86	3.74	3.70E-03	intronic
RAB6B	rs145985321	133563992	C	0.02	0.42	-27.78	6.08	4.86E-06	-22.35	5.81	1.19E-04	-15.79	5.69	5.55E-03	intronic
RAB6B	rs115660540	133568674	G	0.00	0.34	-73.50	15.14	1.20E-06	-62.01	14.47	1.82E-05	-50.47	14.18	3.73E-04	intronic
RAB6B	rs192180274	133574329	T	0.01	0.35	-26.82	13.98	5.52E-02	-33.37	13.37	1.26E-02	-37.38	13.10	4.34E-03	intronic
RAB6B	rs55647813	133574876	T	0.24	0.43	-1.27	2.06	5.37E-01	-4.89	1.97	1.31E-02	-4.49	1.93	2.00E-02	intronic
RAB6B	rs73217250	133579783	T	0.01	0.44	35.80	9.50	1.65E-04	15.39	9.08	9.02E-02	19.74	8.91	2.67E-02	intronic
RAB6B	rs116059608	133583238	A	0.02	0.60	-7.89	4.93	1.10E-01	-4.46	4.72	3.45E-01	-9.71	4.62	3.57E-02	intronic
RAB6B	rs184687940	133595545	T	0.00	0.33	79.15	24.09	1.02E-03	44.43	23.03	5.37E-02	48.44	22.57	3.19E-02	intronic
RAB6B	rs59900352	133602460	C	0.03	0.50	-6.48	5.17	2.10E-01	-11.50	4.95	2.02E-02	-10.00	4.85	3.93E-02	intronic
RAB6B	rs7631892	133605411	A	0.02	0.33	-14.35	6.19	2.05E-02	-15.65	5.92	8.17E-03	-15.60	5.80	7.15E-03	intronic
RAB6B	rs117518401	133614605	T	0.06	0.33	-13.35	4.32	2.00E-03	-11.88	4.13	4.01E-03	-10.71	4.05	8.11E-03	UTR5

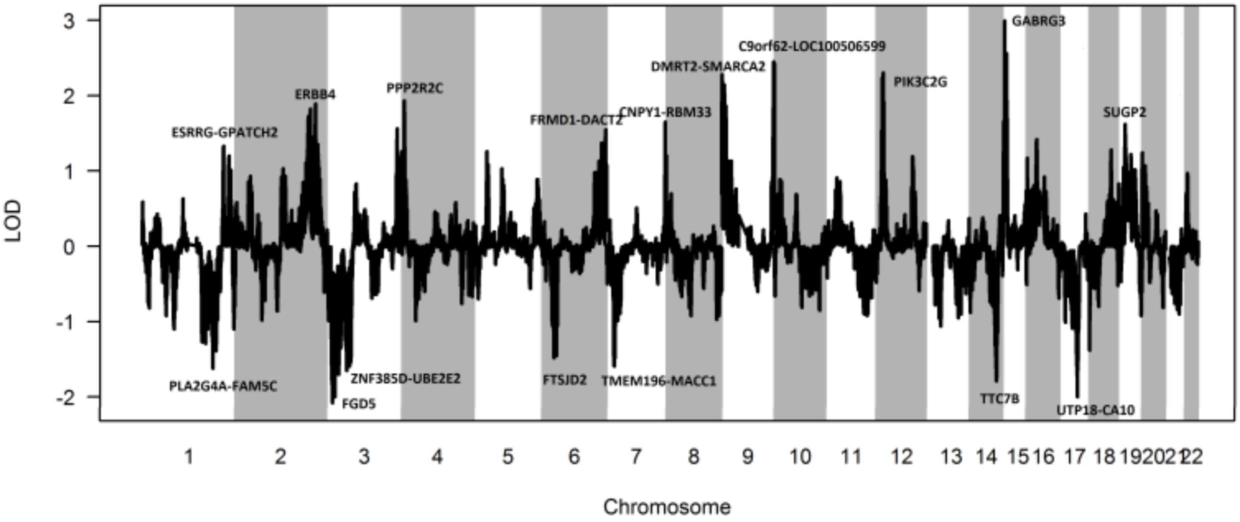
Supplementary Table 9. Effect sizes and P values for top SNPs associated with log_ferritin ($p<10^{-7}$) in JHS before and after adjusting for menopause status. Note: menopause status was only available on 2136/2347 JHS.

