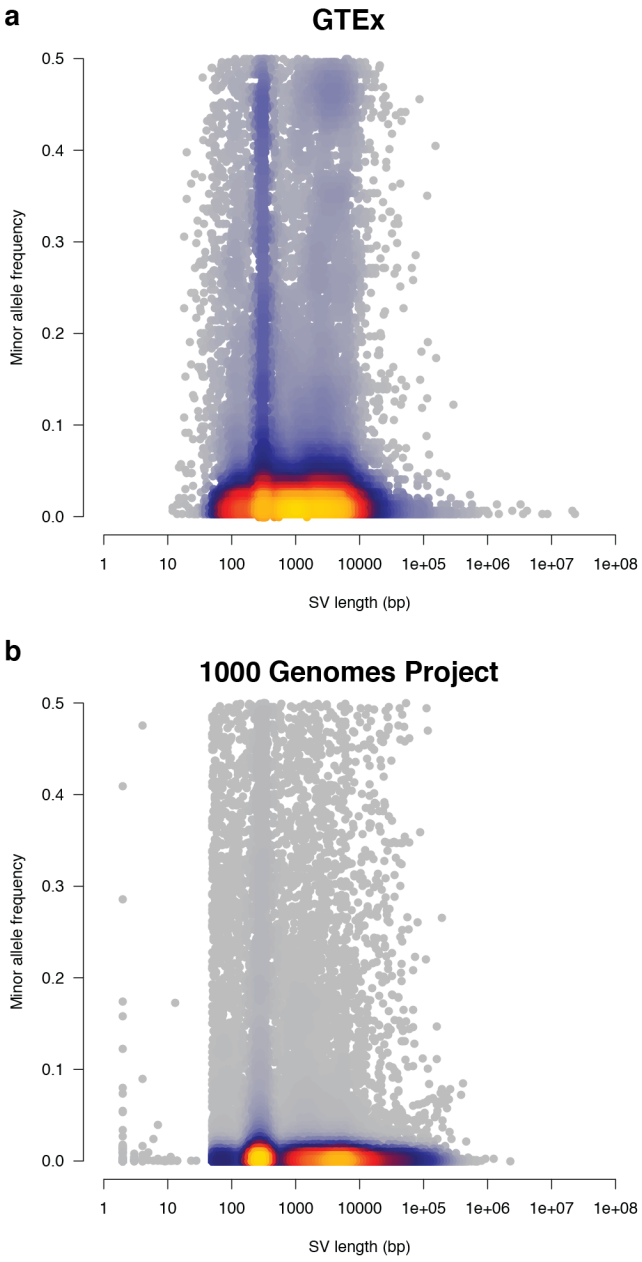
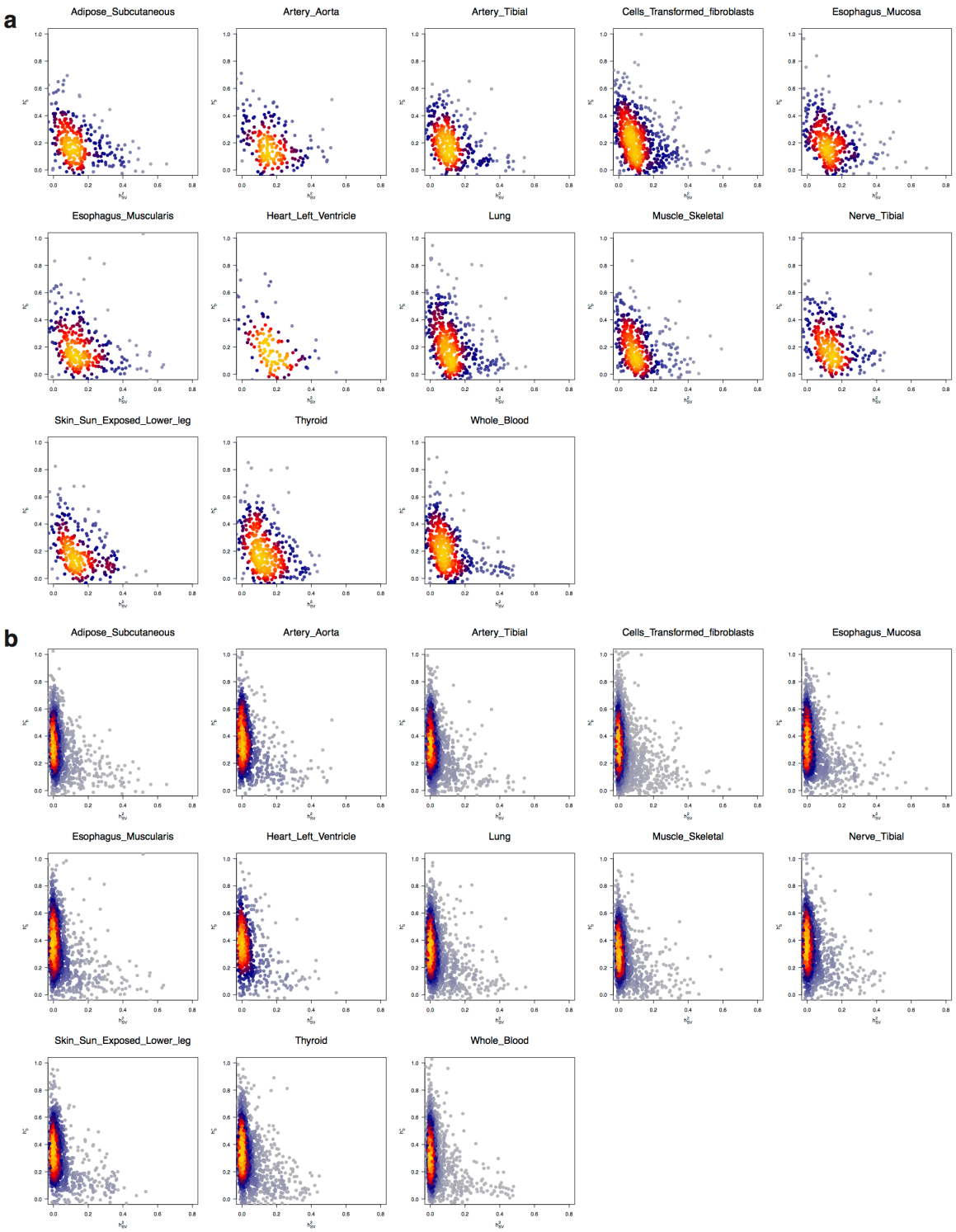
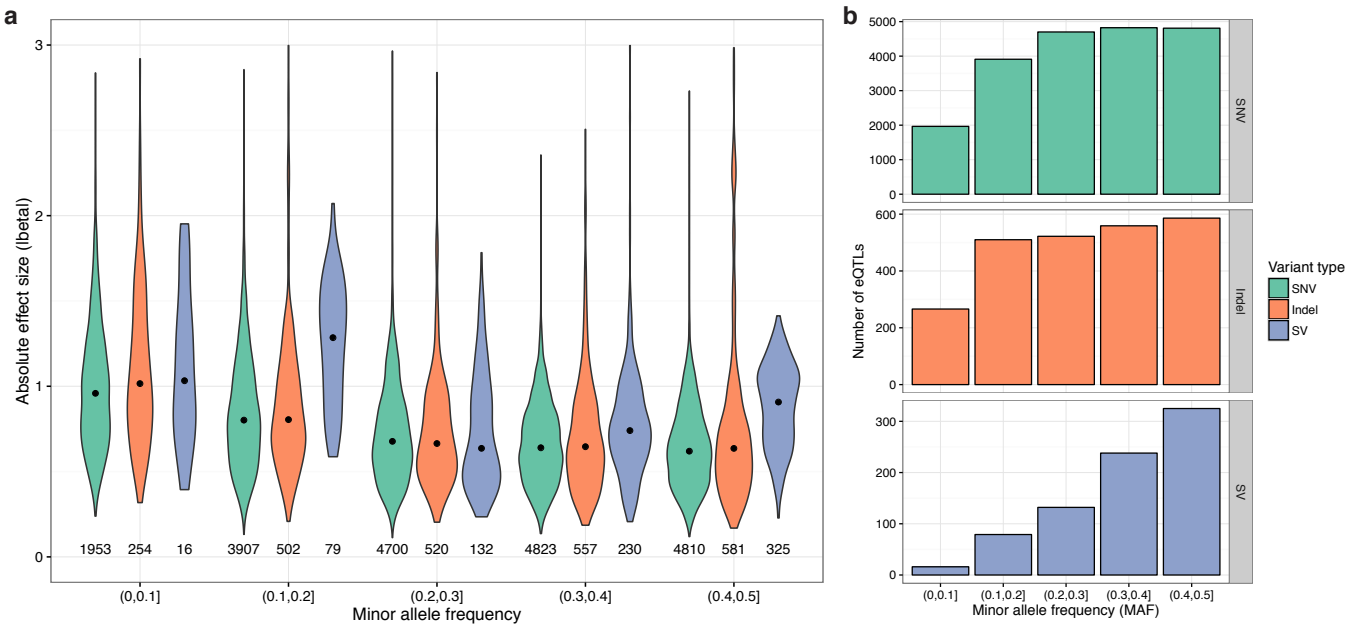
Supplementary Information



