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Supplemental information

Adaptive eQTLs reveal the evolutionary impacts of pleiotropy and tissue-specificity while contributing to health and disease

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Supplementary Information

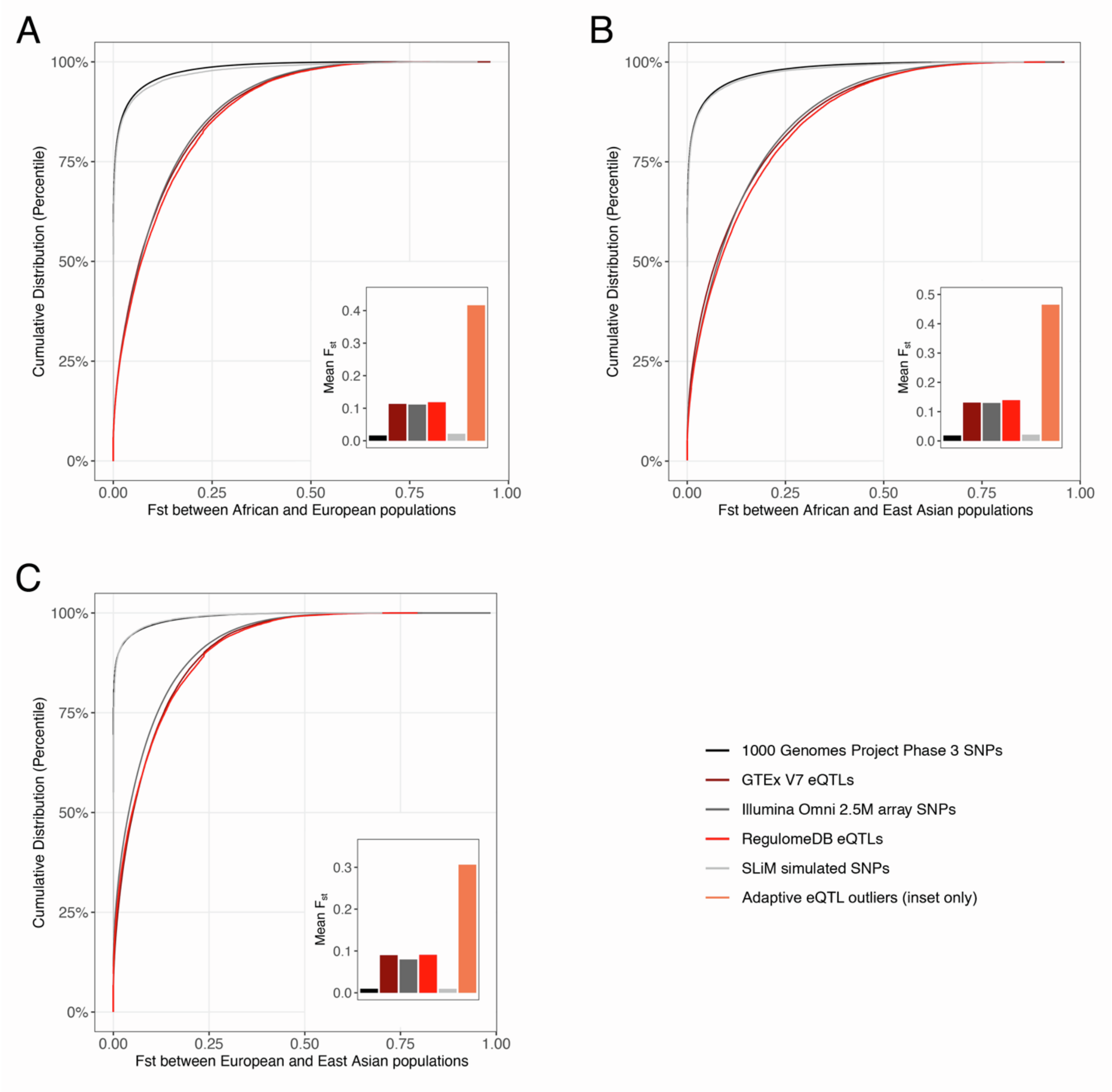

Figure S1. GTEx and RegulomeDB eQTLs tend to have higher values of F_{ST} statistics than random SNPs from the 1KGP. Genetic distances between different pairs of populations were calculated using Weir and Cockerham's F_{ST}: (A) African and European populations, (B) African and East Asian populations, and (C) European and East Asian populations. For each pair of populations, F_{ST} distributions are similar for 1000 Genomes Project and simulated SNPs (i.e., there is overlap between the black and light gray curves). Similarly, F_{ST} distributions are similar for non-adaptive GTEx V7 eQTLs, SNPs on the Illumina Omni 2.5M array, and RegulomeDB eQTLs (i.e., there is overlap between the maroon, medium gray, and red curves).