					Before Adjustment			After Adjustment		
Chr	SNP	EA	EAF	RSQR	β	SE	*P*	β	SE	*P*
X	rs141555380	T	0.14	0.94	0.17	0.03	1.1E-08	0.16	0.03	1.4E-08
X	rs7885619	G	0.15	0.94	0.17	0.03	1.9E-08	0.16	0.03	2.1E-08
X	rs7063597	T	0.14	0.94	0.17	0.03	2.9E-08	0.16	0.03	3.1E-08
X	rs146474788	A	0.14	0.94	0.17	0.03	2.9E-08	0.16	0.03	3.2E-08
X	rs149621038	T	0.16	0.94	0.16	0.03	4.0E-08	0.15	0.03	5.7E-08
X	rs138941436	G	0.15	0.94	0.16	0.03	5.7E-08	0.15	0.03	8.8E-08
X	rs185814586	G	0.13	0.90	0.17	0.03	6.1E-08	0.17	0.03	6.5E-08
X	rs1050828	T	0.14	0.98	0.16	0.03	9.1E-08	0.15	0.03	9.3E-08
10	rs76969309	A	0.05	0.72	0.33	0.06	8.3E-08	0.32	0.06	7.6E-08

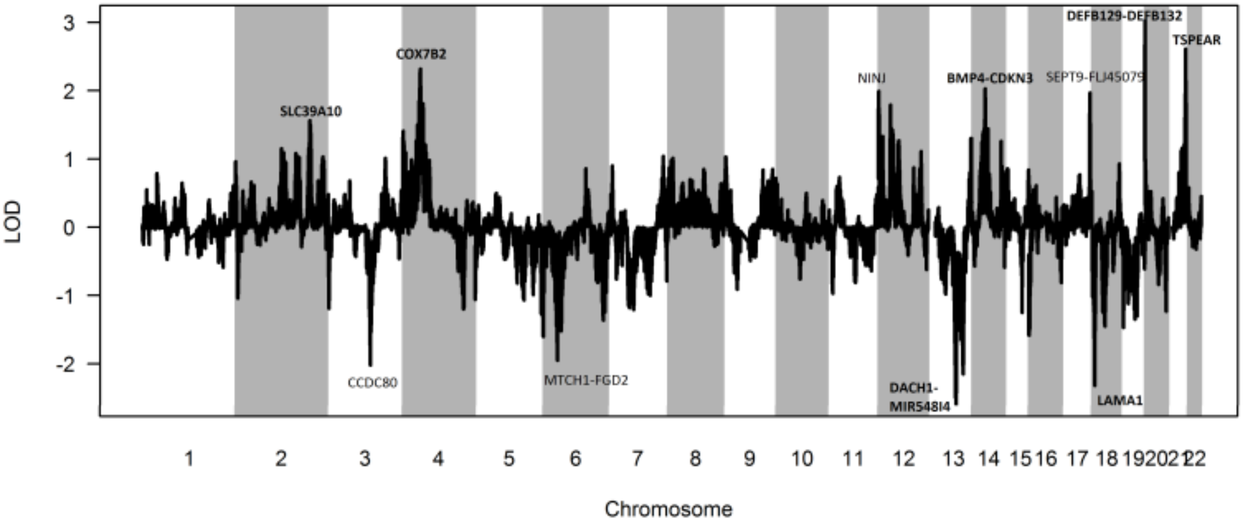
Supplementary Figures



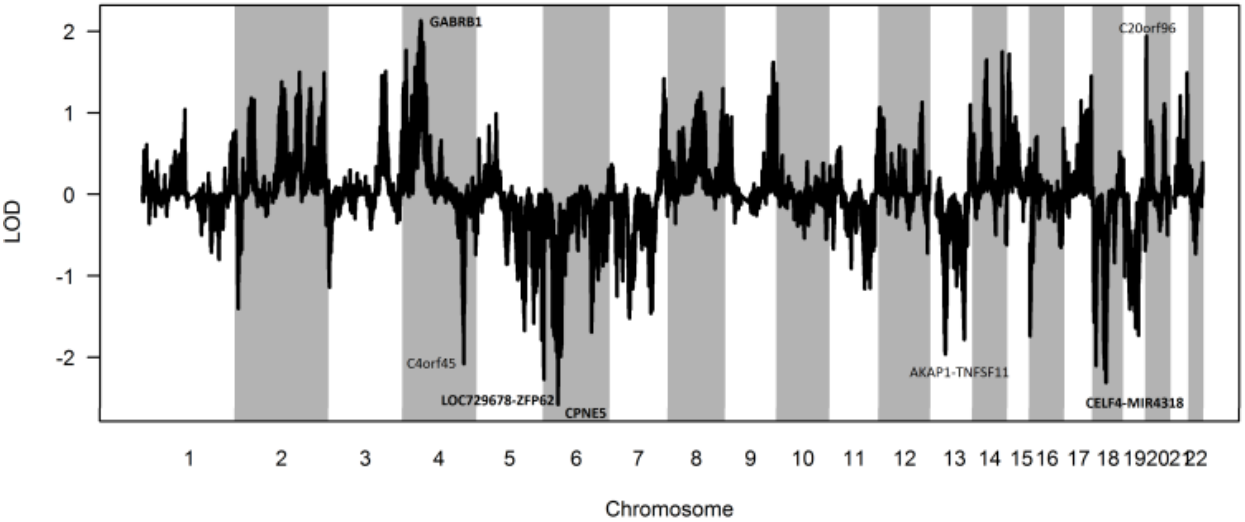
