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Supplemental Data

Cross-Tissue and Tissue-Specific eQTLs:

Partitioning the Heritability of a Complex Trait

Jason M. Torres, Eric R. Gamazon, Esteban J. Parra, Jennifer E. Below, Adan Valladares-Salgado, Niels Wacher, Miguel Cruz, Craig L. Hanis, and Nancy J. Cox

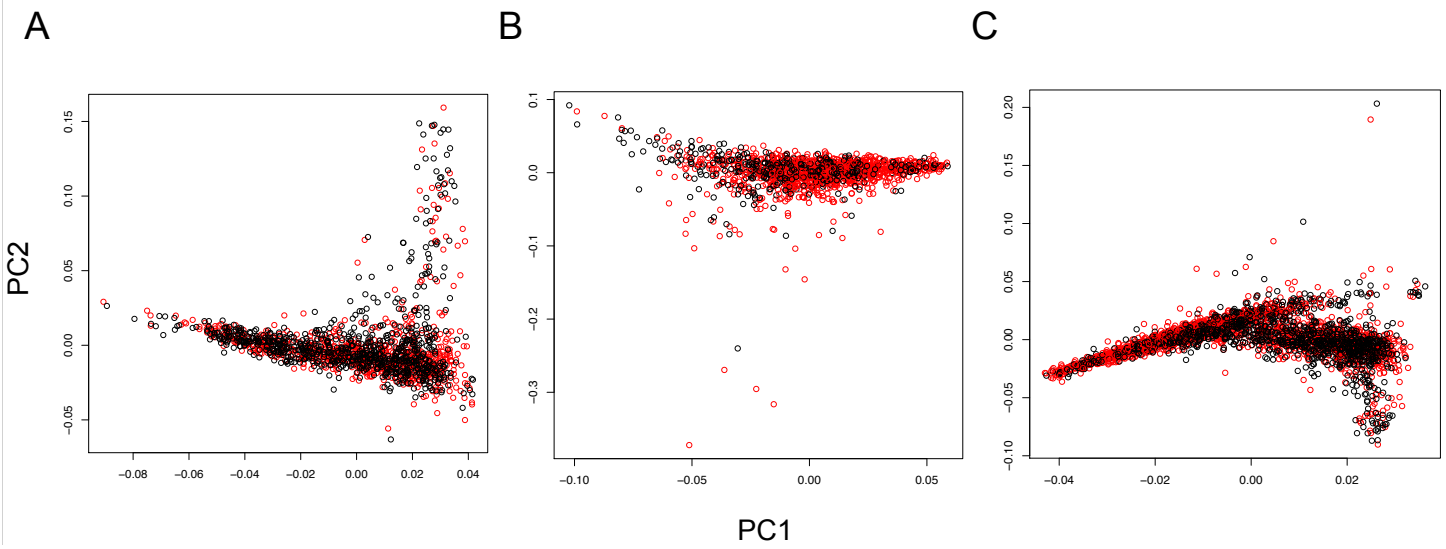

Figure S1. Principal components (PC) analyses of the Hispanic GWAS datasets. Plots of PC1 versus PC2 are shown for the SCT (A), MCM (B), and MH (C) datasets. Black circles indicate controls and red circles indicate cases.

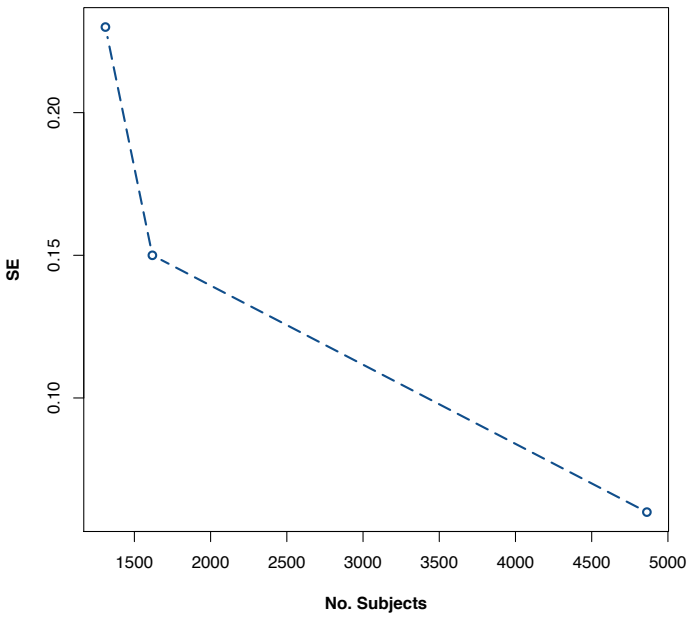

Figure S2. Standard error versus number of subjects represented in each GWAS dataset. From left to right; MCM, SCT, WTCCC.

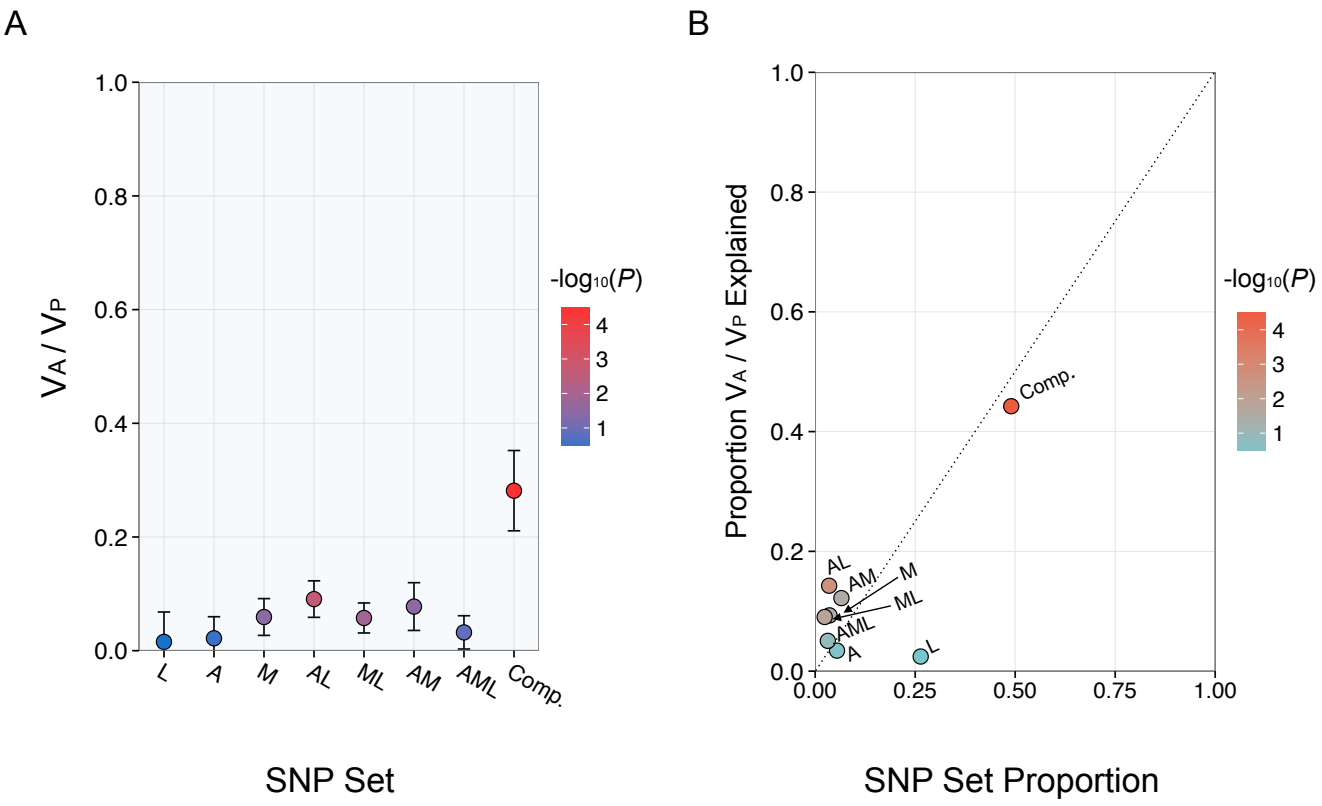

Figure S3. Baseline subset analysis of the WTCCC dataset. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$.