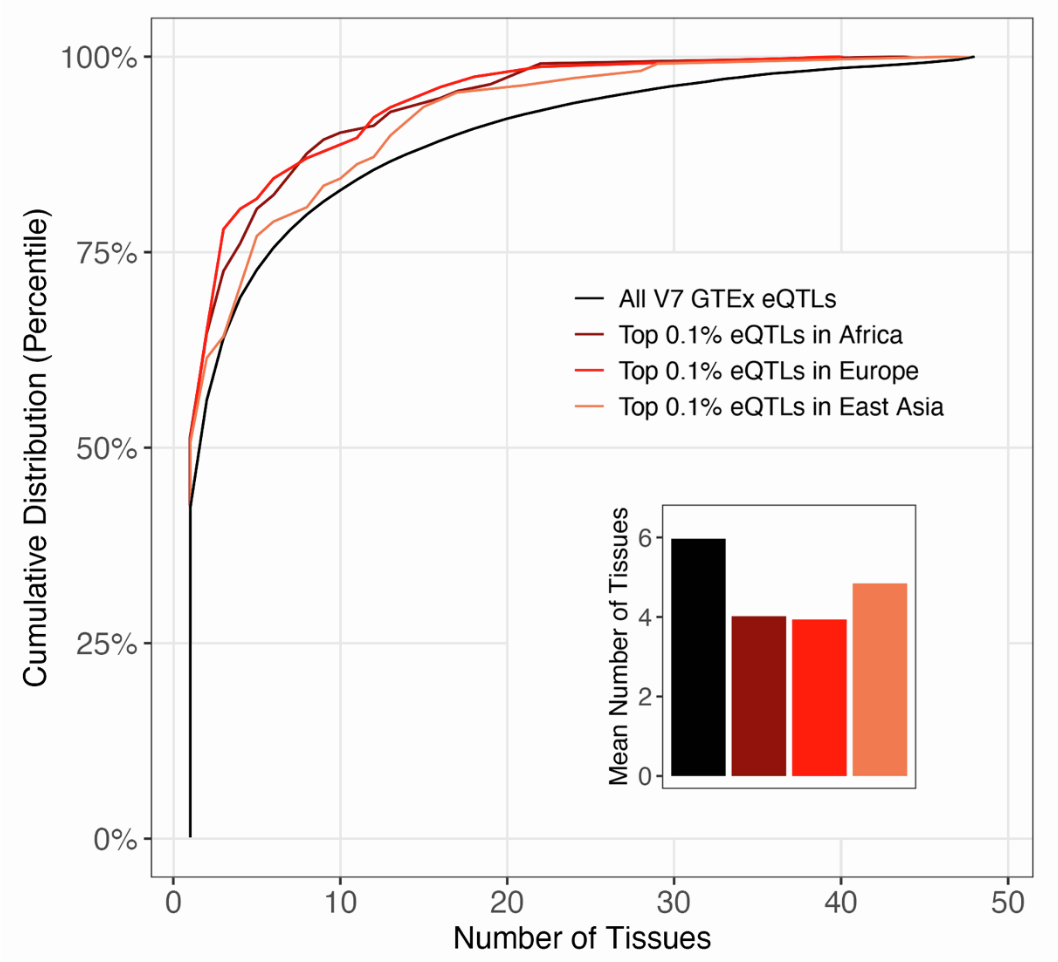

Figure S2. Pleiotropy results are robust to the use of a more stringent adaptive outlier threshold. Here, adaptive outliers are LD-pruned eQTLs that have PBS scores in the top 0.1% of all GTEx eQTLs. Cumulative distributions and mean number of tissues are shown for adaptive and non-adaptive eQTLs. In general, adaptive eQTLs modify gene expression in fewer tissues than non-adaptive eQTLs. For each population, differences in the number of tissues affected by adaptive outliers and the overall set of GTEx eQTLs are statistically significant (p-value < $2.2\ 10^{-16}$ for all comparisons, Wilcoxon rank sum tests).