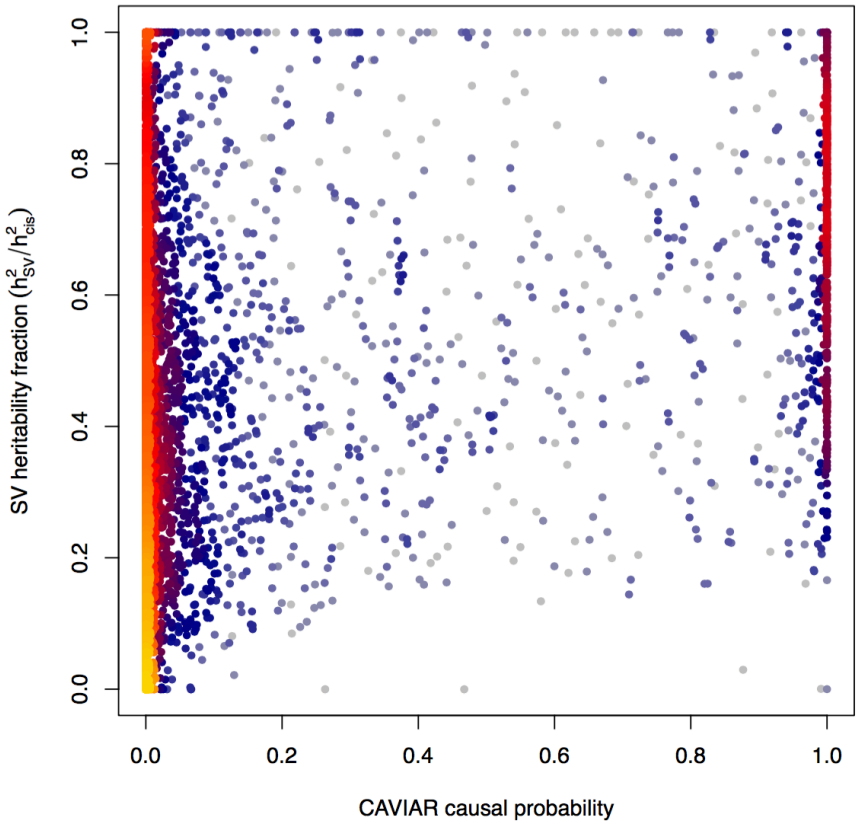
Supplementary Figure 1. Heat scatter plots of SV size by their minor allele frequency (MAF). Distributions show (**a**) the GTEx high confidence SV call set compared to (**b**) the 1000 Genomes Project SV call set from 2,504 individuals (Sudmant *et al.* 2015)



