Annotation	#Source	Model
base	Finucane et al.[1]	baseline/baselineLD
Coding	UCSC Genome Browser and Finucane et al.[1]	baseline/baselineLD
3' UTR	UCSC Genome Browser and Finucane et al.[1]	baseline/baselineLD
5' UTR	UCSC Genome Browser and Finucane et al.[1]	baseline/baselineLD
Promoter	UCSC Genome Browser and Finucane et al.[1]	baseline/baselineLD
Intron	UCSC Genome Browser and Finucane et al.[1]	baseline/baselineLD
ENCODE TF binding	ENCODE[2] and Finucane et al.[1]	baseline/baselineLD
CTCF promoter	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
Promotor-Flanking	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
Transcribed	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
Transcription start size (TSS)	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
Strong enhancer	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
Weak enhancer	Hoffman et al[3] and Finucane et al.[1]	baseline/baselineLD
DHS	ENCODE[2]/Roadmap post-processed by Trynka et al and Finucane et al.[1]	baseline/baselineLD
H3K4me1	Roadmap Epigenomics post-processed by Trynka et al[4] and Finucane et al.[1]	baseline/baselineLD
H3K4me3	Roadmap Epigenomics post-processed by Trynka et al[4] and Finucane et al.[1]	baseline/baselineLD
H3K9ac	Roadmap Epigenomics post-processed by Trynka et al[4] and Finucane et al.[1]	baseline/baselineLD
H3K27ac	Roadmap Epigenomics post-processed by Trynka et al[4] and Finucane et al.[1]	baseline/baselineLD
H3K27ac	Hnisz et al[5] and Finucane et al.[1]	baseline/baselineLD
Super Enhancer	Hnisz et al[5] and Finucane et al.[1]	baseline/baselineLD
Conserved	Lindblad-Toh et al.[6] and Finucane et al.[1]	baseline/baselineLD
FANTOM5 enhancer	Anderson et al.[7] and Finucane et al.[1]	baseline/baselineLD
2 GERP[8] conserved	Gazal et al.[9]	baselineLD
10 MAF bin	Gazal et al.[9]	baselineLD
Predicted Allele Age	Gazal et al.[9]	baselineLD
LLD-AFR	Gazal et al.[9]	baselineLD
Recombination Rate	Gazal et al.[9]	baselineLD
Nucleotide Diversity	Gazal et al.[9]	baselineLD
Background Selection Statistics	Gazal et al.[9]	baselineLD
CpG-Content	Gazal et al.[9]	baselineLD

Supplementary Table 1. List of 75 functional and LD related annotations in baselineLD model. For each of the 24 annotations in the baselineLD a 500bp window around the category is added. In the case of DHS, H3K4me1, H3K4me3, and H3Kac site a 100-bp window is added.

Annotation	S-LDSC Enrichment (se)	GCTA Enrichment(se)	True Enrichment
AllcisQTL	3.32 (0.03)	3.97 (0.01)	4.41
TopcisQTL	60.57 (1.32)	113.98 (0.64)	14.92
95%CredibleSet	5.35 (0.07)	8.72 (0.04)	5.54
MaxCPP	9.83 (0.22)	NA	10.36

Supplementary Table 2. S-LDSC enrichment estimates for four annotations. We simulated 400 replicate data sets. Enrichment is computed by averaging over all 400 data sets (n=400 independent simulations to derive the statistics). True enrichment in each data set is computed using the true causal effect size of each variant.

n_{ge}	n_m	h^2_{ge}	**Annotation**	**S-LDSC Enrichment (se)**	**GCTA (REML) Enrichment (se)**	**True Enrichment**
1	0%	0.16	AllcisQTL	5.35 (0.04)	2.38 (0.02)	8.48
			TopcisQTL	203.47 (2.025)	88.03 (0.86)	91.03
			95%CredibleSet	15.25 (0.17)	8.75 (0.13)	20.35
			MaxCPP	35.55 (0.83)	NA	49.07
10	0%	0.16	AllcisQTL	3.49 (0.03)	4.37 (0.01)	5.55
			TopcisQTL	158.76 (2.01)	137.49 (0.55)	28.66
			95%CredibleSet	10.24 (0.11)	13.07 (0.06)	10.59
			MaxCPP	25.24 (0.44)	NA	34.94
10%	0%	0.16	AllcisQTL	3.37 (0.03)	3.79 (0.01)	4.40
			TopcisQTL	60.20 (1.24)	112.12 (0.49)	15.17
			95%CredibleSet	5.51 (0.07)	8.78 (0.04)	5.65
			MaxCPP	8.97 (0.25)	NA	9.52
10%	10%	0.16	AllcisQTL	3.32 (0.03)	3.97 (0.01)	4.41
			TopcisQTL	60.57 (1.32)	113.98 (0.64)	14.92
			95%CredibleSet	5.35 (0.07)	8.72 (0.04)	5.54
			MaxCPP	9.83 (0.22)	NA	10.36
10%	50%	0.16	AllcisQTL	3.37 (0.03)	3.79 (0.01)	4.40
			TopcisQTL	60.20 (1.24)	112.12 (0.49)	15.17
			95%CredibleSet	5.51 (0.07)	8.78 (0.04)	5.65
			MaxCPP	8.97 (0.25)	NA	9.52
10%	10%	0.1	AllcisQTL	3.55 (0.03)	4.47 (0.01)	4.49
			TopcisQTL	59.42 (1.28)	110.54 (0.65)	13.55
			95%CredibleSet	5.08 (0.07)	8.26 (0.03)	5.30
			MaxCPP	8.37 (0.28)	NA	9.58
10%	10%	0.2	AllcisQTL	3.37 (0.03)	3.79 (0.01)	4.40
			TopcisQTL	61.89 (1.39)	113.33 (0.67)	15.58
			95%CredibleSet	5.58 (0.06)	8.99 (0.04)	5.72
			MaxCPP	9.40 (0.25)	NA	10.86

Supplementary Table 3. S-LDSC and GCTA simulation results for four annotations under different parameter settings. We simulated gene expression and trait phenotypes assuming the same set of variants is causal. The true effect size for gene expression is obtained by sampling from $N(0, h2_{ge}/n_{ce})$ where h^2_{ge} is the heritability of the gene expression and n_{ge} is the total number of causal variants for gene expression. Similarly, the true effect size for trait is obtained by sampling from $N(0, h^2_t/n_t)$ and n_t is the total number of causal variants for traits. We compute enrichment and $\tau*$ for AllcisQTL, TopcisQTL, 95%CredibleSet, and MaxCPP annotations. We observed that S-LDSC estimates for enrichment is upward biased. However, S-LDSC estimates for AllcisQTL, 95%CredibleSet, and MaxCPP annotations are slightly downward biased. In addition, we applied GCTA and observed that GCTA estimates are biased for all three QTL binary annotations (AllcisQTL, TopcisQTL, and 95%CredibleSet). Value of 'NA' indicates that GCTA is not applicable to continues annotation (MaxCPP). Enrichment is computed by averaging over all 400 data sets (n=400 independent simulations to derive the statistics).

Annotation	S-LDSC Enrichment (se)	GCTA Enrichment(se)	True Enrichment
AllcisQTL	1.05 (0.01)	2.59 (0.01)	1.86
TopcisQTL	13.74 (1.30)	77.41 (0.48)	4.74
95%CredibleSet	1.47 (0.05)	5.77 (0.03)	2.09
MaxCPP	3.03 (0.25)	NA	3.36

Supplementary Table 4. S-LDSC and GCTA simulation results for four annotations under alternative simulation framework. We report S-LDSC and GCTA enrichment estimates, averaged across 400 simulations (n=400 independent simulations to derive the statistics). GCTA is not applicable to continuous annotations (MaxCPP).

TissueName	N
Adipose-Subcutaneous	298
Adipose-Visceral-Omentum	185
Adrenal-Gland	126
Artery-Aorta	197
Artery-Coronary	124
Artery-Tibial	285
Brain-Anterior-cingulate-cortex-BA24	72
Brain-Caudate-basal-ganglia	100
Brain-Cerebellar-Hemisphere	89
Brain-Cerebellum	103
Brain-Cortex	96
Brain-Frontal-Cortex-BA9	92
Brain-Hippocampus	82
Brain-Hypothalamus	81
Brain-Nucleus-accumbens-basal-ganglia	93
Brain-Putamen-basal-ganglia	82
Breast-Mammary-Tissue	183
Cells-EBV-transformed-lymphocytes	114
Cells-Transformed-fibroblasts	272
Colon-Sigmoid	124
Colon-Transverse	124
Esophagus-Gastroesophageal-Junction	127
Esophagus-Mucosa	241
Esophagus-Muscularis	218
Heart-Atrial-Appendage	159
Heart-Left-Ventricle	190
Liver	97
Lung	278
Muscle-Skeletal	361
Nerve-Tibial	256
Ovary	85
Pancreas	149
Pituitary	87
Prostate	87
Skin-Not-Sun-Exposed-Suprapubic	197
Skin-Sun-Exposed-Lower-leg	302
Small-Intestine-Terminal-Ileum	77
Spleen	89
Stomach	170
Testis	157
Thyroid	278
Uterus	70
Vagina	79
Whole-Blood	338

Supplementary Table 5. List of 44 tissues in the GTEx dataset. The range of samples in the GTEx data set ranges between 70-361. Tissues are listed in alphabetical order. Let N indicate the eQTL sample size.

See attached Excel file

Supplementary Table 6. List of 47 data sets analyzed in this study. We obtained the summary statistics for each trait from previous published studies where the summary statistics are publicly available. In the case of UK Biobank traits, we computed the summary statistics using BOLT-LMM [10,11]. For some traits we have more than one data set, thus we have 41 independent traits. However, we utilized all the 47 data sets in our meta-analyses as the number of samples that overlap is low. These traits have been selected based on a heritability z-score > 6.

Tissue	**Annotation**	$\tau*$ **(se)**	$\tau*$ **(P)**	**Enrichment (se)**	**Enrichment (P)**
Whole Blood	AllcisQTL	0.01(0.01)	2.33e-01	1.51(0.08)	5.80e-10
Whole Blood	95%CredibleSet	0.07(0.02)	2.21e-03	2.18(0.19)	4.73e-10
Whole Blood	MaxCPP	0.23(0.05)	2.00e-05	5.41(0.82)	7.68e-08
GTEx-FE-Meta-Tissue	AllcisQTL	0.03(0.01)	2.65e-02	1.80(0.04)	9.12e-15
GTEx-FE-Meta-Tissue	95%CredibleSet	0.17(0.02)	2.45e-13	2.75(0.12)	3.45e-21
GTEx-FE-Meta-Tissue	MaxCPP	0.52(0.05)	2.73e-27	5.84(0.40)	1.19e-31

Supplementary Table 7. Enrichment and $\tau*$ for whole blood and FE-Meta-Tissue in the GTEx data set. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics) conditional on baselineLD model. The fraction of SNPs for each annotation in whole blood is as follows: AllcisQTL (6.65%), 95%CredibleSet (2.35%), and MaxCPP (0.11%). The fraction of SNPs for each annotation in GTEx FE-Meta-Tissue is as follows: AllcisQTL (36.04%), 95%CredibleSet (5.87%), and MaxCPP (1.03%).

Annotation	$\tau*$ **(se)**	$\tau*$ **(P)**	**Enrichment (se)**	**Enrichment (P)**
AllciseQTL	0.62(0.06)	9.29e-28	3.25(0.21)	1.33e-28
95%CredibleSet	1.17(0.10)	1.38e-30	8.28(0.64)	1.52e-31
MaxCPP	2.25(0.18)	2.00e-34	32.74(2.61)	1.82e-34

Supplementary Table 8. Enrichment and $\tau*$ for whole blood tissue in the GTEx dataset without conditioning on the baselineLD model. We calculated $\tau*$ by meta-analyzing 41 independent traits (n=41 independent traits to derive the statistics). In this analysis, we have no additional annotation in the model. This result indicate that MaxCPP outperforms other annotations without conditioning on the baselineLD model.