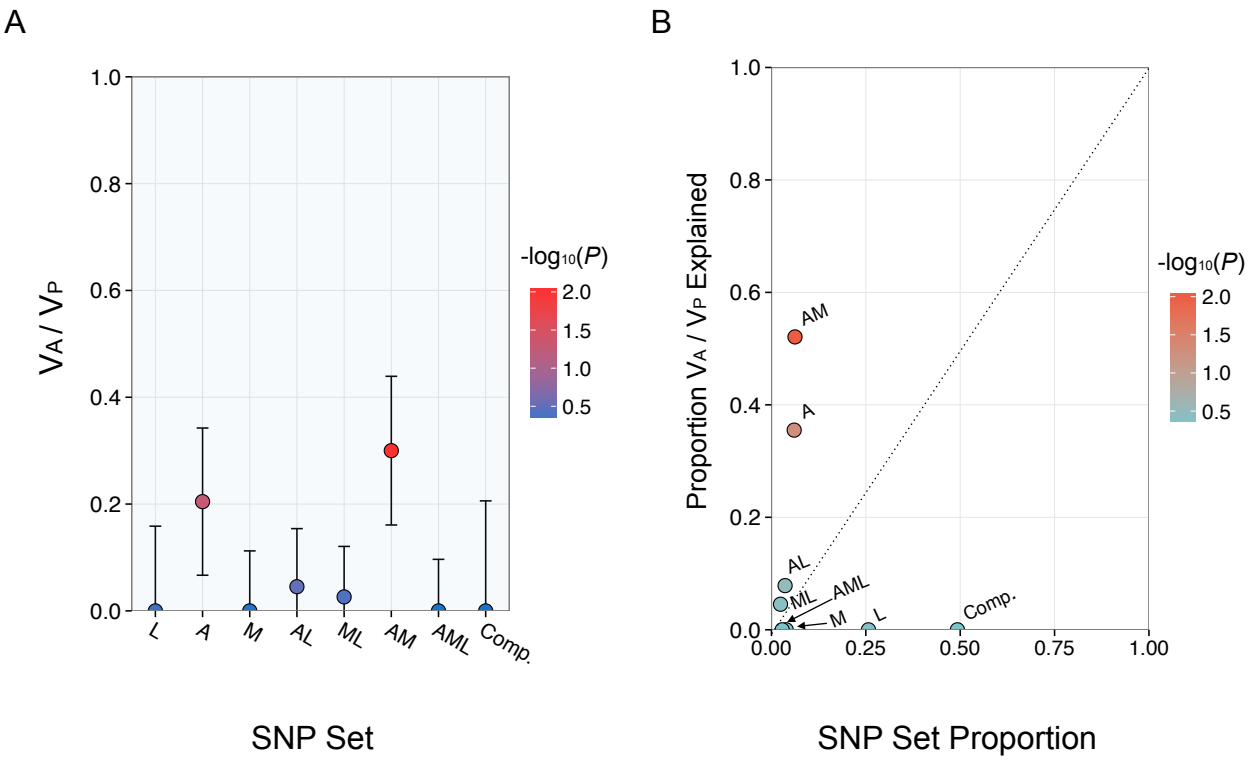

Figure S4. Baseline subset analysis of the merged Hispanic dataset. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$.

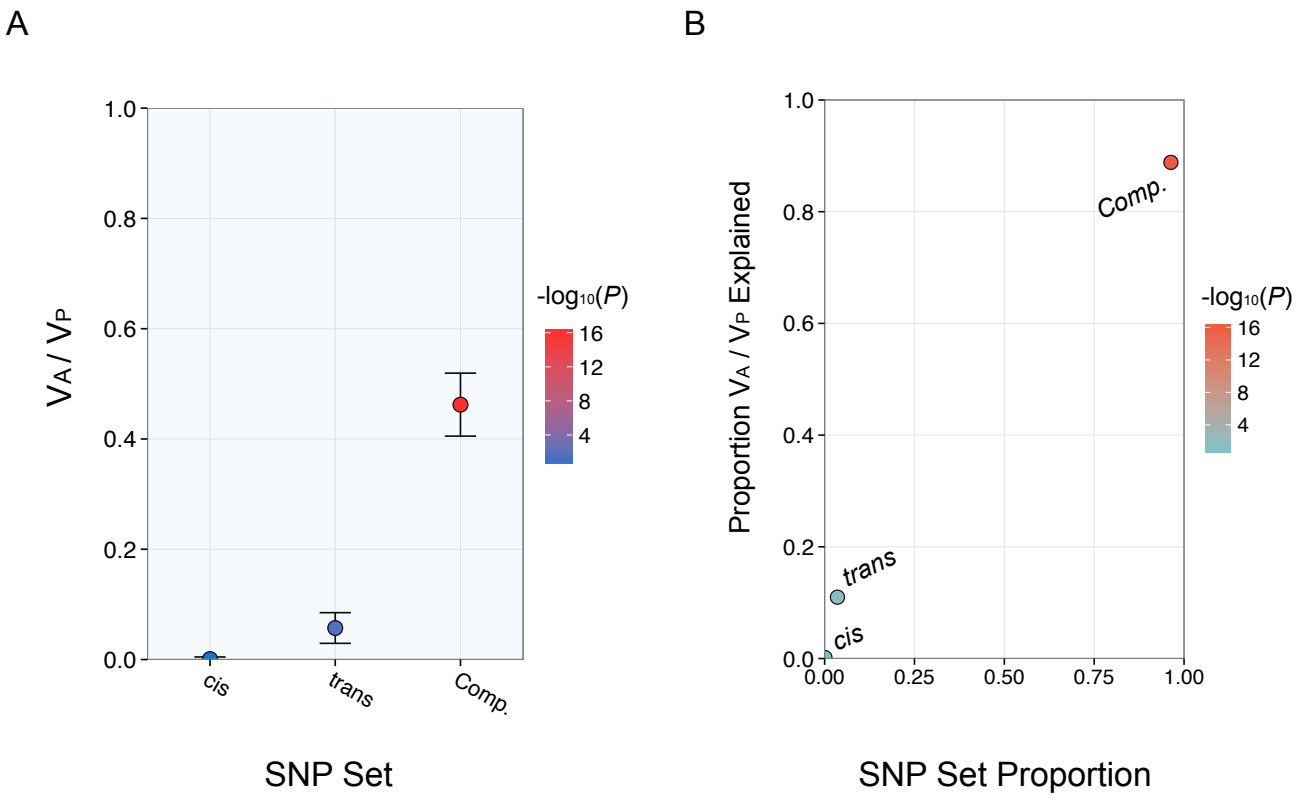

Figure S5. Analysis of heritability from *cis* and *trans* skeletal muscle eQTLs in the WTCCC dataset. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}$(*p*-value).