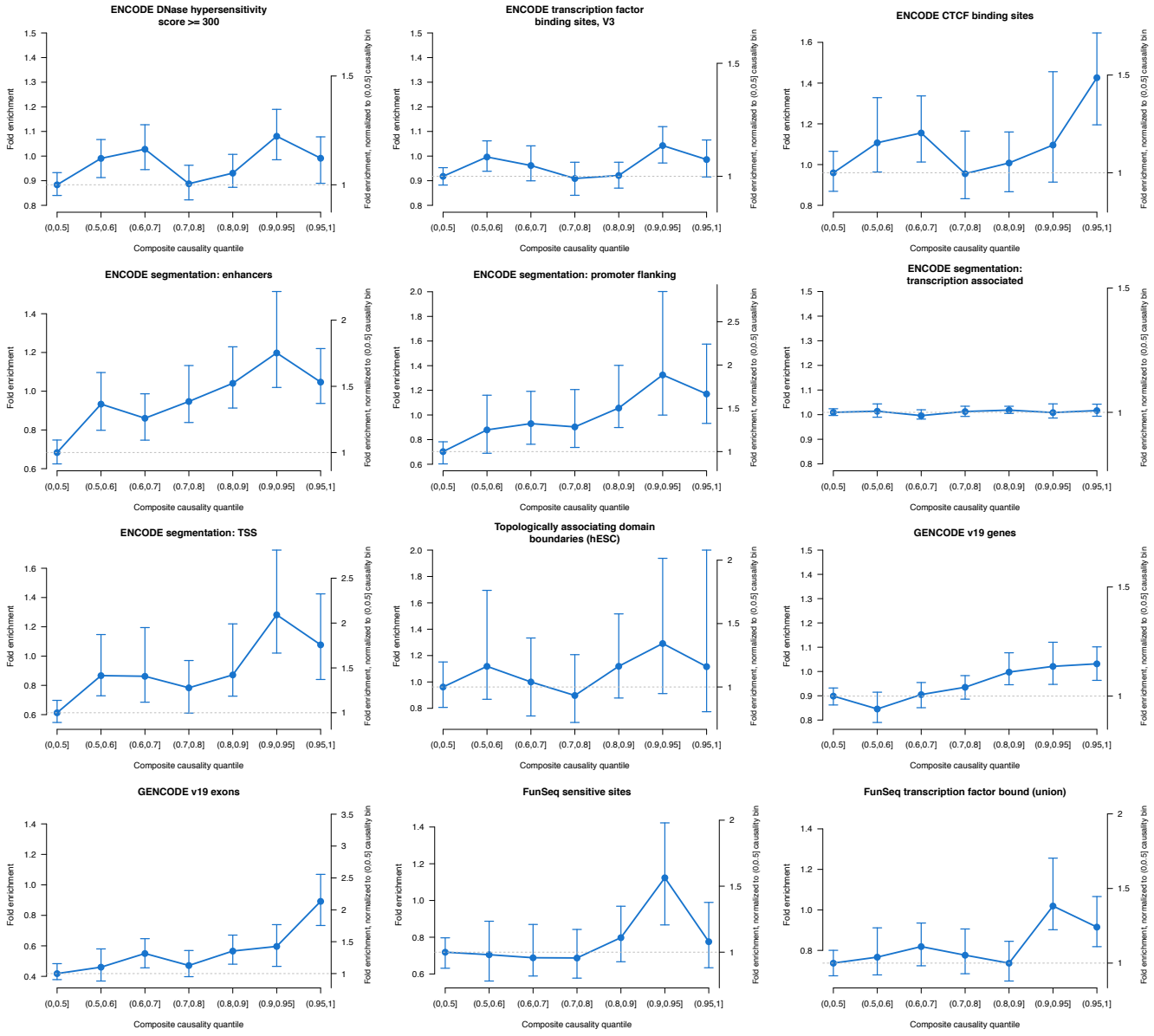
Supplementary Figure 2. Heat scatter plots (grouped by tissue) showing the heritability of each eQTL apportioned to the most significant SV in the *cis* window (x-axis) and the additive effect from the top 1,000 most significant SNVs and indels in the *cis* window for (**b**) SV-only and (**b**) joint eQTL mapping analyses.