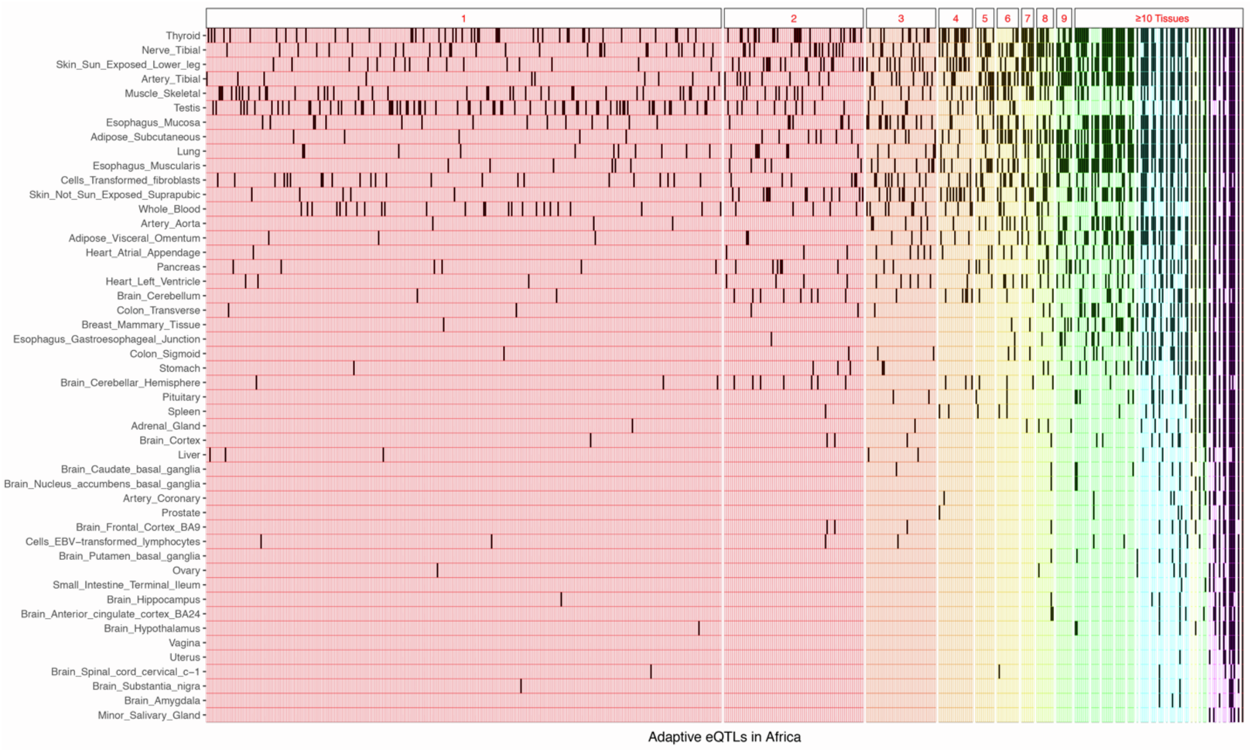

Figure S3. Tissue-specificity of African PBS outliers. A grid of 48 rows and 614 columns is shown, where each row corresponds to a different tissue and each column corresponds to a different adaptive eQTL for the African branch. Filled cells reveal which tissues are affected by each adaptive eQTL. Background colors indicate the number of tissues affected by each adaptive eQTL (e.g., red indicates eQTLs that modify expression in a single tissue). Tissues are rank-ordered by total number of adaptive eQTLs.