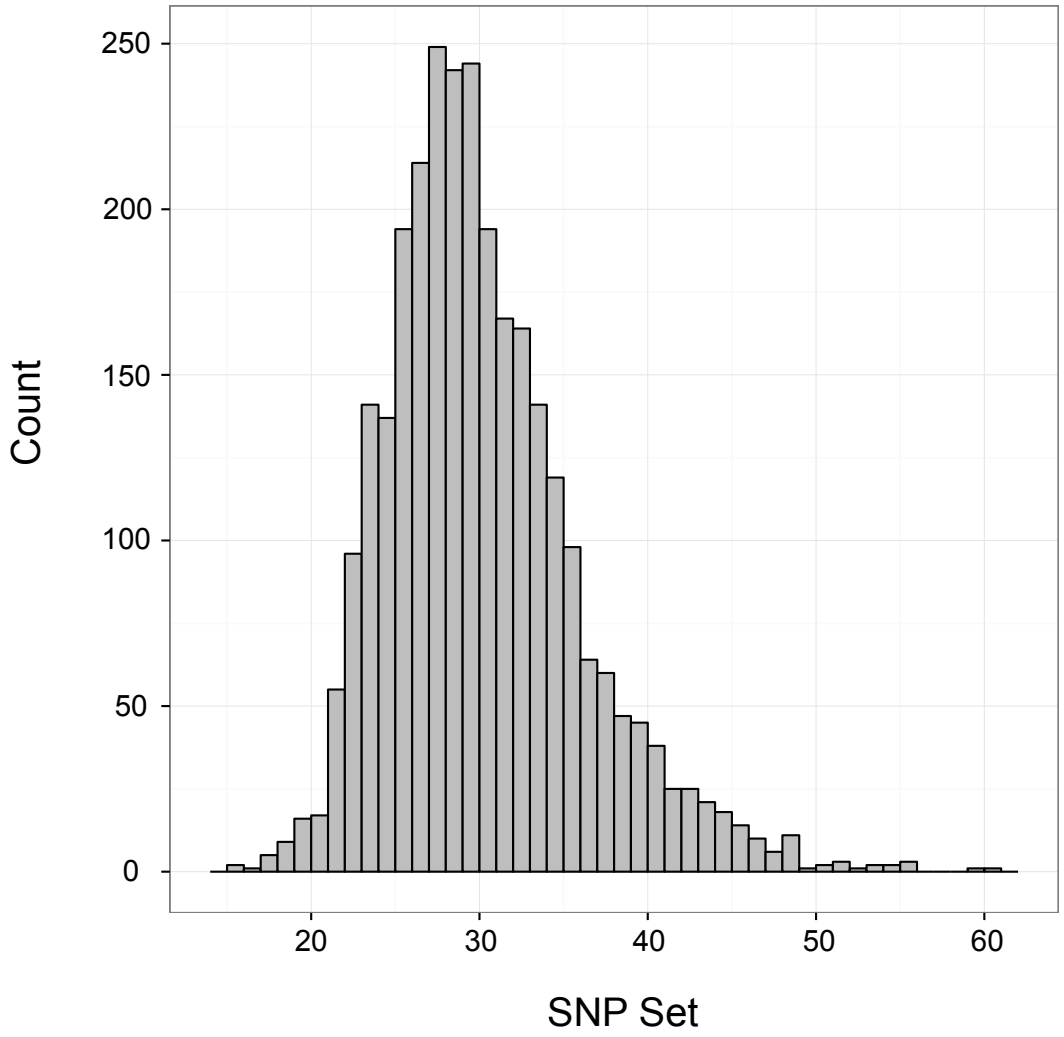

Figure S6. BMI distribution of the merged Hispanic dataset. Mean value with standard deviation, $30.12 \pm 5.74 \ \ kg/m^2$.

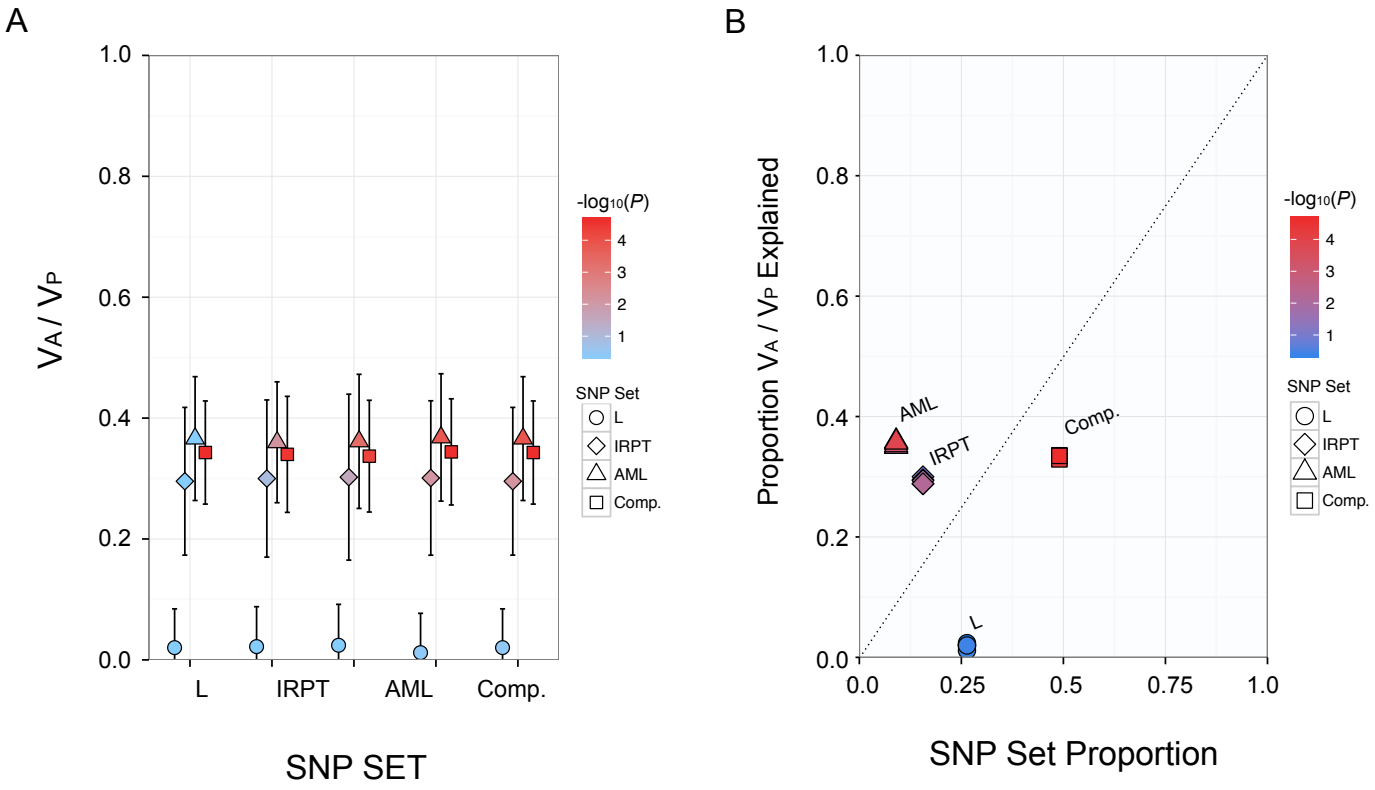

Figure S7. GRM-adjusted partition analysis of the WTCCC dataset.(A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition are shown at each assumed MAF threshold (θ) for causal variants and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. The shape of each point designates the subset identity.

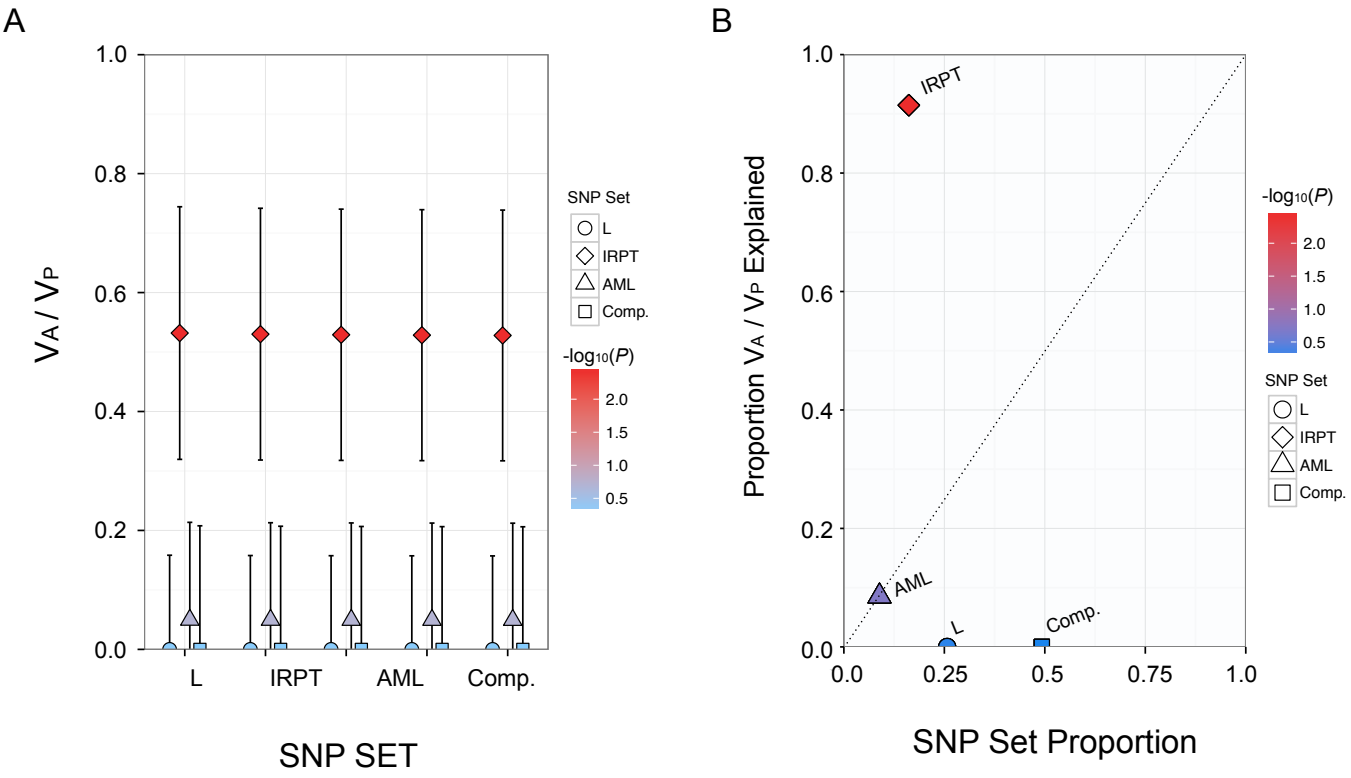

Figure S8. GRM-adjusted partition analysis of the merged Hispanic dataset..(A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition are shown at each assumed MAF threshold (θ) for causal variants and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. The shape of each point designates the subset identity.