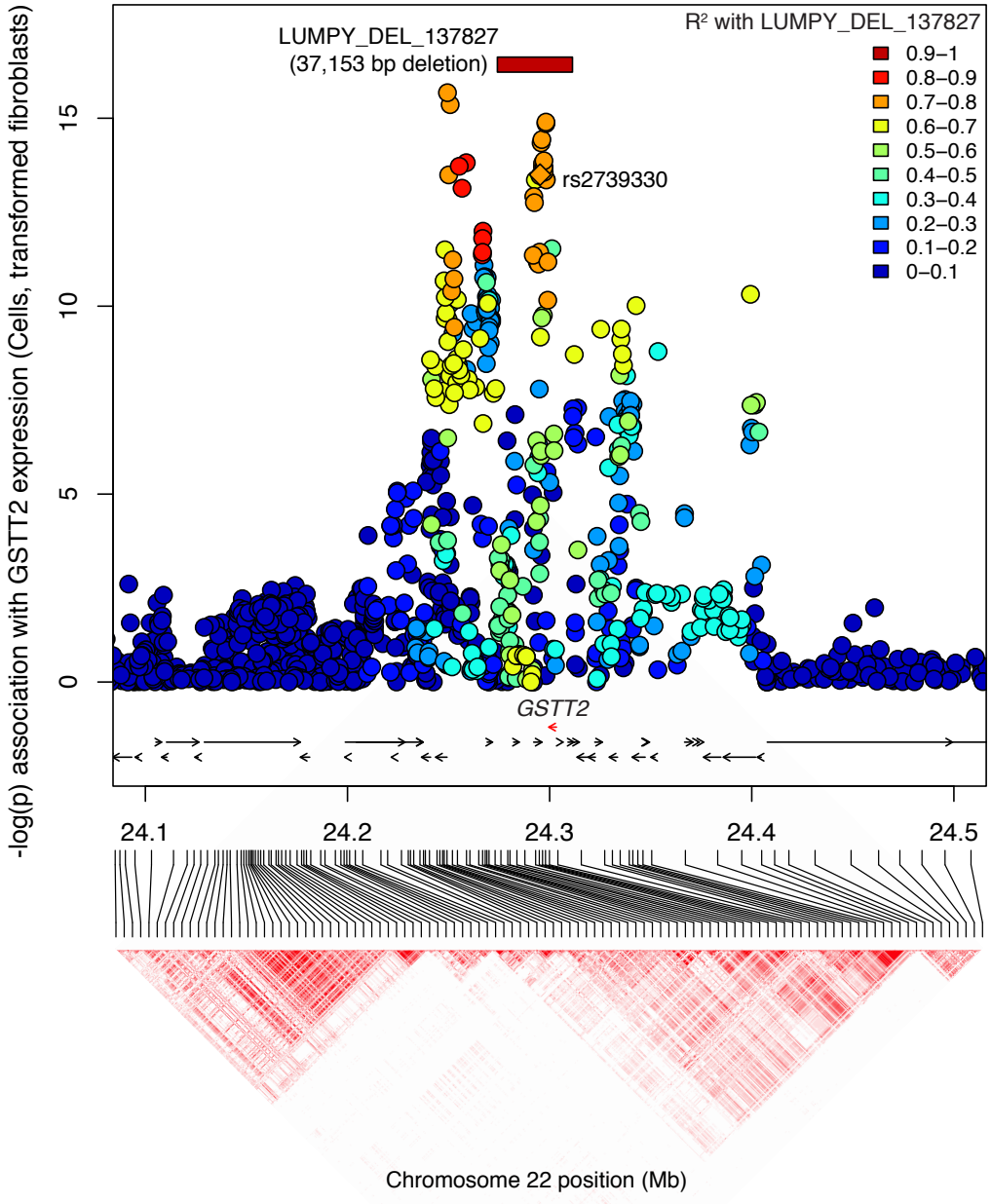
Supplementary Figure 3. Relationship between eQTL effect size and minor allele frequency (MAF). (**a**) Absolute effect size of joint eQTLs within each bin of minor allele frequency (MAF) for SVs, SNVs, and indels. Black dots represent the median of each distribution, and values beneath indicate the number of observations in each distribution. (**b**) Number of eQTLs in each bin of minor allele frequency, by variant type.