Supplementary Fig. 1a. The LOD score of genome-wide admixture scan for TIBC. The LOD score is defined as the log base 10 ratio of the maximum likelihood of the data under a local-ancestry-associated disease model divided by the likelihood of the data under null model. Both the alternative and null model include covariate adjustment for global ancestry. Positive LOD scores show the association of increased African ancestry with higher levels of iron measures, while negative LOD scores show the association of increased African ancestry with lower level of iron measures.



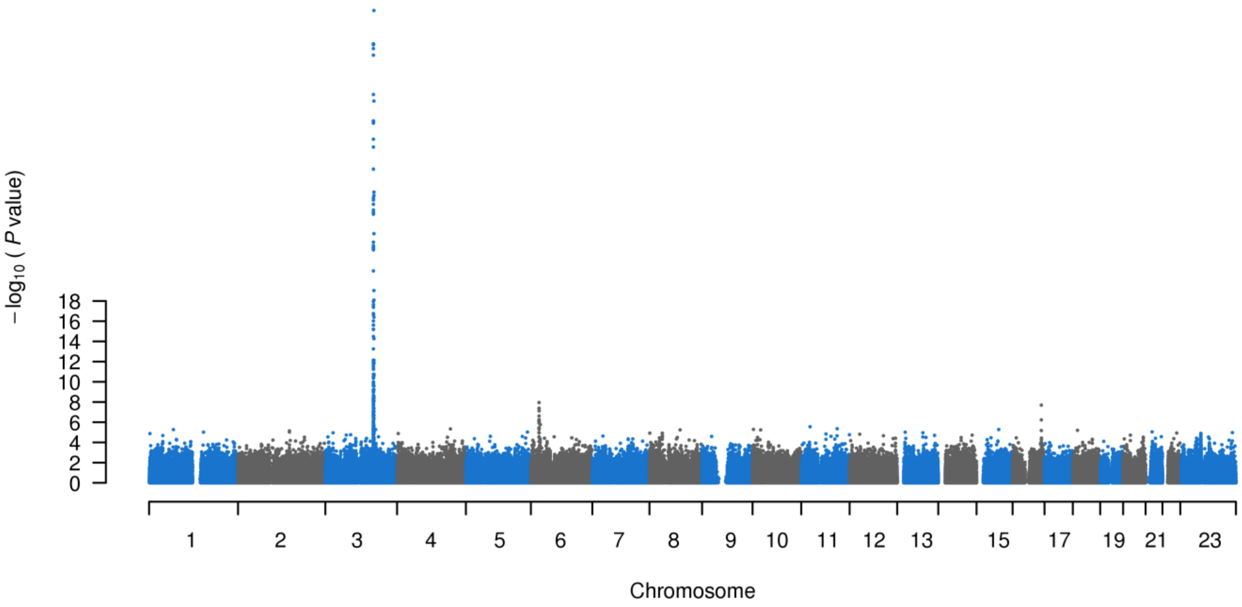
Supplementary Fig. 1b. The LOD scores for local admixture for log_ferritin after adjustment of global ancestry.