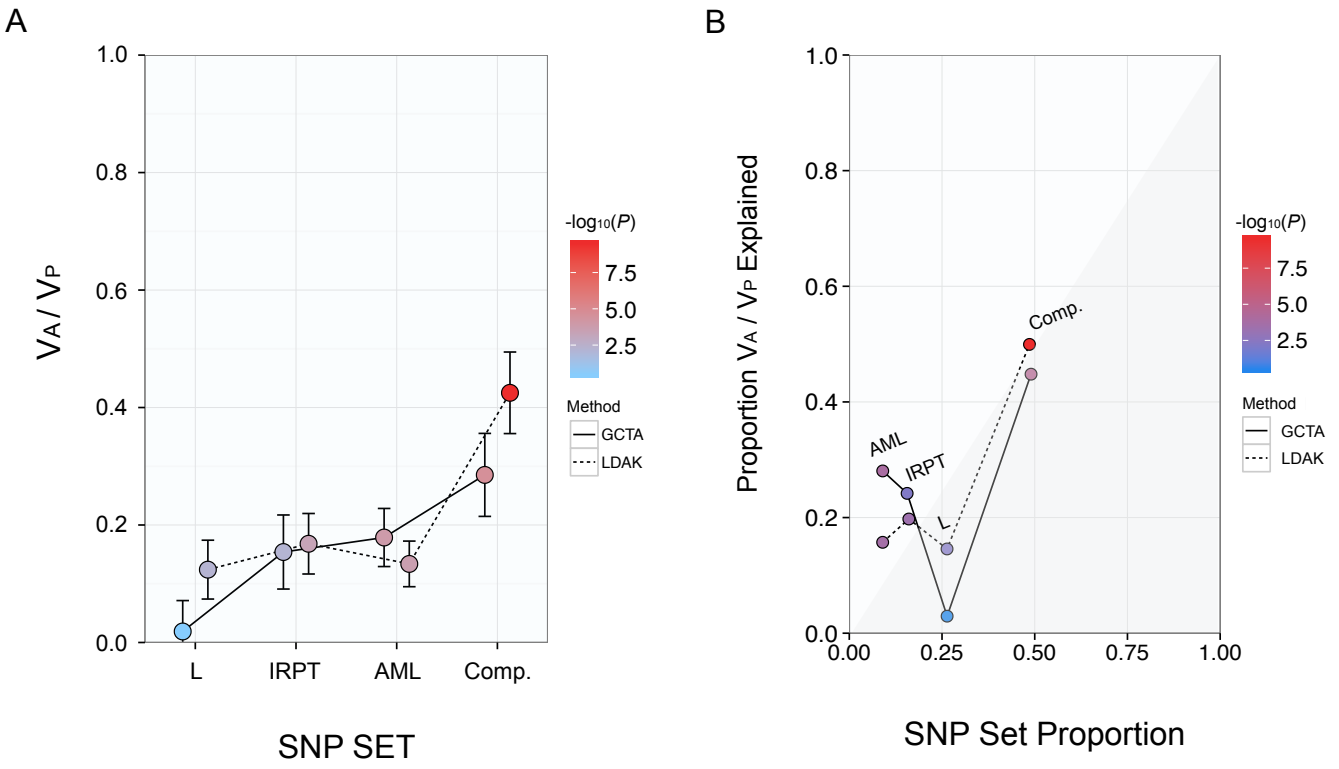

Figure S9. GRM-adjusted partition analysis of the WTCCC dataset. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. Estimates corresponding to the unadjusted GRMs (GCTA) and LD-adjusted GRMs (LDAK) are designated by solid and dashed lines, respectively.

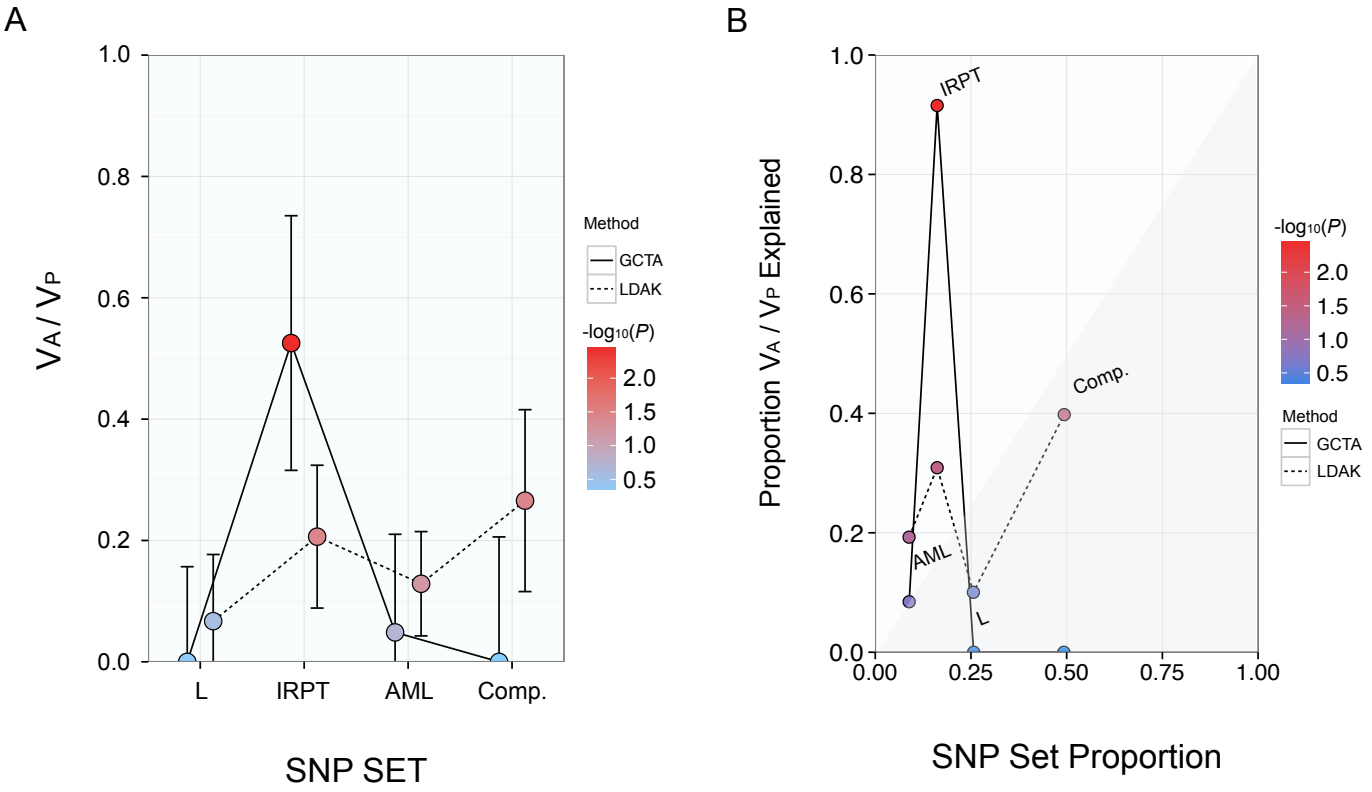

Figure S10. GRM-adjusted partition analysis of the merged Hispanic dataset. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. Estimates corresponding to the unadjusted GRMs (GCTA) and LD-adjusted GRMs (LDAK) are designated by solid and dashed lines, respectively.