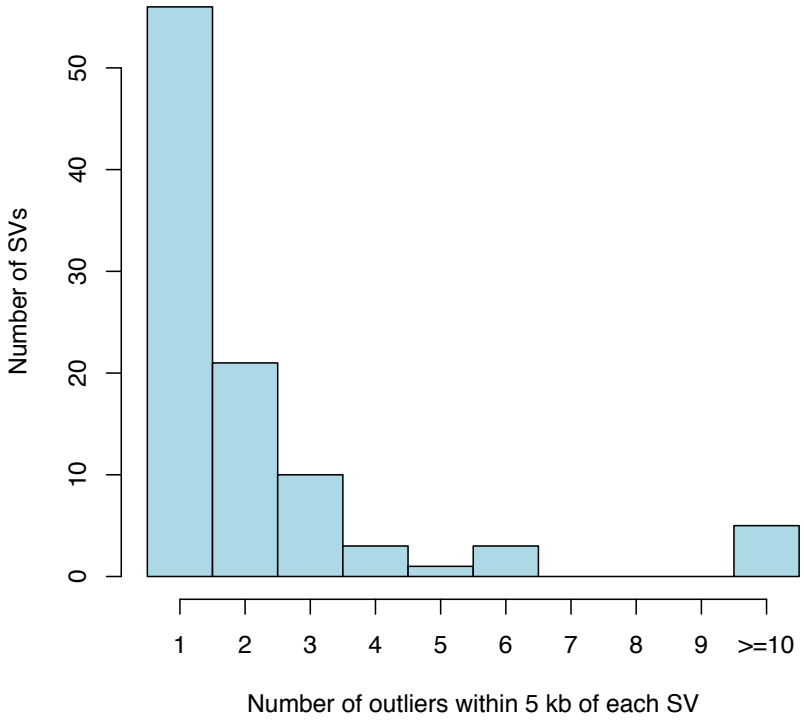
Supplementary Figure 4. Comparison between CAVIAR causal probabilities and the SV heritability fraction (h^2_{SV}/h^2_{cis}) from the GCTA linear mixed model analysis.