TissueName	$\tau*$	N
Adipose-Subcutaneous	0.22	298
Adipose-Visceral-Omentum	0.14	185
Adrenal-Gland	0.12	126
Artery-Aorta	0.19	197
Artery-Coronary	0.03	124
Artery-Tibial	0.22	285
Brain-Anterior-cingulate-cortex-BA24	-0.07	72
Brain-Caudate-basal-ganglia	0.05	100
Brain-Cerebellar-Hemisphere	0.04	89
Brain-Cerebellum	0.08	103
Brain-Cortex	0.03	96
Brain-Frontal-Cortex-BA9	-0.01	92
Brain-Hippocampus	-0.01	82
Brain-Hypothalamus	-0.04	81
Brain-Nucleus-accumbens-basal-ganglia	-0.04	93
Brain-Putamen-basal-ganglia	0.05	82
Breast-Mammary-Tissue	0.11	183
Cells-EBV-transformed-lymphocytes	0	114
Cells-Transformed-fibroblasts	0.18	272
Colon-Sigmoid	0.08	124
Colon-Transverse	0.1	124
Esophagus-Gastroesophageal-Junction	0.08	127
Esophagus-Mucosa	0.13	241
Esophagus-Muscularis	0.14	218
Heart-Atrial-Appendage	0.14	159
Heart-Left-Ventricle	0.12	190
Liver	0.06	97
Lung	0.14	278
Muscle-Skeletal	0.14	361
Nerve-Tibial	0.17	256
Ovary	0.1	85
Pancreas	0.11	149
Pituitary	0.01	87
Prostate	0.03	87
Skin-Not-Sun-Exposed-Suprapubic	0.14	197
Skin-Sun-Exposed-Lower-leg	0.17	302
Small-Intestine-Terminal-Ileum	0	77
Spleen	0.07	89
Stomach	0.15	170
Testis	0.08	157
Thyroid	0.15	278
Uterus	0	70
Vagina	0.05	79
Whole-Blood	0.23	338

Supplementary Table 9. Linear relationship between sample size and the effect of $\tau*$. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets) for MaxCPP annotation conditional on baseline model (n=41 independent traits to derive the statistics). Tissues are obtained from the GTEx data set. Let N indicate the eQTL sample size in GTEx.

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Red Blood Cell Distribution Width (UKBB)	1.52(0.30)	4.59E-07	14.11(2.27)	3.17e-08
HDL	1.45(0.44)	9.35E-04	12.88(3.36)	3.72e-04
Coronary Artery Disease	1.36(0.55)	1.38E-02	11.99(4.40)	6.82e-03
Auto Immune Traits (UKBB)	1.12(0.48)	1.90E-02	9.81(4.01)	1.18e-02
Depressive symptoms	1.10(0.34)	1.40E-03	9.29(2.64)	1.13e-03
Hypothyroidism (UKBB)	1.09(0.46)	1.78E-02	10.09(3.29)	7.18e-03
Red Blood Cell Count (UKBB)	1.09(0.30)	2.99E-04	10.62(2.22)	3.20e-05
Dermatologic Diseases (UKBB)	1.06(0.54)	5.00E-02	10.16(4.09)	2.17e-02
White Blood Cell Count (UKBB)	1.02(0.19)	4.70E-08	9.93(1.40)	1.17e-09
Respiratory and Ear-nose-throat Diseases (UKBB)	1.01(0.31)	1.12E-03	9.38(2.37)	3.59e-04
Age at Menopause (UKBB)	0.96(0.38)	1.22E-02	9.56(2.88)	2.73e-03
Platelet Count (UKBB)	0.86(0.22)	7.63E-05	8.99(1.53)	1.53e-06
Ulcerative Colitis	0.78(0.52)	1.37E-01	8.46(3.99)	5.30e-02
Age first birth	0.72(0.25)	4.08E-03	6.63(1.88)	2.62e-03
Schizophrenia	0.72(0.16)	7.06E-06	6.66(1.19)	2.58e-06
LDL	0.70(0.52)	1.81E-01	7.93(3.95)	7.57e-02
Eosinophil Count (UKBB)	0.68(0.19)	2.64E-04	7.37(1.38)	5.58e-06
Waist-hip Ratio (UKBB)	0.68(0.19)	3.28E-04	6.93(1.35)	3.25e-05
Systolic Blood Pressure (UKBB)	0.67(0.15)	5.35E-06	6.86(1.10)	3.43e-07
Crohn's Disease	0.65(0.46)	1.54E-01	7.21(3.47)	6.24e-02
Eczema (UKBB)	0.59(0.26)	2.17E-02	6.23(1.95)	5.20e-03
FEV1-FVC Ratio (UKBB)	0.58(0.14)	2.93E-05	6.04(1.05)	1.34e-06
Type 2 Diabetes	0.57(0.50)	2.58E-01	6.03(3.70)	1.74e-01
Rheumatoid Arthritis	0.56(0.47)	2.38E-01	6.47(3.60)	1.14e-01
High Cholesterol (UKBB)	0.55(0.25)	3.14E-02	6.34(1.84)	5.01e-03
Forced Vital Capacity (UKBB)	0.52(0.14)	1.82E-04	5.53(1.02)	1.46e-05
BMI	0.51(0.23)	2.64E-02	5.15(1.64)	1.48e-02
BMI (UKBB)	0.43(0.17)	1.24E-02	4.68(1.24)	4.13e-03
Type 2 Diabetes (UKBB)	0.42(0.19)	2.55E-02	4.77(1.38)	6.54e-03
Number children even born	0.39(0.37)	2.91E-01	4.31(2.74)	2.29e-01
Height (UKBB)	0.39(0.15)	7.75E-03	5.11(1.06)	2.70e-04
Years of Education	0.38(0.12)	1.88E-03	4.14(0.88)	4.91e-04
College Education (UKBB)	0.37(0.10)	3.41E-04	4.05(0.76)	8.43e-05
Age at Menarche (UKBB)	0.35(0.16)	3.14E-02	4.15(1.17)	8.27e-03
Height	0.34(0.21)	1.10E-01	4.64(1.57)	2.17e-02
Neuroticism (UKBB)	0.34(0.13)	7.19E-03	3.74(0.93)	3.53e-03
Balding Type I (UKBB)	0.30(0.19)	1.11E-01	3.78(1.41)	4.24e-02
Anorexia	0.28(0.27)	3.13E-01	3.14(2.07)	2.88e-01
Morning Person (UKBB)	0.23(0.11)	3.47E-02	3.12(0.81)	8.59e-03
Smoking Status (UKBB)	0.22(0.11)	4.22E-02	2.96(0.82)	1.63e-02
Heel T Score (UKBB)	0.15(0.16)	3.61E-01	3.00(1.21)	9.58e-02
Tanning (UKBB)	-0.48(0.73)	5.10E-01	-1.65(5.11)	5.92e-01
Sunburn Occasion (UKBB)	-0.48(0.39)	2.24E-01	-1.76(2.77)	3.16e-01
Skin Color (UKBB)	-0.41(0.69)	5.52E-01	-0.89(4.78)	6.86e-01
Hair Color (UKBB)	-0.19(0.43)	6.58E-01	0.54(2.98)	8.74e-01
Ever Smoked	-0.19(0.35)	5.95E-01	-0.16(2.56)	6.52e-01
Autism Spectrum	-0.07(0.33)	8.29E-01	0.78(2.50)	9.30e-01

Supplementary Table 10. Enrichment and $\tau*$ of MaxCPP annotations for FE-Meta-Tissue for all the 41 independent traits (47 data sets). We compute $\tau*$ and enrichment for each trait individually. These values are conditioned on baselineLD model. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Annotation	$\tau*$ **(se)**	$\tau*$ **(P)**
Predicted allele age	-0.167 (0.014)	3.98e-32
LLD AFR	-0.150 (0.007)	4.51e-86
Recombination Rate	-0.176 (0.010)	6.44e-65
Nucleotide diversity	-0.140 (0.009)	3.68e-45
Background selection statistics	0.115 (0.010)	1.45e-26
CpG content	0.180 (0.025)	9.69e-13

Supplementary Table 11. $\tau*$ estimates for 6 continuous annotations introduced in our previous work[9]. We report $\tau*$ estimates meta-analyzed across 41 independent traits (n=41 independent traits to derive the statistics), which are slightly different from the set of traits for which results are reported in Figure 3c of ref.[9].

Tissue	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Muscle-Skeletal	-0.00(0.22)	9.84E-01	3.18(2.98)	4.52E-01
Brain-Caudate-basal-ganglia	-0.00(0.23)	9.88E-01	2.75(4.95)	7.31E-01
Prostate	-0.07(0.26)	7.85E-01	0.51(6.38)	9.65E-01
Brain-Nucleus-accumbens-basal-ganglia	-0.08(0.23)	7.21E-01	1.13(5.20)	9.95E-01
Cells-Transformed-fibroblasts	0.02(0.23)	9.33E-01	3.94(3.17)	3.24E-01
Brain-Frontal-Cortex-BA9	0.03(0.24)	9.06E-01	3.41(5.60)	6.68E-01
Skin-Not-Sun-Exposed-Suprapubic	0.05(0.24)	8.26E-01	3.92(3.75)	4.27E-01
Brain-Anterior-cingulate-cortex-BA24	0.10(0.25)	6.98E-01	5.67(7.51)	5.36E-01
Brain-Hippocampus	0.11(0.24)	6.45E-01	5.84(7.00)	4.79E-01
Pituitary	0.16(0.24)	5.05E-01	6.44(5.48)	3.10E-01
Stomach	0.17(0.22)	4.31E-01	5.86(3.99)	1.85E-01
Adipose-Subcutaneous	0.18(0.21)	3.84E-01	5.54(2.72)	8.25E-02
Brain-Cerebellum	0.21(0.23)	3.63E-01	6.65(4.14)	1.72E-01
Brain-Hypothalamus	0.21(0.25)	3.95E-01	8.49(7.04)	2.73E-01
Vagina	0.22(0.26)	3.95E-01	9.45(8.13)	2.87E-01
Thyroid	0.23(0.21)	2.64E-01	5.79(2.54)	5.16E-02
Esophagus-Muscularis	0.24(0.26)	3.46E-01	5.65(3.27)	1.20E-01
Adrenal-Gland	0.25(0.23)	2.74E-01	7.83(4.43)	1.14E-01
Esophagus-Gastroesophageal-Junction	0.28(0.22)	2.05E-01	8.35(4.36)	7.40E-02
Skin-Sun-Exposed-Lower-leg	0.29(0.22)	1.91E-01	6.46(2.83)	3.83E-02
Nerve-Tibial	0.29(0.23)	2.12E-01	6.51(2.97)	4.78E-02
Brain-Cerebellar-Hemisphere	0.29(0.24)	2.14E-01	8.73(4.81)	1.04E-01
Uterus	0.31(0.26)	2.32E-01	11.88(8.65)	1.55E-01
Testis	0.31(0.33)	3.37E-01	4.93(3.50)	1.73E-01
Artery-Aorta	0.32(0.22)	1.51E-01	8.01(3.33)	3.28E-02
Lung	0.32(0.23)	1.77E-01	7.13(3.20)	3.89E-02
Brain-Cortex	0.35(0.23)	1.34E-01	10.28(5.10)	6.47E-02
Heart-Atrial-Appendage	0.35(0.23)	1.30E-01	8.95(4.15)	4.46E-02
Breast-Mammary-Tissue	0.36(0.21)	9.40E-02	8.72(3.67)	2.32E-02
Ovary	0.39(0.31)	2.03E-01	10.85(6.98)	1.35E-01
Heart-Left-Ventricle	0.42(0.22)	5.91E-02	9.43(3.71)	1.22E-02
Brain-Putamen-basal-ganglia	0.43(0.25)	9.26E-02	13.77(6.55)	5.25E-02
Adipose-Visceral-Omentum	0.44(0.22)	4.25E-02	10.21(3.70)	8.82E-03
Colon-Sigmoid	0.45(0.24)	6.48E-02	11.64(4.97)	2.54E-02
Pancreas	0.45(0.24)	5.76E-02	11.17(4.36)	1.46E-02
Liver	0.48(0.26)	5.85E-02	15.25(6.74)	2.94E-02
Artery-Coronary	0.49(0.23)	3.23E-02	13.08(5.14)	1.17E-02
Cells-EBV-transformed-lymphocytes	0.50(0.24)	3.58E-02	13.56(5.08)	7.99E-03
Esophagus-Mucosa	0.51(0.23)	2.67E-02	10.03(3.22)	3.46E-03
Colon-Transverse	0.53(0.25)	3.16E-02	11.95(4.27)	7.11E-03
GTEx-FE-Meta-Tissue	0.65(0.23)	5.31E-03	7.38(1.75)	2.15E-04
Small-Intestine-Terminal-Ileum	0.66(0.28)	1.63E-02	21.16(8.01)	7.74E-03
Artery-Tibial	0.73(0.23)	1.43E-03	12.44(3.20)	8.43E-05
Spleen	0.74(0.28)	9.61E-03	19.36(6.38)	3.19E-03
Whole-Blood	1.01(0.32)	1.64E-03	17.02(4.36)	1.01E-04