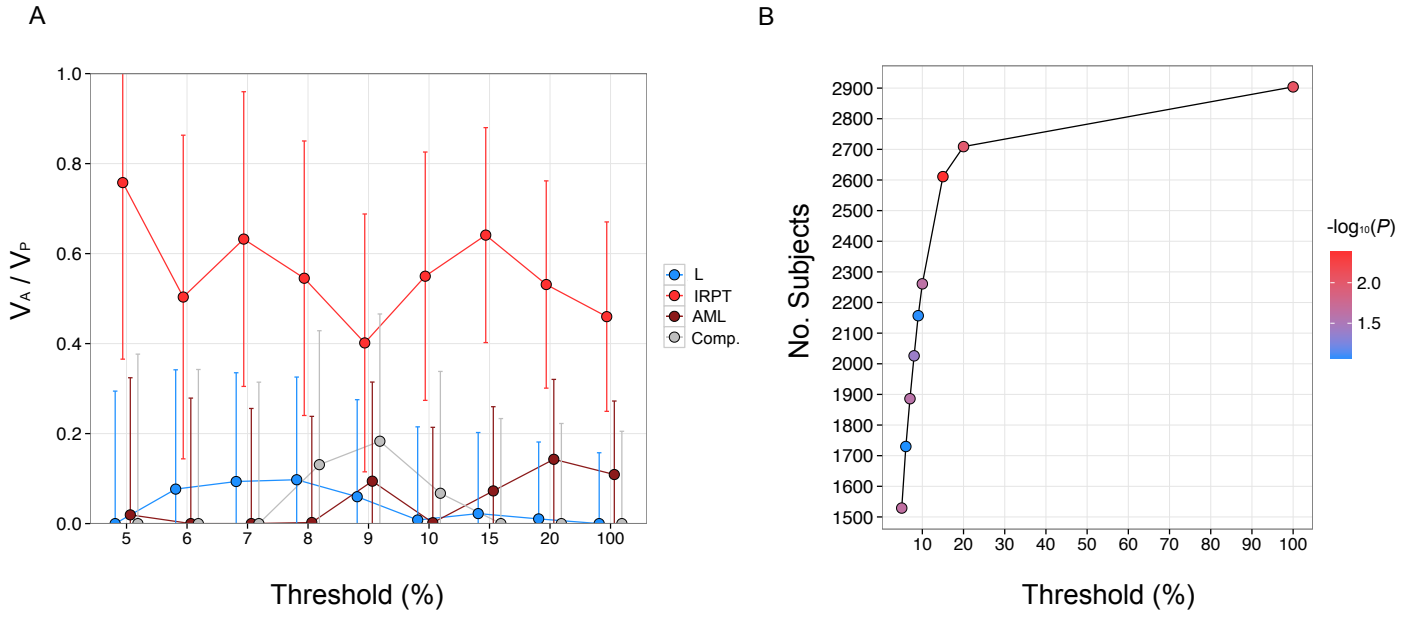

Figure S11. The effect of relatedness thresholds on an eQTL partition analysis of T2D heritability. (A) The IRPT-LCL eQTL partition analysis (explained in detail in the Methods section) was performed at various relatedness thresholds in the merged Hispanic dataset The estimate of heritability (V_A/V_P) is shown for each disjoint subset designated by color at each threshold. (B) The number of retained individuals at each threshold is shown with color corresponding to the significance (-$\log_{10}$(*p*-value)) of the V_A/V_P estimate for the insulin-responsive peripheral tissue (IRPT) subset.

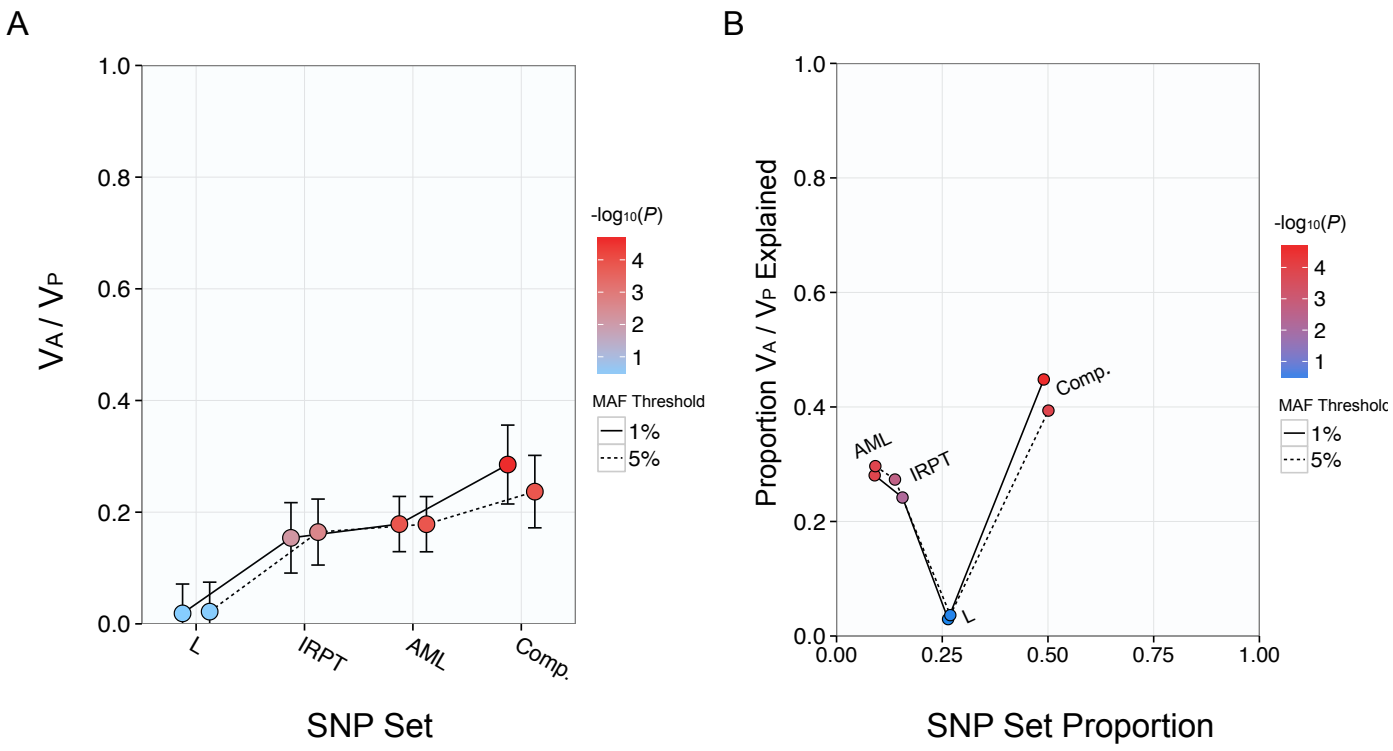

Figure S12. Effect of MAF threshold on partition analysis of the WTCCC dataset.. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. Solid and dashed lines indicate results from a joint analysis performed with a MAF threshold of 1% and 5%, respectively.