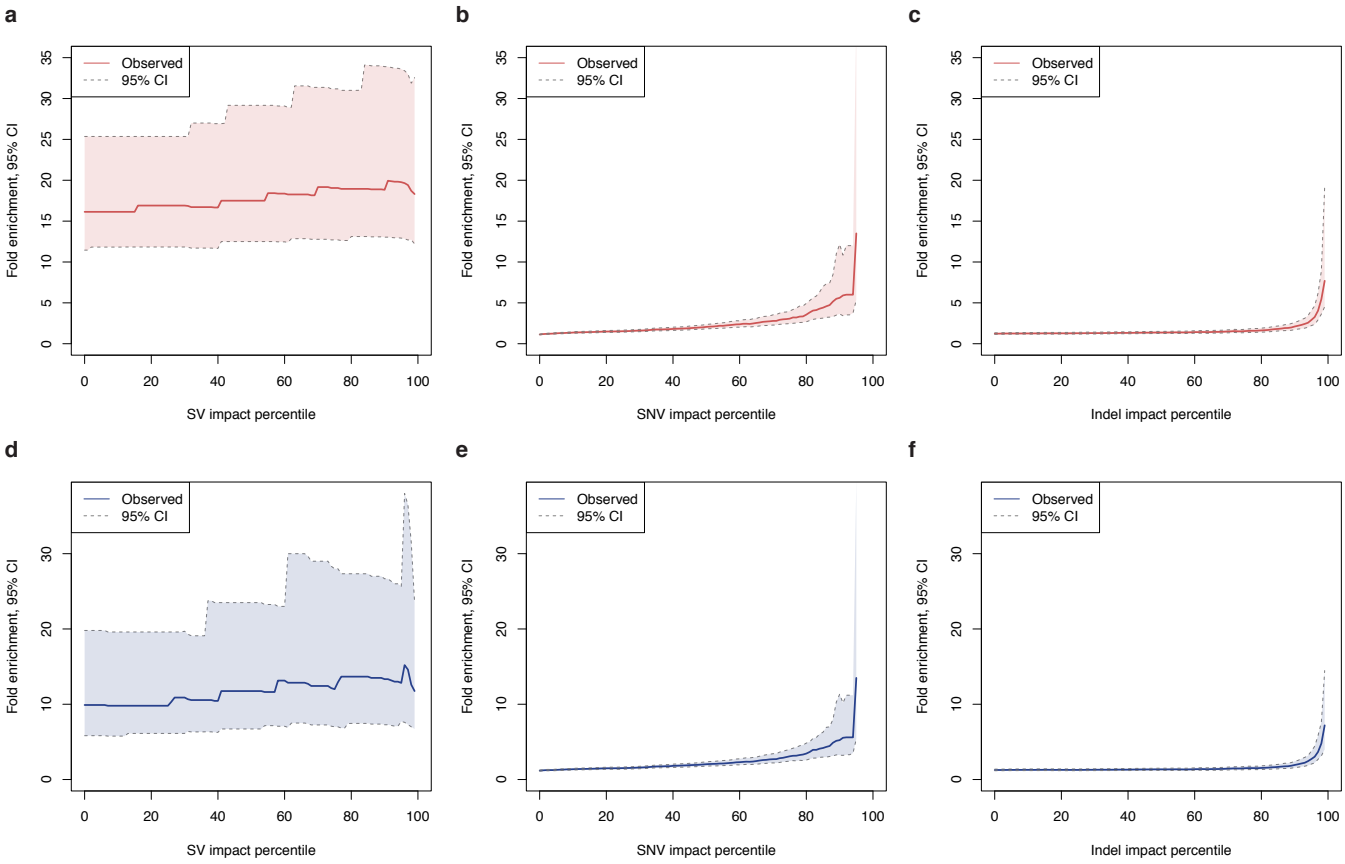
Supplementary Figure 5. Additional genomic features showing fold enrichment for SVs in each composite causality quantile bin compared to the median of 100 permutations with randomly shuffled genomic positions. SVs that overlap with exons of the eGene were excluded. Each annotated feature was allowed 1 kb of flanking sequence on either side for intersection, except GENCODE genes and GENCODE exons (no flanking sequence) and topologically associated domain boundaries (5 kb flanking sequence).