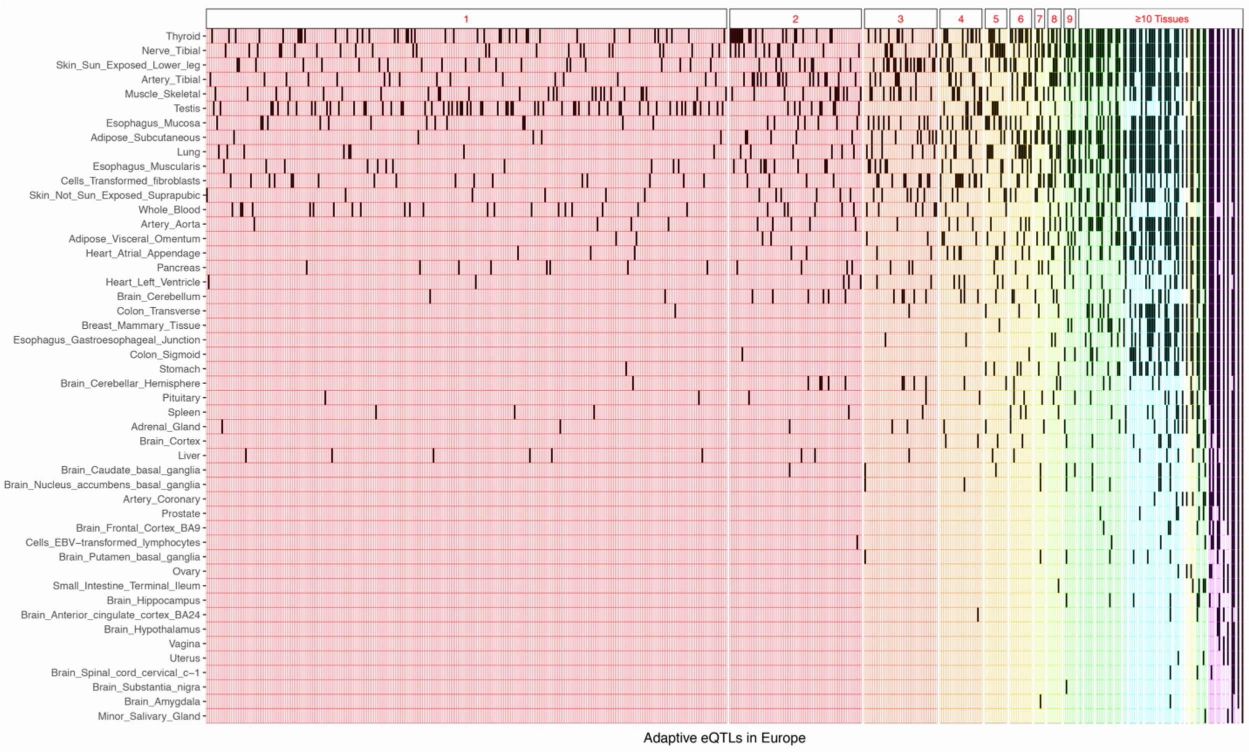

Figure S4. Tissue-specificity of European PBS outliers. A grid of 48 rows and 561 columns is shown, where each row corresponds to a different tissue and each column corresponds to a different adaptive eQTL for the European branch. Filled cells reveal which tissues are affected by each adaptive eQTL. Background colors indicate the number of tissues affected by each adaptive eQTL (e.g., red indicates eQTLs that modify expression in a single tissue). Tissues are rank-ordered by total number of adaptive eQTLs.