Supplementary Table 12. Enrichment and $\tau*$ of MaxCPP annotations for each tissue in GTEx data set in autoimmune disease. We calculated $\tau*$ by meta-analyzing 6 independent autoimmune disease (n=6 independent traits to derive the statistics). Meta-analysis results for each annotation is computed by conditioning on baselineLD model. Tissues are sorted in an increasing oder of $\tau*$ values.We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Trait	**Annotation**	$\tau*$ **(se)**	$\tau*$ **(P)**	**Enrichment (se)**	**Enrichment (P)**
Autoimmune	GTEx-FE-Meta-Tissue	0.41 (0.23)	0.07	6.25(1.71)	1.01e-05
Autoimmune	Whole-Blood	0.91 (0.34)	9.15e-03	16.19(4.64)	5.37e-04
Blood cell	GTEx-FE-Meta-Tissue	0.69 (0.12)	1.86e-08	8.45(0.97)	7.63e-12
Blood cell	Whole-Blood	1.17 (0.24)	1.77e-06	21.11 (3.46)	8.50e-09
Brain-related	GTEx-FE-Meta-Tissue	0.34 (0.06)	6.27e-08	4.30(0.46)	1.57e-06
Brain-related	GTEx-Brain+Nerve	0.28 (0.07)	9.81e-05	5.37 (0.80)	8.95e-08

Supplementary Table 13. Enrichment and $\tau*$ of MaxCPP annotations for the GTEx data set for autoimmune diseases, blood cell traits, and brain related traits. In the case of autoimmune diseases, we calculated $\tau*$ by meta-analyzing 6 independent autoimmune diseases. In the case of blood cell traits, we calculated $\tau*$ by meta-analyzing 5 independent blood cell traits. In the case of brain-related traits, we calculated $\tau*$ by meta-analyzing 8 independent brain-related traits. Brain+Nerve is obtained by computing the MaxCPP annotation for 10 brain and nerve tissues in GTEx. Meta-analysis results for each annotation is computed by conditioning on each other and baselineLD. In whole blood the fraction of SNPs for MaxCPP annotation is 0.11% and in FE-Meta-Tissue the fraction of SNPs for MaxCPP annotation is 1.03%.

Tissue	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Uterus	-0.08(0.11)	4.64E-01	0.25(3.73)	8.43E-01
Brain-Nucleus-accumbens-basal-ganglia	0.19(0.14)	1.81E-01	7.33(3.26)	5.52E-02
Artery-Coronary	0.21(0.11)	4.91E-02	7.55(2.35)	5.63E-03
Prostate	0.24(0.14)	9.52E-02	9.08(3.74)	3.23E-02
Brain-Cerebellum	0.26(0.12)	3.43E-02	7.80(2.27)	2.88E-03
Brain-Cerebellar-Hemisphere	0.28(0.12)	1.86E-02	8.67(2.45)	1.95E-03
Brain-Anterior-cingulate-cortex-BA24	0.28(0.13)	3.41E-02	11.29(3.97)	1.06E-02
Pituitary	0.32(0.12)	9.52E-03	10.42(2.91)	1.32E-03
Brain-Frontal-Cortex-BA9	0.34(0.15)	2.28E-02	10.97(3.54)	5.17E-03
Vagina	0.36(0.12)	2.25E-03	14.09(3.68)	4.63E-04
Cells-EBV-transformed-lymphocytes	0.37(0.15)	1.37E-02	11.28(3.15)	1.19E-03
Ovary	0.38(0.14)	8.14E-03	12.90(3.75)	1.67E-03
Liver	0.40(0.12)	8.53E-04	13.39(3.08)	7.61E-05
Brain-Hippocampus	0.40(0.14)	5.61E-03	14.44(4.21)	1.53E-03
Brain-Hypothalamus	0.42(0.14)	3.11E-03	14.89(4.08)	7.60E-04
Skin-Not-Sun-Exposed-Suprapubic	0.43(0.11)	1.14E-04	9.80(1.76)	8.79E-07
Brain-Cortex	0.43(0.14)	1.90E-03	12.41(3.06)	2.19E-04
Small-Intestine-Terminal-Ileum	0.43(0.14)	2.28E-03	15.39(4.04)	4.04E-04
Esophagus-Mucosa	0.45(0.13)	3.69E-04	9.55(1.90)	6.17E-06
Esophagus-Muscularis	0.45(0.13)	4.29E-04	9.74(1.86)	3.36E-06
Artery-Aorta	0.46(0.11)	3.67E-05	10.01(1.67)	9.30E-08
Spleen	0.46(0.13)	3.26E-04	13.37(2.85)	1.70E-05
Brain-Caudate-basal-ganglia	0.46(0.15)	1.58E-03	12.83(3.13)	1.96E-04
Colon-Sigmoid	0.48(0.14)	6.69E-04	12.81(2.90)	4.08E-05
Esophagus-Gastroesophageal-Junction	0.48(0.16)	2.27E-03	13.05(3.34)	2.52E-04
Testis	0.52(0.11)	4.71E-06	9.30(1.47)	2.30E-08
Thyroid	0.54(0.12)	1.29E-05	9.92(1.59)	1.60E-08
Brain-Putamen-basal-ganglia	0.54(0.16)	5.59E-04	17.04(4.08)	1.06E-04
Artery-Tibial	0.57(0.12)	3.77E-06	10.87(1.68)	6.32E-09
Pancreas	0.57(0.14)	4.39E-05	13.77(2.69)	1.60E-06
Colon-Transverse	0.57(0.16)	3.56E-04	13.04(2.88)	2.09E-05
Adipose-Visceral-Omentum	0.58(0.13)	6.98E-06	13.18(2.22)	7.04E-08
Adrenal-Gland	0.60(0.13)	5.00E-06	14.64(2.53)	1.21E-07
Skin-Sun-Exposed-Lower-leg	0.61(0.14)	2.15E-05	10.90(1.95)	3.15E-07
Muscle-Skeletal	0.63(0.14)	3.51E-06	11.94(1.94)	1.60E-08
Cells-Transformed-fibroblasts	0.64(0.12)	6.82E-08	11.87(1.58)	1.75E-11
Stomach	0.64(0.13)	1.02E-06	14.79(2.38)	1.38E-08
Heart-Atrial-Appendage	0.65(0.13)	6.42E-07	14.66(2.34)	1.02E-08
Breast-Mammary-Tissue	0.66(0.19)	5.69E-04	14.56(3.39)	5.97E-05
Adipose-Subcutaneous	0.67(0.13)	1.74E-07	12.06(1.70)	1.51E-10
Lung	0.71(0.15)	3.08E-06	12.75(2.14)	3.47E-08
Nerve-Tibial	0.73(0.13)	4.20E-08	12.36(1.68)	3.99E-11
Heart-Left-Ventricle	0.73(0.18)	4.71E-05	15.42(3.03)	1.90E-06
GTEx-FE-Meta-Tissue	0.98(0.13)	2.59E-14	9.75(1.00)	4.73E-18
Whole-Blood	1.34(0.24)	2.26E-08	22.73(3.41)	2.76E-10

Supplementary Table 14. Enrichment and $\tau*$ of MaxCPP annotations for each tissue in the GTEx data set in blood cell traits. We calculated $\tau*$ by meta-analyzing 5 independent blood cell traits (n=5 independent traits to derive the statistics). Meta-analysis results for each annotation is computed by conditioning on baselineLD model. Tissues are sorted in an increasing oder of $\tau*$ values.

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Small-Intestine-Terminal-Ileum	0.02(0.07)	8.14E-01	1.73(1.84)	6.95E-01
Liver	0.03(0.07)	6.88E-01	1.99(1.69)	5.58E-01
Artery-Coronary	0.04(0.08)	6.25E-01	2.17(1.80)	5.09E-01
Pituitary	0.05(0.07)	4.45E-01	2.52(1.62)	3.45E-01
Heart-Left-Ventricle	0.07(0.06)	2.50E-01	2.60(1.06)	1.32E-01
Brain-Anterior-cingulate-cortex-BA24	0.07(0.07)	3.20E-01	3.51(2.22)	2.55E-01
Brain-Hippocampus	0.08(0.07)	2.48E-01	3.52(1.96)	1.94E-01
Testis	0.08(0.07)	2.17E-01	2.37(0.88)	1.18E-01
Uterus	0.08(0.11)	4.40E-01	3.94(3.58)	4.02E-01
Brain-Hypothalamus	0.10(0.07)	1.29E-01	4.17(1.95)	1.07E-01
Spleen	0.10(0.07)	1.76E-01	3.47(1.60)	1.25E-01
Ovary	0.10(0.10)	3.25E-01	3.93(2.68)	2.74E-01
Brain-Frontal-Cortex-BA9	0.11(0.07)	1.19E-01	3.77(1.59)	8.22E-02
Brain-Cortex	0.12(0.07)	8.03E-02	4.03(1.54)	5.14E-02
Heart-Atrial-Appendage	0.13(0.07)	5.50E-02	3.69(1.22)	2.70E-02
Adrenal-Gland	0.14(0.07)	4.01E-02	4.01(1.33)	2.44E-02
Brain-Nucleus-accumbens-basal-ganglia	0.14(0.08)	7.85E-02	4.48(1.81)	5.55E-02
Cells-Transformed-fibroblasts	0.15(0.06)	8.91E-03	3.37(0.76)	2.01E-03
Artery-Aorta	0.16(0.07)	2.76E-02	3.72(1.06)	1.09E-02
Esophagus-Gastroesophageal-Junction	0.16(0.07)	1.89E-02	4.46(1.35)	9.96E-03
Pancreas	0.16(0.07)	3.25E-02	4.18(1.33)	1.66E-02
Artery-Tibial	0.16(0.08)	3.27E-02	3.60(1.03)	1.18E-02
Prostate	0.16(0.08)	4.32E-02	5.52(2.12)	3.38E-02
Brain-Cerebellar-Hemisphere	0.17(0.06)	7.16E-03	4.87(1.31)	3.38E-03
Colon-Sigmoid	0.17(0.07)	1.34E-02	4.66(1.34)	6.65E-03
Adipose-Visceral-Omentum	0.18(0.06)	4.34E-03	4.36(1.08)	1.76E-03
Skin-Not-Sun-Exposed-Suprapubic	0.18(0.07)	9.53E-03	4.10(1.07)	3.75E-03
Stomach	0.18(0.07)	7.96E-03	4.64(1.25)	3.69E-03
Colon-Transverse	0.19(0.07)	5.57E-03	4.52(1.15)	2.34E-03
Lung	0.19(0.07)	7.25E-03	3.87(0.95)	2.64E-03
Cells-EBV-transformed-lymphocytes	0.19(0.08)	1.83E-02	5.19(1.67)	1.13E-02
Esophagus-Muscularis	0.21(0.07)	2.19E-03	4.44(1.00)	6.05E-04
Brain-Caudate-basal-ganglia	0.22(0.07)	2.11E-03	6.01(1.53)	1.01E-03
Muscle-Skeletal	0.23(0.07)	9.30E-04	4.58(0.97)	2.41E-04
Thyroid	0.24(0.06)	2.18E-04	4.31(0.80)	3.74E-05
Brain-Cerebellum	0.24(0.07)	2.42E-04	5.72(1.18)	7.92E-05
Whole-Blood	0.24(0.07)	1.08E-03	4.66(1.03)	3.89E-04
Breast-Mammary-Tissue	0.25(0.07)	2.10E-04	5.60(1.16)	8.05E-05
Nerve-Tibial	0.25(0.07)	3.68E-04	4.51(0.89)	8.84E-05
Vagina	0.25(0.08)	1.96E-03	9.19(2.57)	1.56E-03
Brain-Putamen-basal-ganglia	0.25(0.13)	5.60E-02	7.65(3.35)	4.56E-02
Esophagus-Mucosa	0.29(0.07)	9.40E-06	5.30(0.90)	1.96E-06
Skin-Sun-Exposed-Lower-leg	0.31(0.07)	1.15E-05	5.28(0.90)	2.31E-06
Adipose-Subcutaneous	0.35(0.07)	1.40E-07	5.87(0.87)	2.36E-08
Meta-GTEx-BrainNerve	0.43(0.08)	2.09E-08	6.29(0.87)	2.25E-09
GTEx-all-GE	0.45(0.07)	1.15E-11	4.65(0.48)	1.26E-13