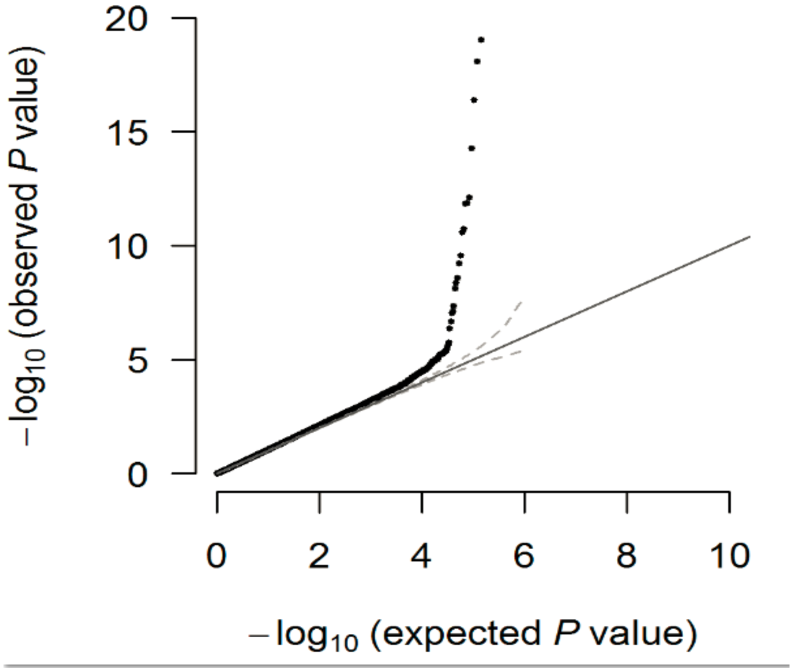
Supplementary Fig. 1c. LOD scores for local admixture for log_iron after adjustment for global ancestry.



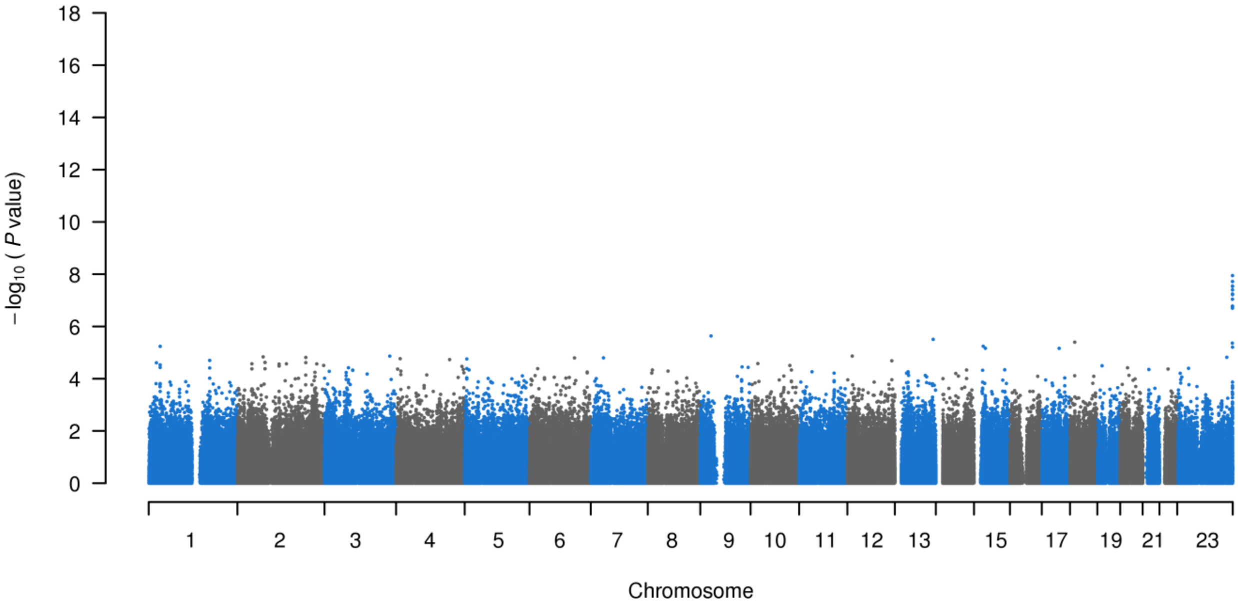
Supplementary Fig. 1d. LOD scores for local admixture for log_SAT after adjustment for global ancestry.