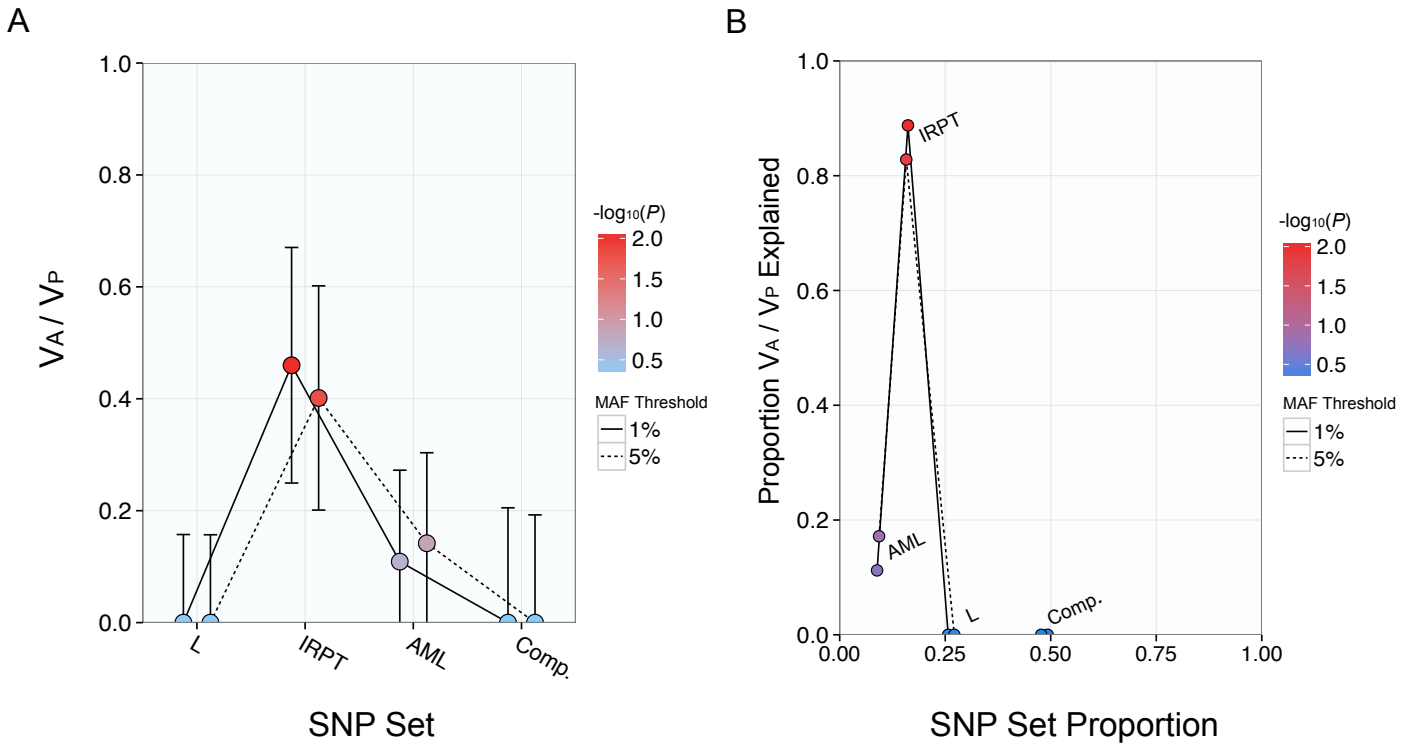

Figure S13. Effect of MAF threshold on partition analysis of the merged Hispanic dataset.. (A) The narrow-sense heritability estimates (V_A/V_P) attributable to disjoint SNP subsets in the IRPT-LCL partition and (B) proportion of explained variance by SNP set proportion for each subset are shown with color corresponding to $-\log_{10}(p\text{-value})$. Solid and dashed lines indicate results from a joint analysis performed with a MAF threshold of 1% and 5%, respectively.

Dataset	Cases (n)	Controls (n)	Age (years)	Sex (n, female)	BMI (kg/m^2)
WTCCC	1,924	2,938	NA	2,298	NA
Starr County	837	781	43.0 ± 11.0	1062	31.0 ± 6.4
Mexico City	967	343	45.5 ± 7.3	833	29.1 ± 4.6

Table S1. Characteristics of study populations. Data are mean ± SD, unless otherwise indicated. NA, not available.

Dataset	V_A/V_P	SE	LRT	P-value	No. SNPs	Prevalence
WTCCC	0.60	0.06	98.24	1.9×10^{-23}	370,139	8%
Starr County	0.56	0.15	13.50	1.2×10^{-04}	1,733,064	20%
Mexico City	0.80	0.23	32.18	7.0×10^{-09}	2,431,591	10%
Merged Hispanic	0.60	0.11	32.79	5.0×10^{-09}	1,652,799	16%

Table S2. Estimates of narrow-sense heritability explained by GWAS-interrogated SNPs. REML estimates of phenotypic variance explained by the additive effect of GWAS SNPs are given with standard error (SE), LRT statistic, *p*-value, number of SNPs, and prevalence of T2D for the WTCCC, Starr County, Mexico City, and Merged Hispanic dataset.

WTCCC				
Covariates	***Va/Vp***	**SE**	**LRT**	**P-value**
—	0.61	0.06	107.85	1.4×10^{-25}
Sex	0.60	0.06	104.57	7.6×10^{-25}
PC1-5	0.60	0.06	98.24	1.9×10^{-23}
Sex+PC1-5	0.59	0.06	95.51	7.4×10^{-23}
Sex+PC1-10	0.56	0.06	79.445	2.5×10^{-19}
Starr County				
Covariates	***Va/Vp***	**SE**	**LRT**	**P-value**
—	0.64	0.15	27.25	8.9×10^{-08}
Sex	0.59	0.15	22.64	9.7×10^{-07}
Age	0.65	0.15	21.85	1.5×10^{-06}
BMI	0.64	0.15	26.66	1.2×10^{-07}
PC1-5	0.59	0.15	17.88	1.2×10^{-05}
Sex+Age	0.61	0.15	18.97	6.7×10^{-06}
Sex+BMI	0.58	0.15	21.14	2.1×10^{-06}
Age+BMI	0.64	0.15	21.65	1.6×10^{-06}
Sex+Age+BMI	0.59	0.15	18.098	1.0×10^{-05}
Sex+Age+BMI+PC1-5	0.56	0.15	13.50	0.0001
Sex+Age+BMI+PC1-10	0.55	0.15	12.411	0.0002
Mexico City				
Covariates	***Va/Vp***	**SE**	**LRT**	**P-value**
—	1.07	0.22	82.95	4.2×10^{-20}
Sex	1.07	0.22	79.63	2.3×10^{-19}
Age	0.91	0.23	46.59	4.4×10^{-12}
BMI	0.94	0.22	70.58	2.2×10^{-17}
PC1-5	1.08	0.23	71.30	1.5×10^{-17}
Sex+Age	0.95	0.23	46.52	4.5×10^{-12}
Sex+BMI	0.96	0.22	69.41	4.0×10^{-17}
Age+BMI	0.78	0.23	38.13	3.3×10^{-10}
Sex+Age+BMI	0.84	0.23	38.92	2.2×10^{-10}
Sex+Age+BMI+PC1-5	0.82	0.23	32.34	6.5×10^{-09}
Sex+Age+BMI+PC1-10	0.80	0.23	32.18	7.0×10^{-09}

Table S3. Evaluation of covariates included in estimation of *chip* heritability. REML estimates of phenotypic variance explained by the additive effect of GWAS SNPs are given for each GWAS dataset with standard error (SE), LRT statistic, *p*-value, number of SNPs, and prevalence of T2D.

WTCCC					
Subset	***Va/Vp***	**SE**	**LRT**	**P-value**	**No. SNPs**
1KB	0.05	0.01	150.09	8.3×10^{-35}	97
10KB	0.06	0.01	130.12	1.9×10^{-30}	429
100KB	0.09	0.01	106.47	2.9×10^{-25}	3043
500KB	0.12	0.02	64.31	5.3×10^{-16}	13931
1MB	0.16	0.02	62.65	1.2×10^{-15}	27116
Starr County					
Subset	***Va/Vp***	**SE**	**LRT**	**P-value**	**No. SNPs**
1KB	0.01	0.02	0.47	0.25	268
10KB	0.02	0.02	0.70	0.20	1546
100KB	0.09	0.04	5.57	9.1×10^{-03}	12063
500KB	0.19	0.06	11.64	3.2×10^{-04}	58852
1MB	0.20	0.08	8.47	1.8×10^{-03}	115591
Mexico City					
Subset	***Va/Vp***	**SE**	**LRT**	**P-value**	**No. SNPs**
1KB	0.08	0.04	6.53	5.3×10^{-03}	445
10KB	0.07	0.04	3.79	0.03	2684
100KB	0.05	0.05	1.08	0.15	20347
500KB	0.23	0.09	6.80	4.6×10^{-03}	91926
1MB	0.23	0.11	4.57	0.02	177167

Table S4. Estimates of narrow-sense heritability explained by subsets comprised of T2D-associated SNPs. Subsets are comprised of T2D-associated SNPs from the NHGRI catalogue and HapMap2 SNPs within 1KB, 10KB, 100KB, 500KB, and 1MB of the associated SNPs. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, and number of SNPs. Results are listed for each GWAS dataset; WTCCC, SCT, MCM.