Supplementary Table 15. Enrichment and $\tau*$ of MaxCPP annotations for each tissue in the GTEx data set in brain related traits. We calculated $\tau*$ by meta-analyzing 8 independent brain related traits (n=8 independent traits to derive the statistics). Meta-analysis results for each annotation is computed by conditioning on each other and baselineLD.

See attached Excel file

Supplementary Table 16. $\tau*$ of MaxCPP annotations for individual tissue and individual trait. We compute the $\tau*$ of each tissue for a given trait in a joint model with FE-Meta-Tissue and baselineLD. We consider the 41 independent traits (47 data sets, n=41 independent traits to derive the statistics) and 11 tissues from GTEx that have sample size > 200. These results are sorted based on the adjusted p-value corrected for multiple hypothesis correction. We obtain only 3 significant traits for blood tissue (FDR $\leq$ 0.05).

Trait	Tissue	$\tau*$	s.e.	pvalue	Adjusted pvalue
UKB-460K.pigment-HAIR	Muscle-Skeletal	0.48	0.32	1.26E-01	0.7077849
Balding Type I (UKBB)	Artery-Tibial	-0.3	0.18	9.41E-02	0.6891582
Anorexia	Whole-Blood	-0.36	0.28	2.05E-01	0.7362254
FEV1-FVC Ratio (UKBB)	Lung	0.64	0.21	2.86E-03	0.2115771
Smoking Status (UKBB)	Artery-Tibial	-0.15	0.1	1.52E-01	0.7202835
Crohn's Disease	Whole-Blood	1.52	0.81	5.95E-02	0.6262367
Tanning (UKBB)	Thyroid	-0.7	0.46	1.32E-01	0.7077849
Skin Color (UKBB)	Esophagus-Mucosa	-0.68	0.48	1.57E-01	0.7202835
Height (UKBB)	Muscle-Skeletal	-0.28	0.13	3.21E-02	0.5324
Age at Menopause (UKBB)	Nerve-Tibial	0.78	0.42	6.25E-02	0.6262367
Ulcerative Colitis	Whole-Blood	1.95	0.73	7.61E-03	0.3900233
High Cholesterol (UKBB)	Nerve-Tibial	-1.03	0.4	9.49E-03	0.3900233
Age at Menarche (UKBB)	Cells-Transformed-fibroblasts	0.23	0.15	1.19E-01	0.7077849
BMI (UKBB)	Whole-Blood	0.21	0.15	1.62E-01	0.7202835
Morning Person (UKBB)	Nerve-Tibial	-0.25	0.13	5.30E-02	0.6262367
Neuroticism (UKBB)	Artery-Tibial	-0.28	0.12	2.17E-02	0.5324
Heel T Score (UKBB)	Adipose-Subcutaneous	0.29	0.16	7.33E-02	0.6335214
White Blood Cell Count (UKBB)	Whole-Blood	1.74	0.42	3.81E-05	0.0184404
Coronary Artery Disease	Artery-Tibial	1.13	0.65	8.44E-02	0.6720459
Depressive symptoms	Thyroid	-0.67	0.32	3.38E-02	0.5324
Red Blood Cell Distribution Width (UKBB)	Whole-Blood	1.78	0.46	1.16E-04	0.028072
HDL	Whole-Blood	1.18	0.48	1.40E-02	0.484
Type 2 Diabetes (UKBB)	Nerve-Tibial	-0.44	0.2	2.99E-02	0.5324
Ever Smoked	Esophagus-Mucosa	-0.56	0.3	6.28E-02	0.6262367
Sunburn Occasion (UKBB)	Nerve-Tibial	-0.28	0.21	1.81E-01	0.7202835
Platelet Count (UKBB)	Whole-Blood	0.85	0.32	8.59E-03	0.3900233
Eczema (UKBB)	Esophagus-Mucosa	0.38	0.3	2.04E-01	0.7362254
Hypothyroidism (UKBB)	Thyroid	1.21	0.46	8.54E-03	0.3900233
College Education (UKBB)	Adipose-Subcutaneous	0.25	0.11	2.53E-02	0.5324
Systolic Blood Pressure (UKBB)	Artery-Tibial	0.44	0.2	3.21E-02	0.5324
Years of Education	Skin-Sun-Exposed-Lower-leg	0.3	0.14	3.39E-02	0.5324
Eosinophil Count (UKBB)	Whole-Blood	1.27	0.35	2.91E-04	0.046948
Dermatologic Diseases (UKBB)	Lung	-0.69	0.49	1.59E-01	0.7202835
Respiratory and Ear-nose-throat Diseases (UKBB)	Whole-Blood	0.57	0.32	7.66E-02	0.6442207
Age first birth	Whole-Blood	0.35	0.22	1.04E-01	0.6991111
Red Blood Cell Count (UKBB)	Muscle-Skeletal	0.44	0.31	1.61E-01	0.7202835
Forced Vital Capacity (UKBB)	Cells-Transformed-fibroblasts	0.28	0.15	6.86E-02	0.6335214
Autism Spectrum	Nerve-Tibial	-0.66	0.3	2.75E-02	0.5324
Waist-hip Ratio (UKBB)	Adipose-Subcutaneous	1.01	0.32	1.88E-03	0.2115771
LDL	Esophagus-Muscularis	-0.71	0.51	1.60E-01	0.7202835
Rheumatoid Arthritis	Artery-Tibial	0.79	0.47	9.54E-02	0.6891582
Schizophrenia	Esophagus-Mucosa	0.3	0.17	7.03E-02	0.6335214
Auto Immune Traits (UKBB)	Esophagus-Mucosa	-0.54	0.5	2.85E-01	0.7812391
Number children even born	Lung	0.51	0.37	1.69E-01	0.7202835

Supplementary Table 17. Top Tissue-specific eQTL MaxCPP annotation for each individual trait. We compute the $\tau*$ of each tissue for a given trait in a joint model with FE-Meta-Tissue and baselineLD. We consider the 41 independent traits (47 data sets) and 11 tissues from GTEx that have sample size > 200. We only report the top tissue for each trait based on significant value of $\tau*$. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
GTEx-FE-Meta-Tissue-All Genes	0.52(0.05)	2.73e-27	5.84(0.40)	1.19e-31
GTEx-FE-Meta-Tissue-AH	0.47(0.05)	4.22e-25	6.39(0.49)	9.83e-29
GTEx-FE-Meta-Tissue-Samocha	0.26(0.03)	2.62e-14	16.41(1.85)	1.24e-16
GTEx-FE-Meta-Tissue-Cassa	0.44(0.04)	5.29e-22	15.99(1.48)	3.63e-24
GTEx-FE-Meta-Tissue-ExAC	0.52(0.04)	7.61e-33	17.06(1.28)	1.20e-35
GTEx-FE-Meta-Tissue-Wang	0.17(0.03)	3.39e-08	8.69(1.23)	9.23e-10

Supplementary Table 18. Comparison of enrichment and $\tau*$ for different gene sets. For each gene set S, we report enrichment and $\tau*$ of MaxCPP(S) conditioned on the baselineLD model, meta-analyzed across 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). The fraction of SNPs in each annotation is as follows: All Genes (1.03%), AH (0.60%), Samocha (0.02%), Cassa (0.06%), ExAC (0.07%), and Wang (0.04%).

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
GTEx-FE-Meta-Tissue-All Genes	0.33 (0.06)	1.93e-08	5.59(0.39)	1.41e-27
GTEx-FE-Meta-Tissue-AH	0.18 (0.04)	0.0001	6.19 (0.57)	3.31e-28
GTEx-FE-Meta-Tissue-All Genes	0.47(0.04)	5.10e-22	5.56(0.39)	2.68e-08
GTEx-FE-Meta-Tissue-Samocha	0.18(0.03)	6.78e-07	15.61(1.89)	1.15e-14
GTEx-FE-Meta-Tissue-All Genes	0.42(0.04)	4.08e-20	5.67(0.39)	5.69e-21
GTEx-FE-Meta-Tissue-Cassa	0.33(0.04)	4.63e-15	15.86(1.47)	3.57e-24
GTEx-FE-Meta-Tissue-All Genes	0.39(0.04)	1.73e-17	5.70(0.39)	1.84e-20
GTEx-FE-Meta-Tissue-ExAC	0.41(0.04)	1.40e-23	16.94(1.29)	2.65e-35
GTEx-FE-Meta-Tissue-All Genes	0.48 (0.04)	6.85e-27	5.63(0.40)	2.58e-07
GTEx-FE-Meta-Tissue-Wang	0.07 (0.03)	0.01	8.10(1.24)	8.53e-09

Supplementary Table 19. Comparison of enrichment and $\tau*$ for different gene sets, conditioned on MaxCPP(All Genes). For each gene set S, we report enrichment and $\tau*$ of maxCPP(S) (and maxCPP(All Genes)) conditioned on the baselineLD model and on MaxCPP(All Genes), meta-analyzed 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). For most gene sets S, the size of MaxCPP(S) is smaller than expected based on the number of genes in S (see Table S20). The fraction of SNPs in each annotation is as follows: All Genes (1.03%), AH (0.60%), Samocha (0.02%), Cassa (0.06%), ExAC (0.07%), and Wang (0.04%).