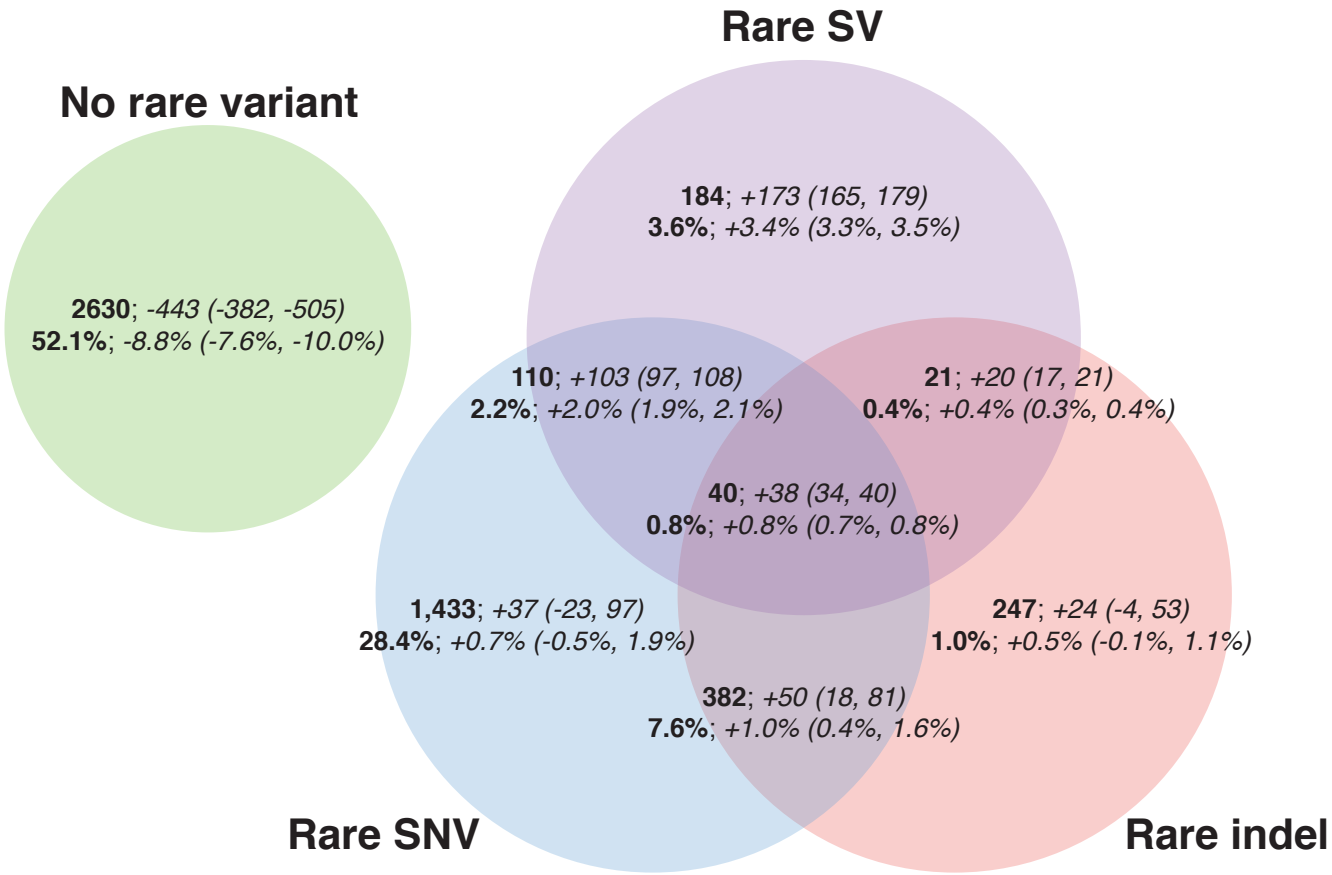
Supplementary Figure 6. A ~37 kb deletion of the GSTT2 (glutathione S-transferase theta-2) linked to a GWAS marker of circulating gamma-glutamyl transferase levels (rs2739440).



Supplementary Figure 7. Histogram showing the number of outlier genes per SV (among the SVs within 5 kb of an outlier gene in the same individual).



Supplementary Figure 8. Fold enrichment of rare variants within 5 kb of expression outliers for (**a**) SVs, (**b**) SNVs, and (**c**) indels gated on impact score percentile. Panels (**d-f**) show the fold enrichment of expression outliers within 5 kb of rare variants for (**d**) SVs, (**e**) SNVs, and (**f**) indels. For SVs, impact score percentile was based on the highest CADD scoring base in the affected interval and the confidence intervals around the SV breakpoints. For SNVs and indels the impact score percentile was derived from the CADD score of the variant.



Supplementary Figure 9. Number and percent of gene expression outliers that have a rare variant of each type within 5 kb of the gene. For each area of the Venn diagram, bold text shows the number (top) and percent (bottom) of the 5,047 expression outliers observed to be within 5 kb of a rare variant in the same individual. Italic text shows the number and percentage of outliers in excess of the median from 1,000 random permutations of the outlier dataset, with the 95% confidence intervals in parentheses.