WTCCC			Hispanic		
Set	**No. SNPs**	**SNP Set Proportion**	**Set**	**No. SNPs**	**SNP Set Proportion**
LCL	134,600	0.354	LCL	569,600	0.345
Adipose	72,290	0.190	Adipose	309,355	0.187
Muscle	60,691	0.160	Muscle	254,357	0.154
GWAS	380,660	1.00	GWAS	1,652,799	1.00

Table S5. Proportion of SNPs designated as eQTLs in each GWAS dataset. The number of SNPs represented in the reference eQTL set and SNP set proportion are shown for each eQTL classification in the WTCCC and merged Hispanic datasets. There are a total of 838,302 SNPs, 616,455 SNPs, and 523,682 SNPs in the LCL adipose, and skeletal muscle eQTL reference sets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.02	0.05	0.12	0.36	0.27	0.03	0.1
IRPT	0.13	0.05	6.16	6.5×10^{-03}	0.16	0.24	1.4
AML	0.15	0.04	13.36	1.3×10^{-04}	0.09	0.28	2.8
Complement	0.25	0.06	16.46	2.5×10^{-05}	0.48	0.45	0.9

Table S6. Estimates of narrow-sense heritability explained by eQTL subsets in the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.01	0.04	0.08	0.39	0.27	0.02	0.1
A	0.02	0.03	0.35	0.28	0.06	0.03	0.6
M	0.05	0.03	3.36	0.03	0.04	0.09	2.3
AM	0.09	0.04	5.06	0.01	0.10	0.17	1.6
AML	0.13	0.04	12.89	1.6×10^{-04}	0.06	0.23	3.6
Complement	0.24	0.06	16.54	2.4×10^{-05}	0.48	0.44	0.9

Table S7. Expanded IRPT-LCL analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	***Va/Vp***	**SE**	**LRT**	**P-value**	**SNP Set Proportion**	**Proportion of *Chip* Heritability**	**Factor**
A ∪ AL	0.11	0.05	5.06	0.01	0.09	0.17	2.0
M ∪ ML	0.18	0.04	9.0	1.4×10^{-03}	0.06	0.19	3.2
Complement	0.39	0.08	27.31	8.7×10^{-08}	0.85	0.63	0.7

Table S8. Index subset analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.02	0.05	0.09	0.39	0.26	0.02	0.1
A	0.02	0.04	0.35	0.28	0.05	0.03	0.6
M	0.06	0.03	3.39	0.03	0.04	0.09	2.6
AL	0.09	0.03	8.21	0.00	0.03	0.14	4.1
ML	0.06	0.03	4.98	0.01	0.02	0.09	3.8
AM	0.08	0.04	3.55	0.03	0.07	0.12	1.9
AML	0.03	0.03	1.26	0.13	0.03	0.05	1.6
Complement	0.28	0.07	16.03	0.00	0.49	0.44	0.9

Table S9. Baseline subset analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
M	0.07	0.03	4.53	0.02	0.04	0.11	3.1
CT	0.23	0.06	14.94	5.5×10^{-05}	0.16	0.37	2.5
Complement	0.32	0.07	19.80	4.3×10^{-06}	0.80	0.52	0.7

Table S10. Index subset analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. M and CT denote muscle-specific and cross-tissue eQTL subsets, respectively.

Subset	Va/Vp	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A ∪ M ∪ AM	0.18	0.06	8.83	1.5×10^{-03}	0.16	0.29	1.8
AL ∪ ML ∪ AML	0.15	0.05	10.43	6.2×10^{-03}	0.09	0.24	2.7
Complement	0.30	0.08	15.59	3.9×10^{-05}	0.75	0.48	0.6

Table S11. Index subset analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	Va/Vp	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.00	0.04	0.00	0.50	0.16	0.00	0.0
CT	0.24	0.06	16.98	1.9×10^{-05}	0.16	0.38	2.4
Complement	0.40	0.07	33.51	3.5×10^{-09}	0.68	0.62	0.9

Table S12. *chip* heritability explained by matched sets of LCL-specific and cross-tissue eQTLs in the WTCCC dataset. In this analysis, the L subset contained the set of the most significant LCL-specific eQTLs so that the SNP set proportion was identical to that of the Cross-tissue set. REML estimates of phenotypic variance explained by the additive effect of GWAS SNPs are given for each GWAS dataset with standard error (SE), LRT statistic, *p*-value, number of SNPs, and prevalence of T2D.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
Cross Tissue (*Cis*)	0.02	0.02	2.47	0.06	0.01	0.04	3.9
Cross Tissue (*Trans*)	0.21	0.06	11.78	3.0×10^{-04}	0.15	0.33	2.3
Complement	0.39	0.07	29.45	2.9×10^{-08}	0.84	0.63	0.7

Table S13. Cis-trans analysis of cross-tissue eQTLs in the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
Muscle (*Cis*)	0.0009	0.004	0.06	0.40	0.0008	0.002	2.2
Muscle (*Trans*)	0.06	0.03	4.29	0.02	0.04	0.11	3.1
Complement	0.46	0.06	68.53	6.3×10^{-17}	0.96	0.89	0.9

Table S14. Cis-trans analysis of muscle-specific eQTLs in the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.00	0.27	0.00	0.49	0.26	0.00	0.0
A	0.08	0.25	0.05	0.41	0.06	0.12	2.2
M	0.27	0.20	2.17	0.07	0.04	0.41	11.4
AM	0.26	0.27	0.83	0.18	0.09	0.39	4.5
AML	0.06	0.26	0.69	0.20	0.06	0.08	1.5
Complement	0.00	0.35	0.00	0.50	0.50	0.00	0.0

Table S15. Expanded IRPT-LCL analysis of the SCT dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.10	0.41	0.00	0.50	0.23	0.10	0.4
A	0.00	0.40	0.00	0.50	0.06	0.00	0.0
M	0.25	0.31	3.19	0.04	0.04	0.25	7.1
AM	0.48	0.47	0.00	0.50	0.10	0.49	4.9
AML	0.00	0.43	0.00	0.50	0.05	0.00	0.0
Complement	0.15	0.58	0.00	0.50	0.52	0.16	0.3

Table S16. Expanded IRPT-LCL analysis of the MCM dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

WTCCC				
Prevalence (%)	***Va/Vp***	**SE**	**LRT**	**P-value**
5	0.52	0.05	98.24	1.9×10^{-23}
10	0.64	0.07	98.24	1.9×10^{-23}
15	0.73	0.08	98.24	1.9×10^{-23}
20	0.79	0.08	98.24	1.9×10^{-23}
25	0.85	0.09	98.24	1.9×10^{-23}
Starr County				
Prevalence (%)	***Va/Vp***	**SE**	**LRT**	**P-value**
5	0.37	0.10	13.50	0.0001
10	0.45	0.12	13.50	0.0001
15	0.52	0.14	13.50	0.0001
20	0.56	0.15	13.50	0.0001
25	0.60	0.16	13.50	0.0001
Mexico City				
Prevalence (%)	***Va/Vp***	**SE**	**LRT**	**P-value**
5	0.65	0.19	32.18	7.0×10^{-09}
10	0.80	0.23	32.18	7.0×10^{-09}
15	0.92	0.27	32.18	7.0×10^{-09}
20	1.00	0.29	32.18	7.0×10^{-09}
25	1.07	0.31	32.18	7.0×10^{-09}

Table S17. Evaluation of the prevalence parameter specified in the estimation of *chip* heritability. REML estimates of phenotypic variance explained by the additive effect of GWAS SNPs are given for each GWAS dataset with standard error (SE), LRT statistic, *p*-value, number of SNPs, and prevalence of T2D.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.00	0.16	0.01	0.47	0.26	0.00	0.0
IRPT	0.46	0.21	5.60	0.01	0.16	0.81	5.0
AML	0.11	0.16	0.72	0.20	0.09	0.19	2.2
Complement	0.00	0.21	0.00	0.50	0.49	0.00	0.0

Table S18. Estimates of narrow-sense heritability explained by eQTL subsets in the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.00	0.16	0.00	0.50	0.26	0.00	0.0
A	0.22	0.14	3.26	0.04	0.06	0.38	6.3
M	0.00	0.11	0.00	0.50	0.04	0.00	0.0
AM	0.27	0.15	3.54	0.03	0.09	0.48	5.2
AML	0.08	0.15	0.60	0.22	0.06	0.15	2.4
Complement	0.00	0.20	0.01	0.45	0.49	0.00	0.0

Table S19. Expanded IRPT-LCL analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.00	0.16	0.03	0.43	0.26	0.00	0.0
A	0.20	0.14	2.65	0.05	0.06	0.36	6.0
M	0.00	0.11	0.00	0.48	0.04	0.00	0.0
AL	0.05	0.11	0.24	0.31	0.04	0.08	2.2
ML	0.03	0.09	0.09	0.38	0.02	0.05	1.9
AM	0.30	0.14	5.55	0.01	0.06	0.52	8.3
AML	0.00	0.10	0.00	0.50	0.03	0.00	0.0
Complement	0.00	0.21	0.00	0.50	0.49	0.00	0.0

Table S20. Baseline subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
M	0.00	0.11	0.00	0.50	0.04	0.00	0.0
CT	0.45	0.19	5.93	0.01	0.15	0.89	5.9
Complement	0.05	0.20	0.05	0.41	0.81	0.11	0.1

Table S21. Index subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. M and CT denote muscle-specific and cross-tissue eQTL subsets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A	0.21	0.13	3.10	0.04	0.06	0.36	6.0
CT	0.37	0.19	4.37	0.02	0.15	0.64	4.2
Complement	0.00	0.21	0.00	0.50	0.79	0.00	0.0