Gene Set (S)	**%SNP**	**E(%SNP)**	**allSNP(S)**		**MaxCPP(S)**	
			$\tau*$ **(s.e.)**	**P**	$\tau*$ **(s.e.)**	**P**
AH	0.60%	0.58%	-0.02(0.01)	2.82e-02	0.18 (0.04)	0.0001
Samocha	0.02%	0.04%	0.06 (0.01)	6.07e-12	0.18 (0.03)	7.60e-07
Cassa	0.06%	0.14%	0.06 (0.01)	6.11e-14	0.33 (0.04)	5.77e-15
ExAC	0.07%	0.15%	0.08 (0.01)	4.61e-18	0.42 (0.04)	1.40e-23
Wang	0.04%	0.09%	0.03 (0.01)	1.77e-03	0.07 (0.03)	0.01

Supplementary Table 20. MaxCPP increases power to detect enriched gene sets. MaxCPP(S) annotation is obtained by considering the maximum CPP restricted to genes in S. allSNP(S) annotation is obtained by considering all the variants in $\pm$ 100Kb around the genes in S. We calculated $\tau*$ by meta-analyzing 41 independent traits (n=41 independent traits to derive the statistics). In the case of MaxCPP(S), $\tau*$ is computed conditional on MaxCPP(all genes) and baselineLD while allSNP(S) $\tau*$ is computed conditional on baselineLD. We observed that effect size ($\tau*$) for MaxCPP is 2-9 times larger compared to allSNP annotation. In addition, in 3 out of 5 gene sets the MaxCPP effect size is more significant. These results indicate that MaxCPP has better power to detect wether a gene set is essential for diseases and complex traits. The %SNP indicates the proportion of SNPs in each annotation, defined as the average value of the annotation. The $E(\%SNP)$ is the expected fraction of SNP in each annotation that is defined as follows: $E(\%SNP) = \%\text{SNP(All Genes)}\frac{|S|}{|G|}$ where $|S|$ is the number of genes in our gene set (S), %SNP(All Genes) is the proportion of SNPs in the MaxCPP annotation when all genes are considered, and $|G|$ is the total number of protein-coding genes ($|G|$=20,551). Our estimates for $E(\%SNP)$ indicates that Cassa, ExAC, Samocha, and Wang gene sets are depleted for eQTL signals.

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Neuroticism (UKBB)	0.64(0.15)	2.27E-05	21.47(4.34)	3.25e-06
Height	1.05(0.32)	9.28E-04	33.35(8.99)	5.05e-04
Platelet Count (UKBB)	1.05(0.32)	9.78E-04	37.66(8.92)	7.73e-05
Anorexia	1.17(0.36)	1.11E-03	34.76(10.66)	1.06e-03
Schizophrenia	0.70(0.22)	1.42E-03	26.04(6.15)	5.89e-05
Sunburn Occasion (UKBB)	0.64(0.20)	1.62E-03	16.00(6.99)	2.67e-02
Height (UKBB)	0.68(0.22)	1.95E-03	23.73(6.02)	3.61e-04
Forced Vital Capacity (UKBB)	0.46(0.15)	2.78E-03	18.31(4.37)	1.06e-04
Crohn's Disease	1.31(0.48)	6.75E-03	42.38(15.81)	4.10e-03
Ulcerative Colitis	1.34(0.50)	6.89E-03	44.59(16.12)	4.34e-03
BMI (UKBB)	0.29(0.12)	1.87E-02	12.77(3.29)	5.14e-04
Systolic Blood Pressure (UKBB)	0.55(0.23)	1.88E-02	22.07(6.70)	1.69e-03
Age first birth	0.72(0.31)	1.89E-02	26.54(9.28)	6.07e-03
Smoking Status (UKBB)	0.27(0.12)	2.29E-02	10.60(3.31)	3.69e-03
Red Blood Cell Count (UKBB)	0.61(0.27)	2.38E-02	27.46(7.96)	1.34e-03
High Cholesterol (UKBB)	1.57(0.70)	2.40E-02	49.11(18.64)	1.34e-02
Heel T Score (UKBB)	0.46(0.20)	2.44E-02	15.72(5.93)	1.27e-02
LDL	1.60(0.72)	2.52E-02	51.38(20.21)	1.82e-02
FEV1-FVC Ratio (UKBB)	0.53(0.24)	2.73E-02	20.60(6.61)	3.51e-03
Morning Person (UKBB)	0.29(0.14)	3.35E-02	11.16(3.86)	8.05e-03
Eosinophil Count (UKBB)	0.44(0.22)	4.85E-02	19.40(6.27)	3.29e-03
Respiratory and Ear-nose-throat Diseases (UKBB)	0.62(0.32)	5.14E-02	26.23(10.05)	1.07e-02
Age at Menarche (UKBB)	0.35(0.21)	8.92E-02	13.89(5.72)	2.44e-02
HDL	0.90(0.53)	9.18E-02	37.60(16.02)	2.24e-02
Hypothyroidism (UKBB)	0.52(0.32)	1.01E-01	24.40(8.43)	4.59e-03
Autism Spectrum	0.61(0.40)	1.30E-01	17.25(11.34)	1.46e-01
Skin Color (UKBB)	0.47(0.31)	1.31E-01	12.37(11.65)	3.01e-01
Depressive symptoms	0.55(0.38)	1.47E-01	24.49(11.16)	2.92e-02
Eczema (UKBB)	0.72(0.51)	1.56E-01	25.77(14.72)	9.10e-02
BMI	0.26(0.19)	1.68E-01	12.44(5.14)	2.44e-02
Number children even born	0.50(0.40)	2.06E-01	18.27(11.09)	1.20e-01
Balding Type I (UKBB)	0.25(0.20)	2.15E-01	10.93(5.82)	8.03e-02
Type 2 Diabetes (UKBB)	0.30(0.25)	2.31E-01	13.27(7.00)	8.05e-02
College Education (UKBB)	0.13(0.12)	2.64E-01	7.94(3.33)	3.76e-02
Tanning (UKBB)	0.24(0.22)	2.73E-01	5.23(9.90)	6.55e-01
Years of Education	0.15(0.15)	3.02E-01	8.63(4.26)	7.50e-02
White Blood Cell Count (UKBB)	0.17(0.18)	3.27E-01	14.84(4.64)	2.53e-03
Waist-hip Ratio (UKBB)	0.20(0.21)	3.38E-01	12.77(5.86)	4.32e-02
Age at Menopause (UKBB)	0.31(0.33)	3.49E-01	18.31(9.88)	7.20e-02
Coronary Artery Disease	0.65(0.77)	3.99E-01	30.14(22.74)	1.84e-01
Type 2 Diabetes	0.42(0.57)	4.61E-01	17.63(15.80)	2.88e-01
Rheumatoid Arthritis	-0.34(0.48)	4.77E-01	-2.61(12.96)	7.82e-01
Red Blood Cell Distribution Width (UKBB)	0.24(0.41)	5.60E-01	20.90(11.26)	8.17e-02
Auto Immune Traits (UKBB)	0.21(0.52)	6.84E-01	15.69(14.93)	3.07e-01
Ever Smoked	-0.12(0.36)	7.33E-01	-3.28(10.23)	6.74e-01
Dermatologic Diseases (UKBB)	-0.17(0.54)	7.45E-01	5.47(14.94)	7.64e-01
Hair Color (UKBB)	0.05(0.27)	8.66E-01	2.07(8.87)	9.02e-01

Supplementary Table 21. Enrichment and $\tau*$ of MaxCPP(ExAC) conditioned on MaxCPP (All Genes) and baselineLD,for each individual trait. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Height (UKBB)	0.63(0.20)	1.43E-03	23.97(5.88)	1.92e-04
Morning Person (UKBB)	0.45(0.14)	1.62E-03	16.58(4.37)	3.46e-04
Height	0.93(0.30)	1.82E-03	32.35(9.31)	9.18e-04
FEV1-FVC Ratio (UKBB)	0.79(0.26)	2.55E-03	29.70(7.85)	4.11e-04
Neuroticism (UKBB)	0.40(0.15)	6.56E-03	15.79(4.41)	7.98e-04
Schizophrenia	0.50(0.18)	6.68E-03	21.69(5.57)	2.38e-04
Age at Menarche (UKBB)	0.52(0.20)	9.43E-03	19.68(6.04)	2.21e-03
Forced Vital Capacity (UKBB)	0.33(0.13)	1.27E-02	15.51(3.99)	3.53e-04
Ulcerative Colitis	1.46(0.60)	1.44E-02	51.72(19.70)	6.75e-03
Platelet Count (UKBB)	0.75(0.31)	1.52E-02	31.49(9.41)	1.49e-03
Age first birth	0.69(0.30)	2.26E-02	27.17(9.77)	7.96e-03
High Cholesterol (UKBB)	0.99(0.43)	2.26E-02	35.68(12.76)	9.20e-03
Respiratory and Ear-nose-throat Diseases (UKBB)	0.59(0.28)	3.38E-02	27.03(9.71)	5.93e-03
Crohn's Disease	0.84(0.40)	3.42E-02	32.42(11.94)	6.57e-03
Systolic Blood Pressure (UKBB)	0.50(0.24)	3.65E-02	22.01(7.40)	4.69e-03
Red Blood Cell Count (UKBB)	0.43(0.21)	3.91E-02	23.74(6.77)	1.02e-03
BMI (UKBB)	0.24(0.12)	4.60E-02	11.92(3.32)	1.20e-03
Anorexia	0.60(0.31)	5.80E-02	20.78(9.91)	4.31e-02
Age at Menopause (UKBB)	0.78(0.42)	5.96E-02	33.13(13.27)	1.36e-02
Eczema (UKBB)	0.96(0.52)	6.53E-02	34.63(16.35)	3.86e-02
HDL	0.83(0.45)	6.80E-02	37.70(15.34)	1.69e-02
Hypothyroidism (UKBB)	0.58(0.33)	7.50E-02	27.52(9.51)	5.36e-03
Auto Immune Traits (UKBB)	1.00(0.58)	8.37E-02	39.37(19.53)	2.92e-02
Eosinophil Count (UKBB)	0.38(0.22)	8.38E-02	18.87(6.73)	6.81e-03
Waist-hip Ratio (UKBB)	0.34(0.23)	1.43E-01	17.50(7.05)	1.89e-02
Autism Spectrum	0.54(0.39)	1.61E-01	16.73(11.92)	1.70e-01
Type 2 Diabetes (UKBB)	0.36(0.27)	1.78E-01	15.74(8.10)	7.00e-02
Ever Smoked	0.48(0.37)	1.96E-01	14.06(11.17)	2.45e-01
Heel T Score (UKBB)	0.23(0.19)	2.32E-01	10.18(5.94)	1.21e-01
LDL	0.70(0.62)	2.62E-01	28.77(20.40)	1.75e-01
BMI	0.24(0.23)	3.03E-01	12.35(6.72)	9.05e-02
Balding Type I (UKBB)	0.17(0.20)	3.79E-01	9.28(6.06)	1.63e-01
Years of Education	0.13(0.16)	4.26E-01	8.19(4.96)	1.49e-01
Smoking Status (UKBB)	0.09(0.11)	4.30E-01	5.91(3.37)	1.44e-01
Number children even born	0.27(0.34)	4.37E-01	12.52(10.66)	2.79e-01
Type 2 Diabetes	-0.38(0.55)	4.86E-01	-5.04(16.87)	7.19e-01
Rheumatoid Arthritis	0.36(0.54)	5.00E-01	17.43(15.96)	2.93e-01
Tanning (UKBB)	-0.21(0.31)	5.02E-01	-7.15(10.57)	4.55e-01
Skin Color (UKBB)	-0.13(0.28)	6.32E-01	-4.28(9.78)	5.91e-01
Coronary Artery Disease	0.27(0.66)	6.87E-01	20.30(20.21)	3.35e-01
Hair Color (UKBB)	-0.10(0.26)	6.95E-01	-2.00(8.67)	7.28e-01
Depressive symptoms	0.12(0.38)	7.49E-01	13.16(11.70)	2.89e-01
Sunburn Occasion (UKBB)	-0.06(0.21)	7.78E-01	-3.09(6.54)	5.37e-01
White Blood Cell Count (UKBB)	0.04(0.16)	8.09E-01	11.50(4.53)	1.93e-02
Dermatologic Diseases (UKBB)	0.09(0.51)	8.54E-01	13.17(15.28)	4.22e-01
College Education (UKBB)	-0.01(0.12)	9.48E-01	4.13(3.60)	3.86e-01
Red Blood Cell Distribution Width (UKBB)	-0.01(0.32)	9.64E-01	14.19(10.04)	1.87e-01