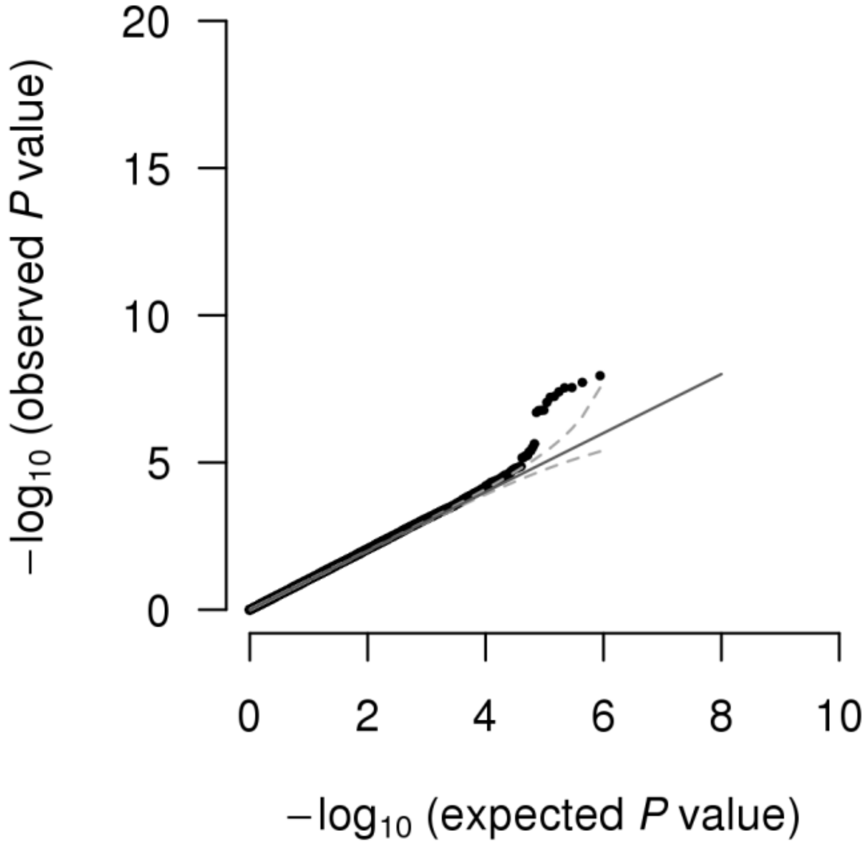
Supplementary Fig. 2a. Manhattan plot of the -$\log_{10}$(P) values by chromosome for TIBC



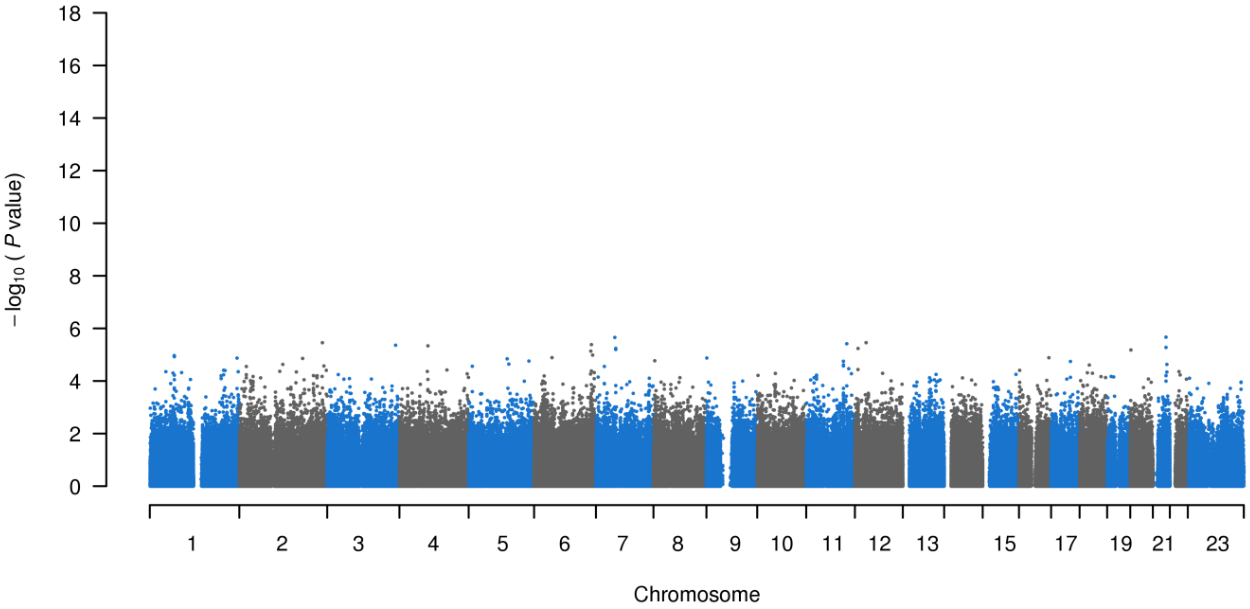
Supplementary Fig.2b. Quantile-Quantile (Q-Q) plots of the P-values across all genotyped SNPs tested for association with TIBC in models adjusting for age, gender, BMI, and 10 eigenvectors calculated from principal component analysis. Horizontal and vertical lines represent expected P values under null distribution and observed P values, respectively. The straight line represents the expected distribution assuming no inflation of the statistics.