	Rare variant type	Num. outliers with rare variant within 5 kb	Num. outliers	Shuffle median	Shuffle 2.5-%tile	Shuffle 97.5-%tile	Fold enrichment of outliers	Fold enrichment (95% CI)
Per outlier	SV	355	5,047	22	14	31	16.1	(11.5, 25.4)
	SNV	1,965	5,047	1,738	1,679	1,797	1.1	(1.1, 1.2)
	Indel	690	5,047	561	519	600	1.2	(1.2, 1.3)
	Any	2,417	5,047	1,974	1,912	2,035	1.2	(1.2, 1.3)
	Rare variant type	Num. rare variants with outlier within 5 kb	Num. rare variants	Shuffle median	Shuffle 2.5-%tile	Shuffle 97.5-%tile	Fold enrichment of rare variants	Fold enrichment (95% CI)
Per variant	SV	99	4,691	10	5	17	9.9	(5.8, 19.8)
	SNV	4,188	4,830,727	3,536	3,349	3,762	1.2	(1.1, 1.3)
	Indel	917	824,836	727	664	786	1.3	(1.2, 1.4)
	Any	5,204	5,660,254	4,275	4,071	4,528	1.2	(1.1, 1.3)

Supplementary Table 3. Fold enrichment of the co-occurrence of gene expression outliers and rare variants in same sample on a per-outlier (top) and per-variant (bottom) basis. Shuffled medians and percentiles represent the number of co-occurrences expected by chance based on 1,000 random permutations of the outlier sample names.

	Type	Variants	Outliers
Deletions	Simple	47	70
	Complex	3	4
Duplications	Simple	32	263
	Complex	6	13
Balanced	Inversions	2	4
	Complex	1	1

Supplementary Table 4. Distribution of simple and complex rearrangements associated with gene expression outliers. After clustering SVs into complex variants present in the same individual(s) and located no more than 100 kb away from each other, a total of 99 SVs associated with expression outliers were collapsed into 91 events.

Cluster ID	Locus	SV IDs	Sample	Class	Coding Region	Outlier Genes
1565	1:25551621-25761207	LUMPY_BND_184573, LUMPY_DUP_176134	GTEX-NPJ7	Complex dup	Yes	ENSG00000117614.5, ENSG00000117616.13, ENSG00000183726.6
1868	1:1388772-1429798	LUMPY_BND_93489, LUMPY_DUP_175996	GTEX-XGQ4	Complex dup	Yes	ENSG00000215915.5
1902	20:32168930-55372800	LUMPY_DEL_135568, LUMPY_DEL_136038	GTEX-P4QR	Complex del	Yes	ENSG00000124126.9
258	11:47153961-47186142	LUMPY_BND_186174, LUMPY_BND_186175, GS_DEL_CNV_11_47153934_47166318, GS_DEL_CNV_11_47173052_47186140	GTEX-Q2AG	Complex del	Yes	ENSG00000149179.9, ENSG00000149182.10
3276	6:127656006-127656010	LUMPY_BND_182569, LUMPY_BND_193281	GTEX-OXRL	Balanced	Yes	ENSG00000093144.14
339	11:77413211-77786061	LUMPY_DUP_177173, LUMPY_DUP_177174	GTEX-UPIC	Complex dup	Yes	ENSG00000087884.10, ENSG00000149262.12
4274	X:78417460-78425402	LUMPY_DEL_174258, LUMPY_DEL_174259	GTEX-X8HC	Complex del	No	ENSG00000147138.1
1126	16:26052128-26052227, 16:26457178-26551538, 16:26910809-27287111	LUMPY_BND_119970, LUMPY_BND_178606, LUMPY_BND_188219, LUMPY_BND_188221, LUMPY_BND_188222, LUMPY_DUP_178610	GTEX-QV31	Complex dup	Yes	ENSG00000155666.7, ENSG00000169189.12
1629	19:50401535-50401536, 19:52871602-52970915	LUMPY_BND_179537, LUMPY_DUP_179549	GTEX-X261	Complex dup	Yes	ENSG00000269834.1, ENSG00000221923.4, ENSG00000167555.9
4136	X:100747271-100747272	LUMPY_BND_195398	GTEX-OXRN	Complex dup	Yes	ENSG00000196440.7, ENSG00000198960.6

Supplementary Table 5. Complex SVs associated with expression outliers. Complex SVs were identified by clustering rare SVs located no more than 100 kb away from each other and present in the same individual(s).