Supplementary Table 22. Enrichment and $\tau*$ of MaxCPP(Cassa) conditioned on MaxCPP (All Genes) and baselineLD, for each individual trait. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
BMI (UKBB)	0.56(0.16)	6.90E-04	34.32(8.86)	2.88e-04
Anorexia	0.94(0.36)	9.62E-03	51.96(19.95)	9.07e-03
Neuroticism (UKBB)	0.52(0.20)	1.06E-02	31.54(10.83)	5.27e-03
BMI	0.53(0.22)	1.65E-02	33.16(11.57)	4.76e-03
Number children even born	1.05(0.48)	2.72E-02	59.73(25.43)	2.05e-02
Systolic Blood Pressure (UKBB)	0.32(0.15)	2.82E-02	24.40(7.95)	3.51e-03
Red Blood Cell Count (UKBB)	0.76(0.38)	4.79E-02	51.01(21.02)	1.94e-02
Smoking Status (UKBB)	0.25(0.13)	6.05E-02	16.34(6.92)	2.69e-02
Schizophrenia	0.44(0.24)	6.80E-02	30.06(12.41)	1.97e-02
Heel T Score (UKBB)	0.35(0.20)	7.15E-02	21.92(10.77)	4.92e-02
Age at Menarche (UKBB)	0.29(0.18)	1.00E-01	19.88(9.58)	5.04e-02
Morning Person (UKBB)	0.21(0.13)	1.13E-01	14.25(6.85)	5.22e-02
Ulcerative Colitis	0.92(0.59)	1.18E-01	56.93(31.51)	7.74e-02
Height (UKBB)	0.24(0.15)	1.18E-01	18.13(8.18)	4.11e-02
College Education (UKBB)	0.16(0.11)	1.27E-01	13.11(5.68)	3.47e-02
Eczema (UKBB)	0.47(0.32)	1.34E-01	31.29(15.93)	6.07e-02
High Cholesterol (UKBB)	0.77(0.51)	1.36E-01	46.72(26.29)	8.48e-02
Height	0.35(0.24)	1.56E-01	23.27(12.93)	8.59e-02
LDL	0.84(0.64)	1.93E-01	52.67(32.97)	1.18e-01
Tanning (UKBB)	-0.57(0.44)	1.94E-01	-29.89(25.59)	2.40e-01
HDL	-0.49(0.38)	1.96E-01	-11.51(18.96)	5.05e-01
Crohn's Disease	0.60(0.47)	1.98E-01	38.79(25.59)	1.33e-01
Years of Education	0.19(0.15)	2.03E-01	14.38(7.88)	9.00e-02
Sunburn Occasion (UKBB)	0.48(0.45)	2.83E-01	24.21(25.58)	3.41e-01
Rheumatoid Arthritis	-0.47(0.50)	3.47E-01	-17.39(26.16)	4.83e-01
Type 2 Diabetes (UKBB)	0.16(0.18)	3.65E-01	13.71(9.10)	1.64e-01
Ever Smoked	0.38(0.44)	3.84E-01	20.37(23.58)	4.11e-01
Age first birth	0.20(0.24)	4.08E-01	17.65(13.15)	2.04e-01
Auto Immune Traits (UKBB)	-0.39(0.48)	4.18E-01	-9.73(24.90)	6.67e-01
Hair Color (UKBB)	-0.22(0.30)	4.73E-01	-9.77(17.34)	5.34e-01
Balding Type I (UKBB)	-0.14(0.20)	4.83E-01	-2.65(10.31)	7.24e-01
Skin Color (UKBB)	-0.28(0.43)	5.06E-01	-14.47(24.95)	5.37e-01
Eosinophil Count (UKBB)	0.16(0.24)	5.09E-01	16.15(12.56)	2.27e-01
Forced Vital Capacity (UKBB)	0.07(0.11)	5.30E-01	9.86(6.01)	1.41e-01
FEV1-FVC Ratio (UKBB)	-0.07(0.12)	5.68E-01	3.08(6.06)	7.32e-01
Autism Spectrum	-0.19(0.36)	5.89E-01	-8.96(19.06)	5.92e-01
Platelet Count (UKBB)	0.22(0.41)	5.92E-01	21.02(21.37)	3.48e-01
Type 2 Diabetes	0.26(0.49)	6.02E-01	20.14(25.82)	4.60e-01
Red Blood Cell Distribution Width (UKBB)	0.12(0.37)	7.50E-01	21.25(19.58)	3.03e-01
Depressive symptoms	0.11(0.37)	7.56E-01	15.80(19.38)	4.42e-01
Waist-hip Ratio (UKBB)	-0.04(0.14)	7.60E-01	5.35(6.95)	5.28e-01
Hypothyroidism (UKBB)	-0.07(0.22)	7.61E-01	7.27(10.30)	5.37e-01
Dermatologic Diseases (UKBB)	-0.10(0.51)	8.44E-01	5.31(26.92)	8.72e-01
White Blood Cell Count (UKBB)	0.03(0.20)	8.62E-01	12.39(10.44)	2.76e-01
Coronary Artery Disease	0.08(0.52)	8.82E-01	16.95(28.04)	5.63e-01
Respiratory and Ear-nose-throat Diseases (UKBB)	0.03(0.29)	9.20E-01	11.67(14.09)	4.48e-01
Age at Menopause (UKBB)	-0.01(0.29)	9.80E-01	9.82(15.18)	5.63e-01

Supplementary Table 23. Enrichment and $\tau*$ of MaxCPP (Samocha) conditioned on MaxCPP (All Genes) and baselineLD, for each individual trait. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
LDL	1.71(1.11)	1.24E-01	69.35(41.44)	1.02e-01
Red Blood Cell Distribution Width (UKBB)	0.89(0.51)	8.06E-02	46.15(19.07)	1.87e-02
HDL	0.79(0.92)	3.92E-01	41.07(34.84)	2.49e-01
Respiratory and Ear-nose-throat Diseases (UKBB)	0.76(0.36)	3.72E-02	36.30(14.64)	1.52e-02
Red Blood Cell Count (UKBB)	0.72(0.34)	3.46E-02	36.63(13.21)	7.98e-03
Eczema (UKBB)	0.70(0.60)	2.44E-01	30.97(22.20)	1.80e-01
Ulcerative Colitis	0.60(0.66)	3.62E-01	30.07(23.96)	2.12e-01
High Cholesterol (UKBB)	0.51(0.62)	4.11E-01	24.98(22.07)	2.84e-01
Age at Menopause (UKBB)	0.44(0.42)	3.00E-01	25.86(15.67)	1.10e-01
Platelet Count (UKBB)	0.42(0.32)	1.95E-01	24.19(11.62)	4.70e-02
Type 2 Diabetes	0.41(0.55)	4.58E-01	20.81(20.13)	3.18e-01
Coronary Artery Disease	0.41(0.53)	4.41E-01	26.44(19.96)	1.83e-01
Balding Type I (UKBB)	0.39(0.23)	9.56E-02	17.70(8.47)	4.59e-02
Schizophrenia	0.32(0.17)	6.12E-02	18.14(6.20)	6.82e-03
Ever Smoked	0.31(0.32)	3.29E-01	10.90(11.39)	3.90e-01
Eosinophil Count (UKBB)	0.31(0.24)	1.96E-01	18.69(8.91)	4.77e-02
Height	0.22(0.27)	4.19E-01	12.87(9.79)	2.26e-01
Dermatologic Diseases (UKBB)	0.21(0.67)	7.59E-01	17.41(23.78)	4.90e-01
Depressive symptoms	0.20(0.40)	6.25E-01	15.87(14.88)	3.13e-01
BMI	0.18(0.22)	4.11E-01	11.68(8.20)	1.93e-01
Type 2 Diabetes (UKBB)	0.18(0.19)	3.36E-01	11.47(6.86)	1.23e-01
Hypothyroidism (UKBB)	0.17(0.41)	6.75E-01	16.03(13.20)	2.49e-01
Systolic Blood Pressure (UKBB)	0.17(0.15)	2.55E-01	12.99(5.71)	3.70e-02
Crohn's Disease	0.16(0.50)	7.54E-01	12.78(17.37)	4.96e-01
Rheumatoid Arthritis	0.16(0.50)	7.50E-01	12.34(17.59)	5.14e-01
Age at Menarche (UKBB)	0.16(0.18)	3.82E-01	9.85(6.62)	1.82e-01
Smoking Status (UKBB)	0.16(0.11)	1.41E-01	8.83(4.01)	5.06e-02
Height (UKBB)	0.14(0.19)	4.66E-01	10.39(6.82)	1.73e-01
BMI (UKBB)	0.11(0.11)	3.08E-01	8.79(4.18)	6.42e-02
Heel T Score (UKBB)	0.10(0.15)	5.23E-01	6.70(5.62)	3.07e-01
Years of Education	0.09(0.16)	5.56E-01	7.47(5.57)	2.47e-01
Auto Immune Traits (UKBB)	0.06(0.55)	9.17E-01	11.56(19.68)	5.87e-01
Autism Spectrum	0.06(0.41)	8.77E-01	3.09(14.64)	8.87e-01
Neuroticism (UKBB)	0.04(0.12)	7.01E-01	5.31(4.22)	3.07e-01
Morning Person (UKBB)	0.02(0.12)	8.79E-01	3.90(4.46)	5.15e-01
Skin Color (UKBB)	-0.67(0.51)	1.87E-01	-23.84(17.55)	1.76e-01
Tanning (UKBB)	-0.54(0.56)	3.39E-01	-19.74(20.18)	3.08e-01
Hair Color (UKBB)	-0.41(0.32)	2.08E-01	-13.30(12.13)	2.49e-01
Age first birth	-0.29(0.23)	2.10E-01	-3.78(8.32)	5.67e-01
Anorexia	-0.28(0.34)	4.10E-01	-6.88(12.25)	5.24e-01
Number children even born	-0.19(0.37)	5.99E-01	-2.60(13.56)	7.91e-01
Sunburn Occasion (UKBB)	-0.18(0.42)	6.78E-01	-7.11(13.90)	5.58e-01
FEV1-FVC Ratio (UKBB)	-0.14(0.13)	2.51E-01	0.87(4.68)	9.78e-01
Forced Vital Capacity (UKBB)	-0.10(0.11)	3.96E-01	2.25(4.27)	7.71e-01
Waist-hip Ratio (UKBB)	-0.09(0.12)	4.81E-01	3.85(4.31)	5.09e-01
White Blood Cell Count (UKBB)	-0.04(0.18)	8.41E-01	8.72(6.54)	2.38e-01
College Education (UKBB)	-0.00(0.10)	9.69E-01	3.88(3.63)	4.30e-01