Table S22. Index subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. A and CT denote adipose-specific and cross-tissue eQTL subsets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A ∪ AL	0.32	0.16	4.35	0.02	0.10	0.63	6.5
M ∪ ML	0.05	0.13	0.12	0.36	0.06	0.09	1.4
Complement	0.14	0.21	0.47	0.25	0.84	0.28	0.34

Table S23. Index subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Facto
A ∪ M ∪ AM	0.53	0.19	8.29	1.2×10^{-03}	0.16	0.91	5.6
AL ∪ ML ∪ AML	0.05	0.14	0.10	0.38	0.09	0.09	1.0
Complement	1.0×10^{-06}	0.22	0.00	0.50	0.75	1.7×10^{-06}	2.3×10

Table S24. Index subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
L	0.01	0.13	0.01	0.47	0.26	0.02	0.1
Complement	0.48	0.16	8.896	1.4×10^{-03}	0.74	0.98	1.3

Table S25. Index subset analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. L denotes LCL-specific eQTL subset.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
M	0.00	0.19	0.00	0.50	0.04	0.00	0.0
CT	0.46	0.32	2.32	0.06	0.15	0.65	4.3
Complement	0.25	0.36	0.24	0.31	0.81	0.35	0.4

Table S26. Index subset analysis of the merged Hispanic dataset with BMI < 30. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. M and CT denote muscle-specific and cross-tissue eQTL subsets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A	0.01	0.23	0.00	0.48	0.06	0.02	0.3
CT	0.50	0.32	2.45	0.06	0.15	0.76	5.0
Complement	0.15	0.37	0.15	0.35	0.79	0.22	0.3

Table S27. Index subset analysis of the merged Hispanic dataset with BMI < 30. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. A and CT denote adipose-specific and cross-tissue eQTL subsets, respectively.

Subset	Va/Vp	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
M	0.06	0.25	0.06	0.41	0.04	0.08	2.2
CT	0.25	0.42	0.34	0.28	0.15	0.34	2.3
Complement	0.42	0.45	0.91	0.17	0.81	0.57	0.7

Table S28. Index subset analysis of the merged Hispanic dataset with BMI ≥ 30. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. M and CT denote muscle-specific and cross-tissue eQTL subsets, respectively.

Subset	Va/Vp	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A	0.65	0.31	4.15	0.02	0.06	0.80	13.3
CT	0.11	0.42	0.07	0.40	0.15	0.14	0.9
Complement	0.05	0.45	0.01	0.46	0.79	0.06	0.1

Table S29. Index subset analysis of the merged Hispanic dataset with BMI ≥ 30. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. A and CT denote adipose-specific and cross-tissue eQTL subsets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
A	0.62	0.31	3.87	0.02	0.06	0.69	11.4
CT	0.00	0.42	0.00	0.50	0.15	0.00	0.0
Complement	0.28	0.45	0.45	0.25	0.79	0.31	0.4

Table S30. Index subset analysis of the merged Hispanic dataset with BMI ≥ 30. BMI was not included as a covariate in this analysis. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained. A and CT denote adipose-specific and cross-tissue eQTL subsets, respectively.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
"Lean" cohort							
A ∪ AM	0.15	0.30	0.25	0.31	0.12	0.22	1.8
Complement	0.54	0.31	2.8	0.05	0.88	0.78	0.9
"Non-lean" cohort							
A ∪ AM	0.69	0.38	3.23	0.04	0.12	0.77	6.3
Complement	0.20	0.38	0.29	0.30	0.88	0.23	0.3

Table S31. Index subset analysis of the merged Hispanic. SNPs were partitioned into the set comprised of the union of adipose-specific eQTLs and eQTLs mapped in both adipose and muscle tissue ($A \cup AM$) and the complement set of SNPs. For the "lean" (BMI < 30) and "non-lean" (BMI ≥ 30) cohort, REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
				GCTA			
L	0.02	0.0	0.12	0.36	0.26	0.03	0.1
IRPT	0.15	0.06	6.16	6.5×10^{-03}	0.16	0.24	1.5
AML	0.18	0.05	13.36	1.2×10^{-04}	0.09	0.28	3.1
Comp.	0.29	0.07	16.46	2.5×10^{-05}	0.49	0.45	0.9
				LDAK			
L	0.12	0.05	6.34	5.9×10^{-03}	0.26	0.15	0.6
IRPT	0.17	0.05	11.00	4.5×10^{-04}	0.16	0.20	1.3
AML	0.13	0.04	12.26	2.3×10^{-04}	0.09	0.16	1.8
Comp.	0.43	0.07	38.25	$3.11 \times 10z^{-10}$	0.49	0.50	1.0

Table S32. GRM-adjusted estimates of narrow-sense heritability explained by eQTL subsets in the WTCCC dataset. Heritability estimates corresponding to the unadjusted GRM (GCTA) and LD-adjusted GRM (LDAK) for each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
				GCTA			
L	0.00	0.16	0.01	0.47	0.26	0.00	0.0
IRPT	0.53	0.21	7.2	3.6×10^{-03}	0.16	0.92	5.8
AML	0.05	0.16	0.76	0.19	0.09	0.08	0.9
Comp.	0.00	0.21	0.00	0.5	0.49	0.00	0.0
				LDAK			
L	0.07	0.11	0.38	0.27	0.26	0.10	0.4
IRPT	0.21	0.12	3.20	0.037	0.16	0.31	1.9
AML	0.13	0.09	2.28	0.07	0.09	0.19	2.1
Comp.	0.27	0.15	3.20	0.04	0.50	0.40	0.8

Table S33. GRM-adjusted estimates of narrow-sense heritability explained by eQTL subsets in the merged Hispanic dataset. Heritability estimates corresponding to the unadjusted GRM (GCTA) and LD-adjusted GRM (LDAK) for each subset are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Threshold (%)	Subjects (n)	Va/Vp	SE
2.5	667	0.80	0.40
5	1540	0.60	0.20
10	2272	0.60	0.14
15	2628	0.62	0.12
20	2730	0.60	0.11
None	2928	0.48	0.10

Table S34. Evaluation of genetic relatedness thresholds applied to the merged Hispanic dataset. REML estimates of phenotypic variance explained by GWAS SNPs are given with standard error (SE) and number of subjects retained (n) for each relatedness threshold.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
				MAF 1%			
L	0.02	0.05	0.12	0.36	0.26	0.03	0.1
A ∪ M ∪ AM	0.15	0.06	6.16	6.5×10^{-03}	0.16	0.24	1.6
AML	0.18	0.05	13.36	1.3×10^{-03}	0.09	0.28	3.1
Complement	0.29	0.07	16.46	2.5×10^{-05}	0.49	0.45	0.9
				MAF 5%			
L	0.02	0.05	0.17	0.34	0.27	0.04	0.1
A ∪ M ∪ AM	0.16	0.06	8.0	2.3×10^{-03}	0.14	0.27	2.0
AML	0.18	0.05	13.32	1.3×10^{-03}	0.09	0.30	3.2
Complement	0.24	0.06	13.35	1.3×10^{-03}	0.50	0.39	0.8

Table S35. Effect of MAF threshold on partition analysis of the WTCCC dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset in an IRPT-LCL partition analysis are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.

Subset	*Va/Vp*	SE	LRT	P-value	SNP Set Proportion	Proportion of *Chip* Heritability	Factor
				MAF 1%			
L	0.02	0.05	0.12	0.36	0.26	0.03	0.1
A ∪ M ∪ AM	0.15	0.06	6.16	6.5×10^{-03}	0.16	0.24	1.6
AML	0.18	0.05	13.36	1.3×10^{-03}	0.09	0.28	3.1
Complement	0.29	0.07	16.46	2.5×10^{-05}	0.49	0.45	0.9
				MAF 5%			
L	0.02	0.05	0.17	0.34	0.27	0.04	0.1
A ∪ M ∪ AM	0.16	0.06	8.0	2.3×10^{-03}	0.14	0.27	2.0
AML	0.18	0.05	13.32	1.3×10^{-03}	0.09	0.30	3.2
Complement	0.24	0.06	13.35	1.3×10^{-03}	0.50	0.39	0.8

Table S36. Effect of MAF threshold on partition analysis of the merged Hispanic dataset. REML estimates of phenotypic variance explained by the additive effect of SNPs from each subset in an IRPT-LCL partition analysis are given with standard error (SE), LRT statistic, *p*-value, SNP set proportion, and proportion of *chip* heritability explained. Factor relates SNP set proportion to proportion of *chip* heritability explained.