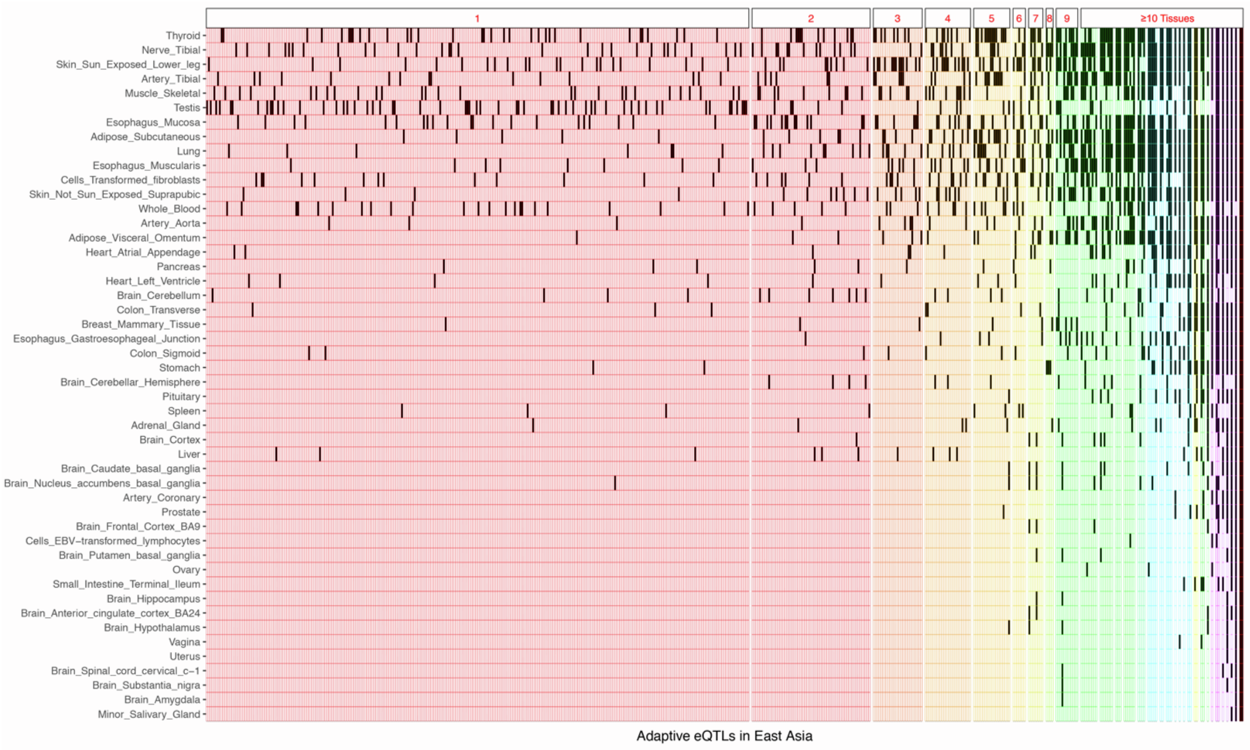

Figure S5. Tissue-specificity of East Asian PBS outliers. A grid of 48 rows and 524 columns is shown, where each row corresponds to a different tissue and each column corresponds to a different adaptive eQTL for the East Asian branch. Filled cells reveal which tissues are affected by each adaptive eQTL. Background colors indicate the number of tissues affected by each adaptive eQTL (e.g., red indicates eQTLs that modify expression in a single tissue). Tissues are rank-ordered by total number of adaptive eQTLs.