Supplementary Table 24. Enrichment and $\tau*$ of MaxCPP (Wang) conditioned on MaxCPP (All Genes) and baselineLD, for each individual trait. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Trait	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
Height (UKBB)	0.64(0.26)	1.23E-02	7.71(1.65)	1.32e-04
Neuroticism (UKBB)	0.49(0.22)	2.61E-02	5.69(1.28)	3.26e-04
LDL	2.18(0.99)	2.76E-02	16.55(6.63)	1.98e-02
White Blood Cell Count (UKBB)	0.72(0.33)	3.10E-02	12.95(2.18)	2.16e-07
Ever Smoked	1.11(0.52)	3.46E-02	4.10(3.51)	3.74e-01
FEV1-FVC Ratio (UKBB)	0.44(0.21)	4.15E-02	7.85(1.45)	2.40e-06
Anorexia	0.97(0.49)	4.80E-02	6.91(3.10)	4.76e-02
Height	0.58(0.32)	6.88E-02	7.00(2.23)	8.25e-03
Ulcerative Colitis	1.35(0.81)	9.48E-02	13.88(5.31)	9.73e-03
High Cholesterol (UKBB)	0.86(0.55)	1.19E-01	9.77(3.06)	6.19e-03
College Education (UKBB)	0.23(0.15)	1.35E-01	5.01(0.93)	2.58e-05
Number children even born	0.82(0.57)	1.51E-01	7.54(3.74)	8.01e-02
Forced Vital Capacity (UKBB)	0.24(0.19)	1.99E-01	6.57(1.39)	8.40e-05
Age at Menarche (UKBB)	0.32(0.27)	2.25E-01	5.48(1.57)	5.00e-03
Hair Color (UKBB)	-0.83(0.80)	3.00E-01	-2.68(4.02)	3.74e-01
Autism Spectrum	-0.59(0.58)	3.12E-01	-1.47(3.35)	4.45e-01
Schizophrenia	0.20(0.23)	3.85E-01	7.59(1.49)	1.74e-05
Sunburn Occasion (UKBB)	-0.53(0.62)	3.92E-01	-3.87(2.77)	1.02e-01
Tanning (UKBB)	-0.89(1.04)	3.95E-01	-5.14(5.78)	3.07e-01
Smoking Status (UKBB)	-0.15(0.18)	4.20E-01	2.44(1.09)	1.83e-01
Type 2 Diabetes (UKBB)	-0.29(0.38)	4.37E-01	3.78(2.02)	1.71e-01
Waist-hip Ratio (UKBB)	-0.30(0.40)	4.51E-01	5.92(1.57)	1.58e-03
Years of Education	0.15(0.22)	4.93E-01	4.79(1.28)	3.55e-03
HDL	0.52(0.82)	5.29E-01	15.21(5.58)	1.05e-02
Balding Type I (UKBB)	0.21(0.35)	5.48E-01	4.66(2.07)	6.94e-02
Morning Person (UKBB)	0.11(0.19)	5.63E-01	3.59(1.11)	2.01e-02
Age first birth	0.22(0.39)	5.69E-01	7.64(2.71)	1.42e-02
Eczema (UKBB)	-0.24(0.43)	5.74E-01	5.43(2.60)	8.45e-02
BMI (UKBB)	0.09(0.18)	6.21E-01	5.12(1.54)	9.25e-03
Depressive symptoms	0.27(0.57)	6.34E-01	10.52(3.62)	8.35e-03
Rheumatoid Arthritis	0.39(0.83)	6.36E-01	8.15(5.18)	1.55e-01
Crohn's Disease	0.29(0.65)	6.60E-01	8.49(4.05)	5.78e-02
Red Blood Cell Count (UKBB)	-0.17(0.39)	6.68E-01	10.24(2.81)	1.33e-03
Coronary Artery Disease	-0.38(0.89)	6.70E-01	10.79(5.14)	4.64e-02
BMI	-0.12(0.32)	7.16E-01	4.81(1.98)	5.88e-02
Skin Color (UKBB)	-0.30(1.09)	7.79E-01	-2.12(6.21)	6.15e-01
Eosinophil Count (UKBB)	0.08(0.35)	8.10E-01	7.86(2.05)	7.96e-04
Respiratory and Ear-nose-throat Diseases (UKBB)	-0.11(0.51)	8.30E-01	9.16(3.09)	7.70e-03
Red Blood Cell Distribution Width (UKBB)	-0.11(0.56)	8.37E-01	14.00(3.11)	5.18e-05
Platelet Count (UKBB)	-0.07(0.43)	8.68E-01	8.91(2.12)	2.58e-04
Dermatologic Diseases (UKBB)	0.10(0.93)	9.14E-01	10.77(5.78)	8.67e-02
Hypothyroidism (UKBB)	0.05(0.54)	9.20E-01	10.55(3.89)	1.58e-02
Heel T Score (UKBB)	0.02(0.25)	9.22E-01	3.15(1.46)	1.39e-01
Age at Menopause (UKBB)	-0.05(0.53)	9.26E-01	9.57(4.08)	3.19e-02
Systolic Blood Pressure (UKBB)	-0.01(0.27)	9.76E-01	6.99(1.68)	3.61e-04
Type 2 Diabetes	-0.01(0.87)	9.90E-01	6.12(5.12)	3.21e-01
Auto Immune Traits (UKBB)	0.00(0.98)	9.96E-01	10.06(5.58)	7.72e-02

Supplementary Table 25. Enrichment and $\tau*$ of MaxCPP (AH) conditioned on MaxCPP (All Genes) and baselineLD, for each individual trait. We obtained the standard error using block jackknife. We used 200 blocks per genome (n=200 blocks are used to derive the statistics).

Annotation	Cell Type	N
eQTL	CD14+ monocytes	194
eQTL	CD16+ neutrophils	192
eQTL	Naive CD4+ T Cell	169
hQTL-H3K27ac	CD14+ monocytes	162
hQTL-H3K27ac	CD16+ neutrophils	174
hQTL-H3K27ac	Naive CD4+ T Cell	143
hQTL-H3K4me1	CD14+ monocytes	172
hQTL-H3K4me1	CD16+ neutrophils	173
hQTL-H3K4me1	Naive CD4+ T Cell	104
sQTL	CD14+ monocytes	194
sQTL	CD16+ neutrophils	192
sQTL	Naive CD4+ T Cell	169
meQTL	CD14+ monocytes	196
meQTL	CD16+ neutrophils	197
meQTL	Naive CD4+ T Cell	132

Supplementary Table 26. Cell types and molecular QTL in the BLUEPRINT data set.

See attached Excel file

Supplementary Table 27. Enrichment and $\tau*$ for CD14+ monocytes, CD16+ neutrophils, naive CD4+ T cells and FE-Meta-Tissue in the BLUEPRINT data set. We report results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations, conditioned on the baselineLD model and meta-analyzed across 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). In each case, we report results for AllcisQTL, 95%CredibleSet and MaxCPP.

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
eQTL	0.38(0.05)	3.88e-12	5.44(0.55)	3.26e-16
H3K27ac-hQTL	0.45(0.06)	1.65e-13	4.28(0.37)	2.59e-19
H3K4me1-hQTL	0.43(0.05)	5.61e-15	4.27(0.36)	1.29e-20
meQTL	0.28(0.04)	9.01e-12	2.81(0.19)	8.36e-22
sQTL	0.19(0.04)	8.50e-07	3.61(0.40)	1.39e-10

Supplementary Table 28. Enrichment and $\tau*$ of MaxCPP annotations for FE-Meta-Tissue in the BLUEPRINT data set. We report MaxCPP results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations conditioned on baselineLD model and meta-analyzed across 41 independent traits (47 data sets, n=41 independent traits to derive the statistics).

QTL Type	**Tissue 1 (T1)**	**Tissue 2 (T2)**	**Replication T1 in T2 (%)**	**Replication T2 in T1 (%)**
eQTL	GTEx FE-Meta-Tissue	GTEx Whole Blood	16.08%	94.20%
	GTEx FE-Meta-Tissue	BLUEPRINT MONO	29.74%	77.95%
	GTEx FE-Meta-Tissue	BLUEPRINT NEUT	25.89%	77.06%
	GTEx FE-Meta-Tissue	BLUEPRINT TCEL	26.55%	80.01%
	GTEx Whole Blood	BLUEPRINT MONO	55.11%	24.66%
	GTEx Whole Blood	BLUEPRINT NEUT	52.22%	26.54%
	GTEx Whole Blood	BLUEPRINT TCEL	48.85%	25.12%
	BLUEPRINT MONO	BLUEPRINT TCEL	57.09%	65.63%
	BLUEPRINT NEUT	BLUEPRINT MONO	67.42%	59.36%
	BLUEPRINT NEUT	BLUEPRINT TCEL	56.20%	56.88%
H3K27ac-hQTL	BLUEPRINT MONO	Waszak et al.	1.40%	56.68%
	BLUEPRINT NEUT	Waszak et al.	1.49%	50.09%
	BLUEPRINT TCEL	Waszak et al.	1.68%	42.86%
	BLUEPRINT FE-Meta-Tissue	Waszak et al.	0.95%	80.61%
	BLUEPRINT MONO	BLUEPRINT TCEL	39.33%	62.53%
	BLUEPRINT NEUT	BLUEPRINT MONO	66.01%	55.03%
	BLUEPRINT NEUT	BLUEPRINT TCEL	42.67%	56.56%
H3K4me1-hQTL	BLUEPRINT MONO	Waszak et al.	0.95%	68.55%
	BLUEPRINT NEUT	Waszak et al.	1.04%	58.02%
	BLUEPRINT TCEL	Waszak et al.	1.35%	35.90%
	BLUEPRINT FE-Meta-Tissue	Waszak et al.	0.74%	83.25%
	BLUEPRINT MONO	BLUEPRINT TCEL	28.33%	77.07%
	BLUEPRINT NEUT	BLUEPRINT MONO	78.03%	60.58%
	BLUEPRINT NEUT	BLUEPRINT TCEL	32.32%	68.25%
meQTL	BLUEPRINT MONO	BLUEPRINT TCEL	69.09%	80.29%
	BLUEPRINT NEUT	BLUEPRINT MONO	82.25%	82.46%
	BLUEPRINT NEUT	BLUEPRINT TCEL	69.15%	80.25%
sQTL	BLUEPRINT MONO	BLUEPRINT TCEL	50.14%	40.70%
	BLUEPRINT NEUT	BLUEPRINT MONO	52.72%	40.72%
	BLUEPRINT NEUT	BLUEPRINT TCEL	46.27%	29.01%

Supplementary Table 29. High replication rates of cis-eQTL and other molecular QTL in GTEx and BLUEPRINT data. For each pair of data sets, we report the proportion of cis-QTL detected at FDR<5% in the first data set that are detected at FDR<5% in the second data set. In the eQTL analysis, we determined that BLUEPRINT eQTL have a much higher replication rate in GTEx FE-Meta-Tissue (avg=78%) than in GTEx Whole Blood (avg=25%). In the hQTL analyses, we determined that hQTL from Waszak et al.[12] (H3K27ac-hQTL and H3K4me3-hQTL) attain moderately high replication rates in individual BLUEPRINT cell types (avg=52%) and even higher replication rates in BLUEPRINT FE-Meta-Tissue (avg=82%). We elected to not include the Waszak et al. hQTL data in our main disease/trait heritability analyses, due to its much smaller size (n=45) and much lower power (much lower replication rates of BLUEPRINT hQTL in Waszak et al. data); we also determined that the hQTL replication rate from one BLUEPRINT cell type to another BLUEPRINT cell type (avg=56%) is comparable to the eQTL replication rate from one BLUEPRINT cell type to another BLUEPRINT cell type (avg=60%). The meQTL replication rate from one BLUEPRINT cell type to another BLUEPRINT cell type (avg=77%) was also high. The sQTL replication rate from one BLUEPRINT cell type to another BLUEPRINT cell type (avg=43%) was moderately high.