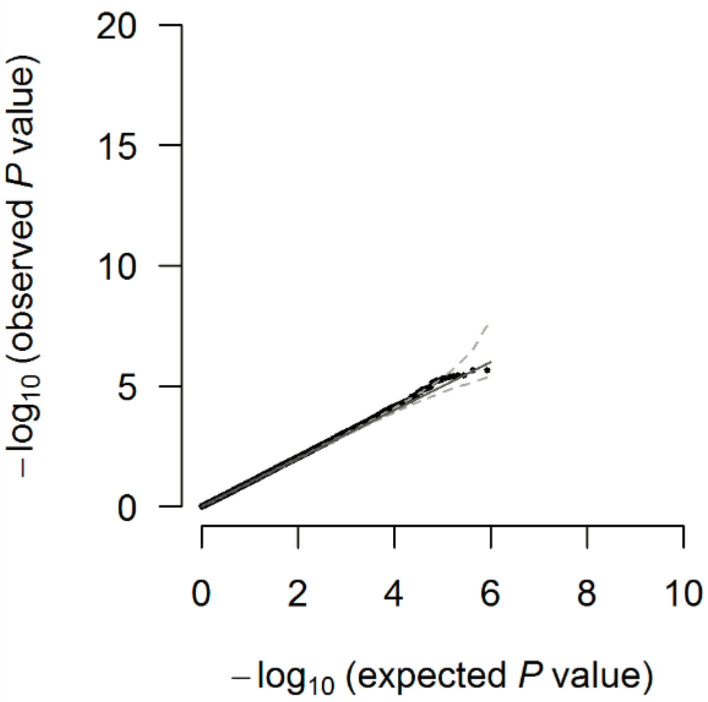
Supplementary Fig. 3a. Manhattan plot of the -log$_{10}$(P) values by chromosome for log_ferritin



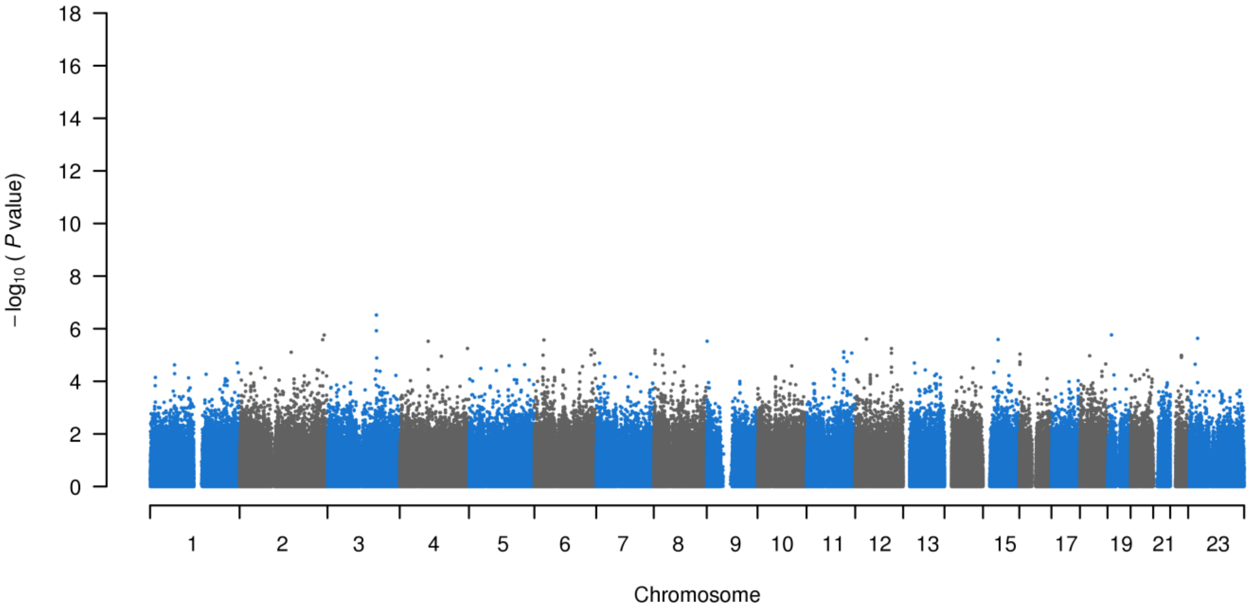
Supplementary Fig.3b. Quantile-Quantile (Q-Q) plots of the P-values across all genotyped SNPs tested for association with log_ferritin