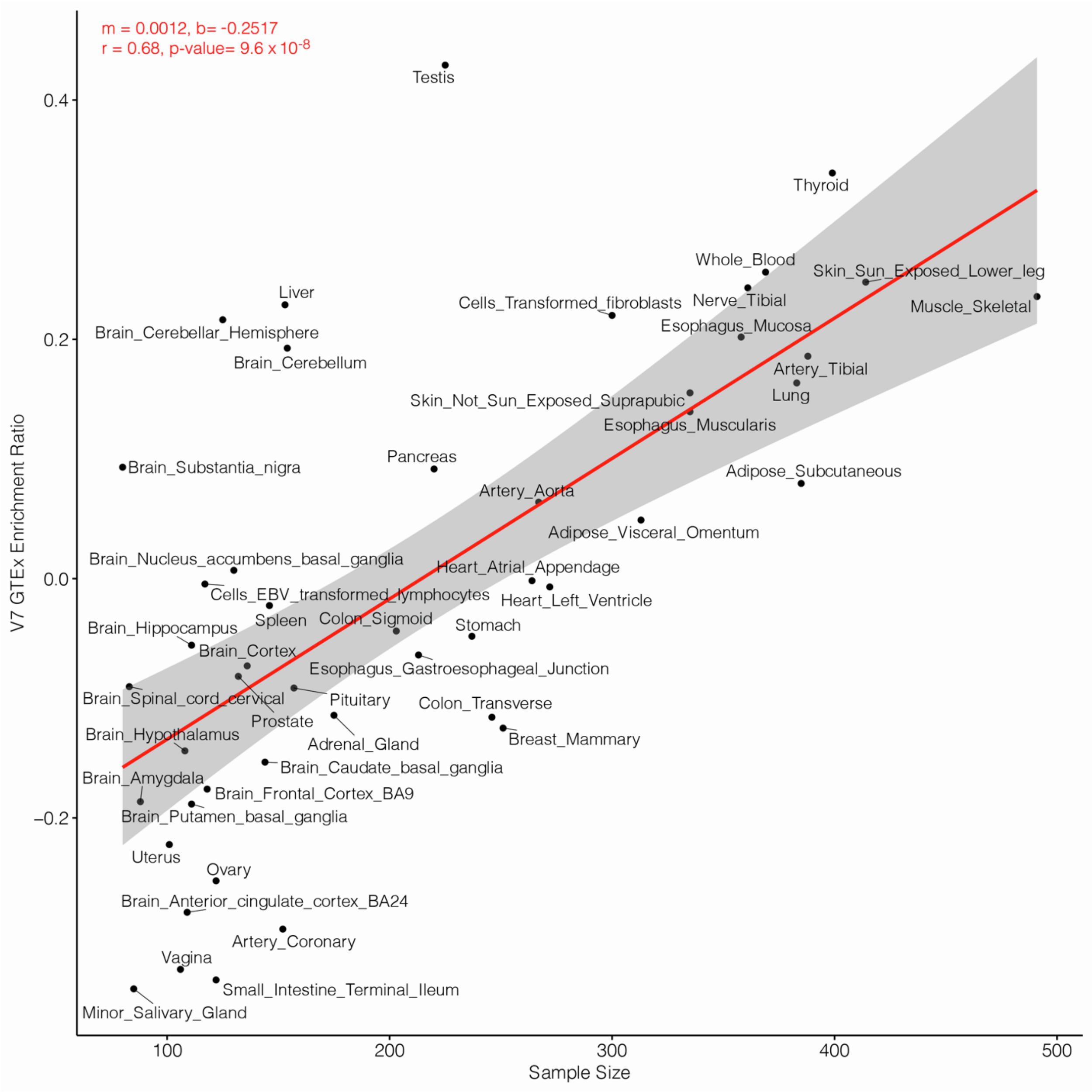

Figure S6. Enrichment ratios are not independent of sample size per tissue. Equation for the regression line: Enrichment Ratio = 0.0012 x (Sample Size) – 0.2517. Tissues with positive adjusted enrichment ratios are above the red line, and tissues with negative adjusted enrichment ratios are below the red line.