Tissue	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
FE-Meta-Tissue-H3K27ac-hQTL	0.45(0.06)	1.65E-13	4.28(0.37)	2.59E-19
MONO-H3K4me1-hQTL	0.44(0.06)	4.09E-15	4.92(0.43)	2.52E-20
FE-Meta-Tissue-H3K4me1-hQTL	0.43(0.05)	5.61E-15	4.27(0.36)	1.29E-20
FE-Meta-Tissue-eQTL	0.38(0.05)	3.88E-12	5.44(0.55)	3.26E-16
NEUT-H3K4me1-hQTL	0.35(0.05)	1.33E-12	4.83(0.46)	2.93E-17
MONO-eQTL	0.33(0.05)	4.61E-11	5.77(0.62)	6.19E-15
NEUT-eQTL	0.33(0.05)	4.68E-12	6.02(0.63)	8.90E-16
NEUT-H3K27ac-hQTL	0.33(0.05)	1.13E-12	5.63(0.56)	4.40E-17
FE-Meta-Tissue-METH	0.28(0.04)	9.01E-12	2.81(0.19)	8.36E-22
TCEL-eQTL	0.26(0.05)	2.35E-08	4.95(0.57)	6.37E-12
NEUT-meQTL	0.26(0.04)	4.42E-09	3.54(0.31)	2.02E-16
MONO-meQTL	0.25(0.04)	7.74E-09	3.49(0.31)	1.02E-15
MONO-H3K27ac-hQTL	0.23(0.04)	5.65E-08	4.36(0.47)	9.45E-13
FE-Meta-Tissue-sQTL	0.19(0.04)	8.50E-07	3.61(0.40)	1.39E-10
TCEL-meQTL	0.18(0.03)	2.39E-07	3.18(0.28)	7.89E-15
MONO-sQTL	0.15(0.04)	5.56E-05	5.28(0.88)	1.03E-06
NEUT-sQTL	0.14(0.03)	1.83E-06	5.25(0.75)	1.55E-08
TCEL-sQTL	0.10(0.04)	1.17E-02	3.94(0.83)	4.00E-04
TCEL-H3K27ac-hQTL	0.06(0.04)	1.00E-01	2.95(0.56)	4.68E-04
TCEL-H3K4me1-hQTL	0.02(0.03)	6.00E-01	2.06(0.51)	3.62E-02

Supplementary Table 30. Enrichment and $\tau*$ of MaxCPP annotations for CD14+ monocytes, CD16+ neutrophils, naive CD4+ T cells and FE-Meta-Tissue in the BLUEPRINT data set. We report results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations, conditioned on the baselineLD model and meta-analyzed across 41 independent traits (47 data sets, n=41 independent traits to derive the statistics)

Tissue	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
FE-Meta-Tissue-H3K27ac-hQTL	1.46(0.22)	4.68E-11	10.05(1.29)	1.19E-14
MONO-H3K4me1-hQTL	1.32(0.20)	1.91E-11	11.73(1.56)	1.74E-14
FE-Meta-Tissue-eQTL	1.27(0.21)	3.07E-09	14.54(2.18)	1.37E-11
FE-Meta-Tissue-H3K4me1-hQTL	1.24(0.20)	6.54E-10	9.64(1.28)	9.16E-13
TCEL-eQTL	1.15(0.21)	4.19E-08	16.32(2.66)	5.37E-10
NEUT-H3K4me1-hQTL	0.98(0.19)	3.69E-07	10.53(1.82)	2.92E-09
FE-Meta-Tissue-sQTL	0.95(0.23)	2.75E-05	11.70(2.30)	2.62E-06
NEUT-H3K27ac-hQTL	0.89(0.22)	3.51E-05	12.37(2.49)	5.63E-07
MONO-eQTL	0.85(0.20)	1.53E-05	12.43(2.36)	1.87E-07
NEUT-eQTL	0.83(0.21)	1.05E-04	13.01(2.76)	3.18E-06
NEUT-meQTL	0.75(0.20)	2.37E-04	6.96(1.28)	1.58E-06
NEUT-sQTL	0.70(0.21)	7.20E-04	20.32(5.12)	1.74E-04
FE-Meta-Tissue-METH	0.69(0.20)	6.16E-04	4.63(0.77)	2.51E-06
TCEL-sQTL	0.65(0.31)	3.77E-02	15.87(6.20)	1.49E-02
MONO-H3K27ac-hQTL	0.64(0.20)	1.25E-03	9.37(2.14)	1.35E-05
TCEL-H3K4me1-hQTL	0.62(0.24)	1.11E-02	13.04(3.99)	2.44E-03
MONO-meQTL	0.49(0.22)	2.48E-02	5.39(1.37)	1.33E-03
TCEL-H3K27ac-hQTL	0.48(0.22)	3.28E-02	10.29(3.25)	2.89E-03
TCEL-meQTL	0.40(0.27)	1.38E-01	5.17(1.98)	3.06E-02
MONO-sQTL	0.38(0.23)	9.69E-02	11.37(5.19)	4.50E-02

Supplementary Table 31. Enrichment and $\tau*$ of MaxCPP annotations for CD14+ monocytes, CD16+ neutrophils, naive CD4+ T cells and FE-Meta-Tissue in the BLUEPRINT data set in autoimmune disease. We report results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations, conditioned on the baselineLD model and meta-analyzed across six autoimmune diseases (n=6 independent traits to derive the statistics).

Tissue	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
NEUT-eQTL	1.14(0.14)	2.04E-16	17.07(1.70)	3.28E-21
MONO-H3K4me1-hQTL	1.12(0.10)	1.58E-28	10.17(0.69)	4.12E-34
FE-Meta-Tissue-H3K27ac-hQTL	1.11(0.20)	2.51E-08	8.24(1.05)	1.05E-11
Meta-Tissue-eQTL	1.11(0.11)	3.94E-23	13.09(1.05)	8.07E-29
MONO-eQTL	1.04(0.13)	1.44E-16	14.76(1.45)	6.21E-21
FE-Meta-Tissue-H3K4me1-hQTL	1.02(0.10)	4.96E-26	8.08(0.55)	3.94E-32
NEUT-H3K27ac-hQTL	0.99(0.27)	2.91E-04	13.80(3.04)	2.25E-05
NEUT-H3K4me1-hQTL	0.90(0.17)	1.35E-07	10.01(1.45)	5.90E-10
MONO-H3K27ac-hQTL	0.79(0.13)	2.31E-09	10.80(1.35)	2.46E-13
NEUT-meQTL	0.77(0.10)	1.66E-15	7.24(0.66)	5.09E-22
MONO-meQTL	0.75(0.09)	8.17E-18	7.17(0.60)	7.87E-26
FE-Meta-Tissue-METH	0.69(0.08)	5.67E-17	4.73(0.31)	5.90E-28
TCEL-eQTL	0.68(0.11)	2.83E-10	11.00(1.30)	2.69E-14
TCEL-meQTL	0.54(0.09)	5.49E-09	6.31(0.72)	6.71E-14
MONO-sQTL	0.47(0.12)	3.69E-05	13.40(2.61)	2.06E-06
FE-Meta-Tissue-sQTL	0.44(0.10)	3.23E-06	6.66(0.95)	3.16E-09
TCEL-sQTL	0.43(0.17)	1.30E-02	11.47(3.51)	2.98E-03
NEUT-sQTL	0.43(0.11)	1.05E-04	13.37(2.74)	6.79E-06
TCEL-H3K27ac-hQTL	0.41(0.11)	1.09E-04	8.82(1.52)	2.64E-07
TCEL-H3K4me1-hQTL	0.25(0.09)	3.84E-03	6.71(1.44)	7.91E-05

Supplementary Table 32. Enrichment and $\tau*$ of MaxCPP annotations for CD14+ monocytes, CD16+ neutrophils, naive CD4+ T cells and FE-Meta-Tissue in the BLUEPRINT data set in blood cell traits. We report results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations, conditioned on the baselineLD model and meta-analyzed across five blood cell traits (n=5 independent traits to derive the statistics).

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
GTEx-eQTL	0.38(0.03)	6.44e-29	4.88(0.31)	1.10e-34
BL-eQTL	0.12(0.04)	3.04e-03	3.79(0.44)	2.21e-10
BL-H3K27ac-hQTL	0.19(0.05)	1.30e-04	3.51(0.33)	1.30e-14
BL-H3K4me1-hQTL	0.17(0.04)	3.67e-06	3.57(0.30)	8.01e-18
BL-meQTL	0.12(0.03)	3.16e-05	2.55(0.17)	2.28e-19
BL-sQTL	0.02(0.03)	3.48e-01	2.55(0.32)	1.01e-06

Supplementary Table 33. Enrichment and $\tau*$ of MaxCPP annotations for FE-Meta-Tissue in the GTEx and BLUEPRINT data sets in a joint analysis. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). Meta-analysis results for eQTL from GTEx and eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations from BLUEPRINT conditioned on each other and baselineLD model.

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
eQTL	0.22(0.04)	1.44e-07	4.44(0.47)	1.21e-13
H3K27ac-hQTL	0.20(0.05)	9.75e-05	3.55(0.33)	4.54e-15
H3K4me1-hQTL	0.18(0.04)	1.79e-06	3.62(0.30)	2.21e-18
meQTL	0.14(0.03)	1.68e-06	2.62(0.17)	7.49e-21
sQTL	0.06(0.03)	2.70e-02	2.81(0.33)	3.29e-08

Supplementary Table 34. Enrichment and $\tau*$ for FE-Meta-Tissue in the BLUEPRINT data set. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). Meta-analysis results for eQTL, 2 hQTL (H3K27ac and H3K4me1), sQTL, and meQTL annotations conditioned on each other and baselineLD model.

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
FE Meta Tissue GTEx	0.49(0.06)	1.96e-17	5.65(0.40)	1.14e-31
TSS	-0.00(0.05)	9.49e-01	5.44(0.51)	3.32e-18
FE Meta Tissue GTEx	0.50(0.06)	5.21e-15	5.65(0.40)	1.16e-31
TES	0.00(0.06)	9.45e-01	5.36(0.47)	9.25e-21
FE Meta Tissue GTEx	0.46(0.04)	2.51e-27	5.64(0.40)	8.92e-32
TSS<10K	0.05(0.04)	2.48e-01	6.30(0.85)	5.43e-10
FE Meta Tissue GTEx	0.57(0.05)	1.63e-27	5.64(0.40)	7.99e-32
TES<10K	-0.14(0.04)	2.52e-03	3.77(0.69)	1.08e-04

Supplementary Table 35. Enrichment and $\tau*$ for TSS/TES-related annotations from GTEx. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). Meta-analysis results are conditioned on the baselineLD model and MaxCPP. The TSS annotation consists of the MaxCPP annotation restricted to variants that are closer to the TSS and the TES annotation consist of the MaxCPP annotation restricted to variants that are closer to the TES. In addition, TSS<10K consists of variants whose distance to TSS is less than 10Kb and TES<10K consists of variants whose distance to TES is less than 10Kb. We did not detect any significantly positive $\tau*$, although the $\tau*$ for TES<10K was slightly and significantly negative, indicating a reduction in heritability for this annotation conditional on the baselineLD model and MaxCPP.

Annotation	$\tau*$ (se)	$\tau*$ (P)	Enrichment (se)	Enrichment (P)
FE Meta Tissue BLUEPRINT	0.35(0.06)	1.44e-08	5.45(0.55)	2.51e-16
TSS	0.02(0.04)	7.05e-01	4.76(0.76)	7.34e-07
FE Meta Tissue BLUEPRINT	0.22(0.06)	8.25e-05	5.35(0.54)	5.04e-16
TES	0.07(0.04)	9.12e-02	6.10(0.72)	1.94e-12
FFE Meta Tissue BLUEPRINT	0.29(0.06)	2.11e-07	5.39(0.54)	4.24e-16
TSS<10K	0.09(0.06)	9.74e-02	6.87(1.46)	2.94e-05
FE Meta Tissue BLUEPRINT	0.30(0.05)	2.72e-08	5.40(0.54)	4.01e-16
TES<10K	0.04(0.04)	2.71e-01	5.88(0.95)	2.82e-07

Supplementary Table 36. Enrichment and $\tau*$ for TSS/TES-related annotations obtained from the BLUEPRINT gene expression data set. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics). Meta-analysis results are conditioned on the baselineLD model and MaxCPP. The TSS annotation consists of the MaxCPP annotation restricted to variants that are closer to the TSS and the TES annotation consist of the MaxCPP annotation restricted to variants that are closer to the TES. In addition, TSS<10K consists of variants whose distance to TSS is less than 10Kb and TES<10K consists of variants whose distance to TES is less than 10Kb. We did not detect any significantly positive $\tau*$.

See attached Excel file

Supplementary Table 37. MaxCPP enrichment and $\tau*$ estimates are not sensitive to the maximum number of causal variants per locus modeled by CAVIAR. We report MaxCPP enrichment and $\tau*$ estimates for each of 44 GTEx tissues with CAVIAR modeling either up to six or up to three causal variants per locus. We determined that results were not statistically different. We calculated $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics)

See attached Excel file

Supplementary Table 38. Results using baselineLD model v1.1 and baselineLD model v1.0 are highly concordant. We report enrichment and $\tau*$ estimates for each of 44 GTEx tissues using baselineLD model v1.1 and baselineLD model v1.0, where v1.1 is identical to v1.0 (as described in ref. 39) except that an error in the promoter annotation has been fixed. We determined that results were not statistically different. We calculated enrichment and $\tau*$ by meta-analyzing 41 independent traits (47 data sets, n=41 independent traits to derive the statistics).

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