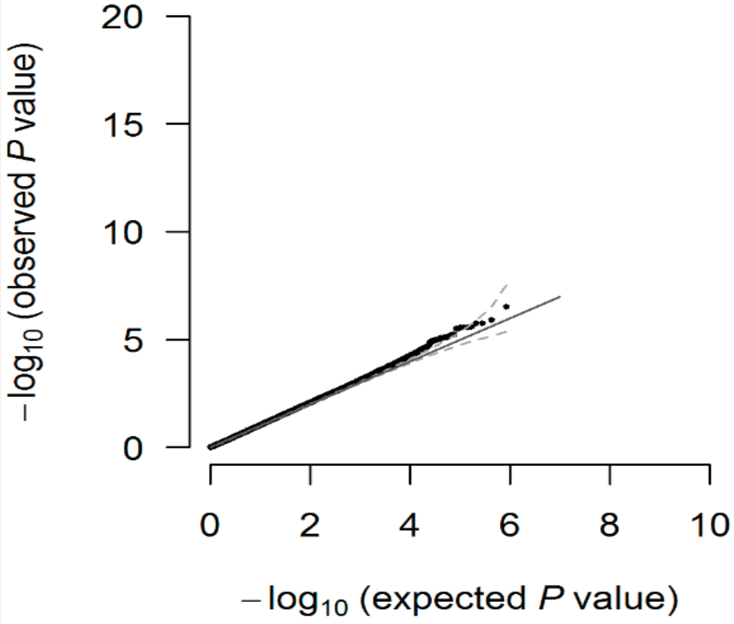
Supplementary Fig. 4a. Manhattan plot of the -$\log_{10}$(P) values by chromosome for log_iron



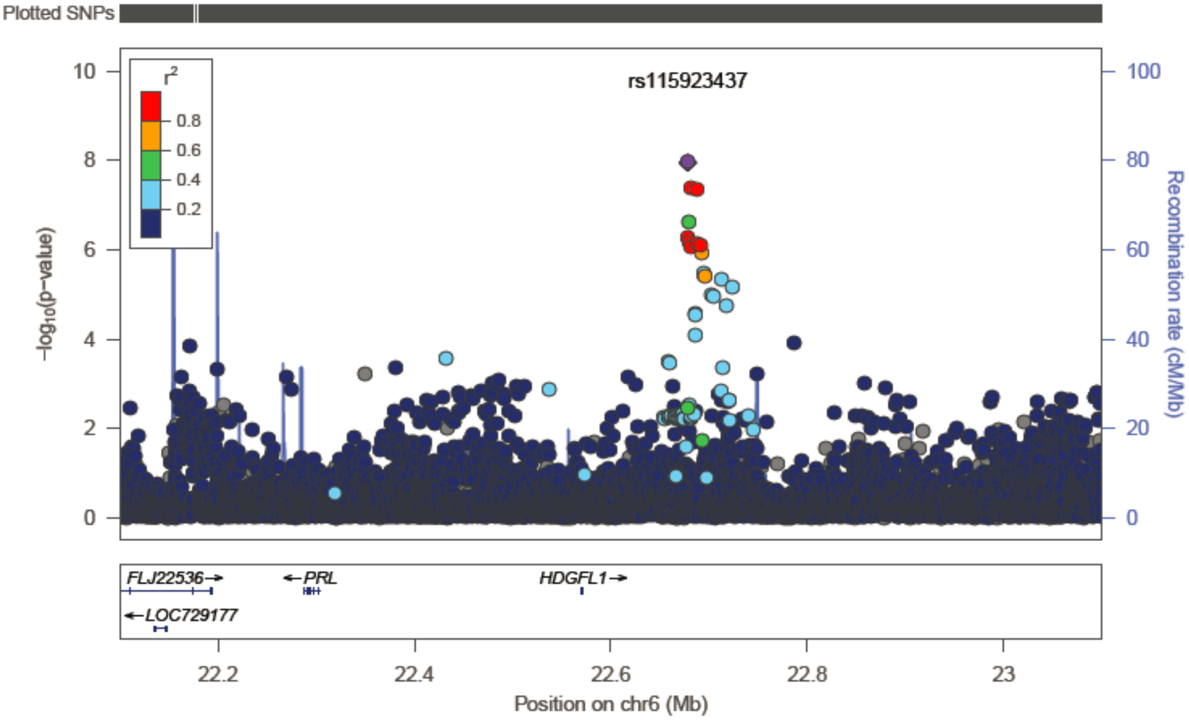
Supplementary Fig.4b. Quantile-Quantile (Q-Q) plots of the P-values across all genotyped SNPs tested for association with log_iron



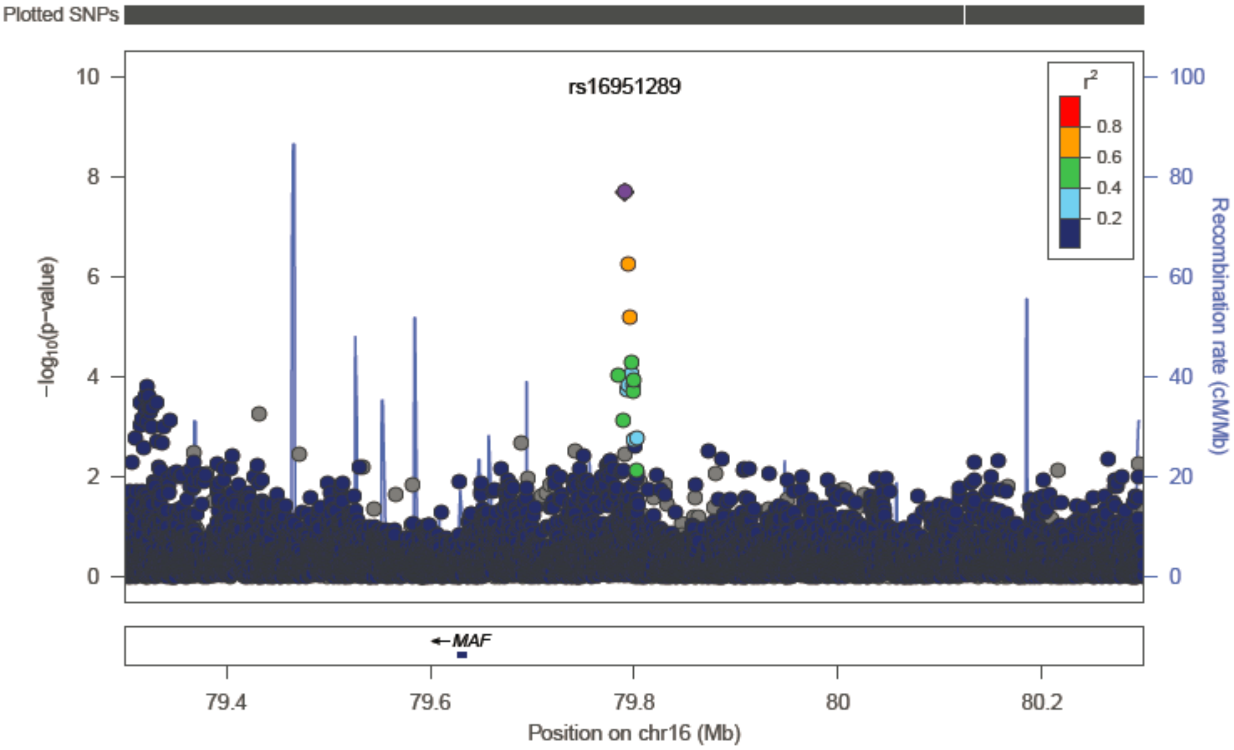
Supplementary Fig. 5a. Manhattan plot of the $-\log_{10}(P)$ values by chromosome for log_SAT



Supplementary Fig.5b. Quantile-Quantile (Q-Q) plots of the P-values across all genotyped SNPs tested for association with log_SAT



Supplementary Fig.6. Regional plot of the -$\log_{10}$(P) values for the SNPs at the *HDGFL1* risk locus for TIBC.



Supplementary Fig.7. Regional plot of the -$\log_{10}$(P) values for the SNPs at the *MAF* risk locus for TIBC