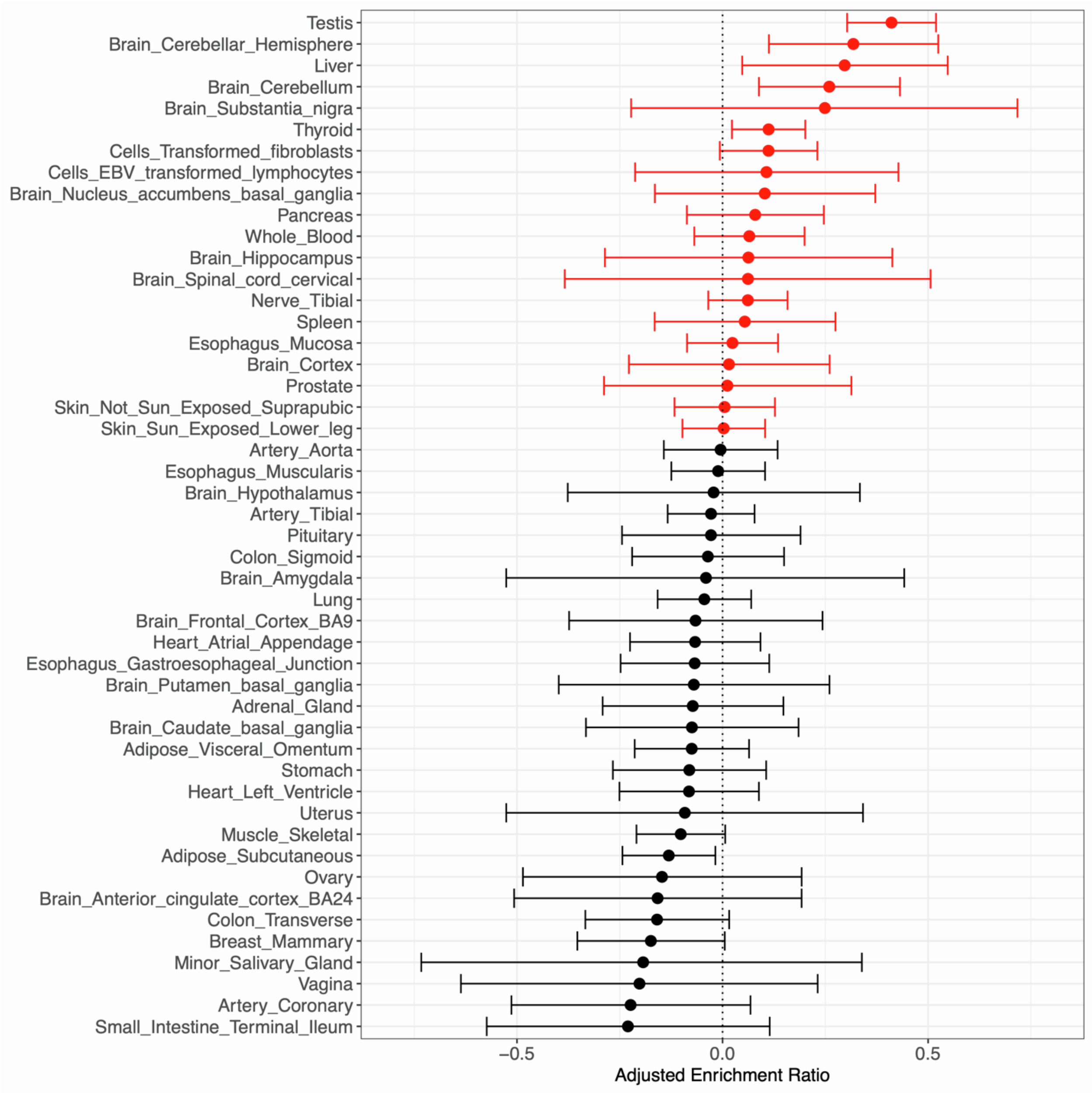

Figure S7. Tissue enrichment results after correcting for the sample size differences using a linear model. Here, adaptive outliers are LD-pruned eQTLs that have PBS scores in the top 1% of all GTEx eQTLs. 95% confidence intervals for each adjusted enrichment ratio are shown. Adjusted enrichment ratios are the residuals from Figure S7. Note that there is no single optimal way to correct for sample sizes (nonlinear regression would give different adjusted enrichment ratios).

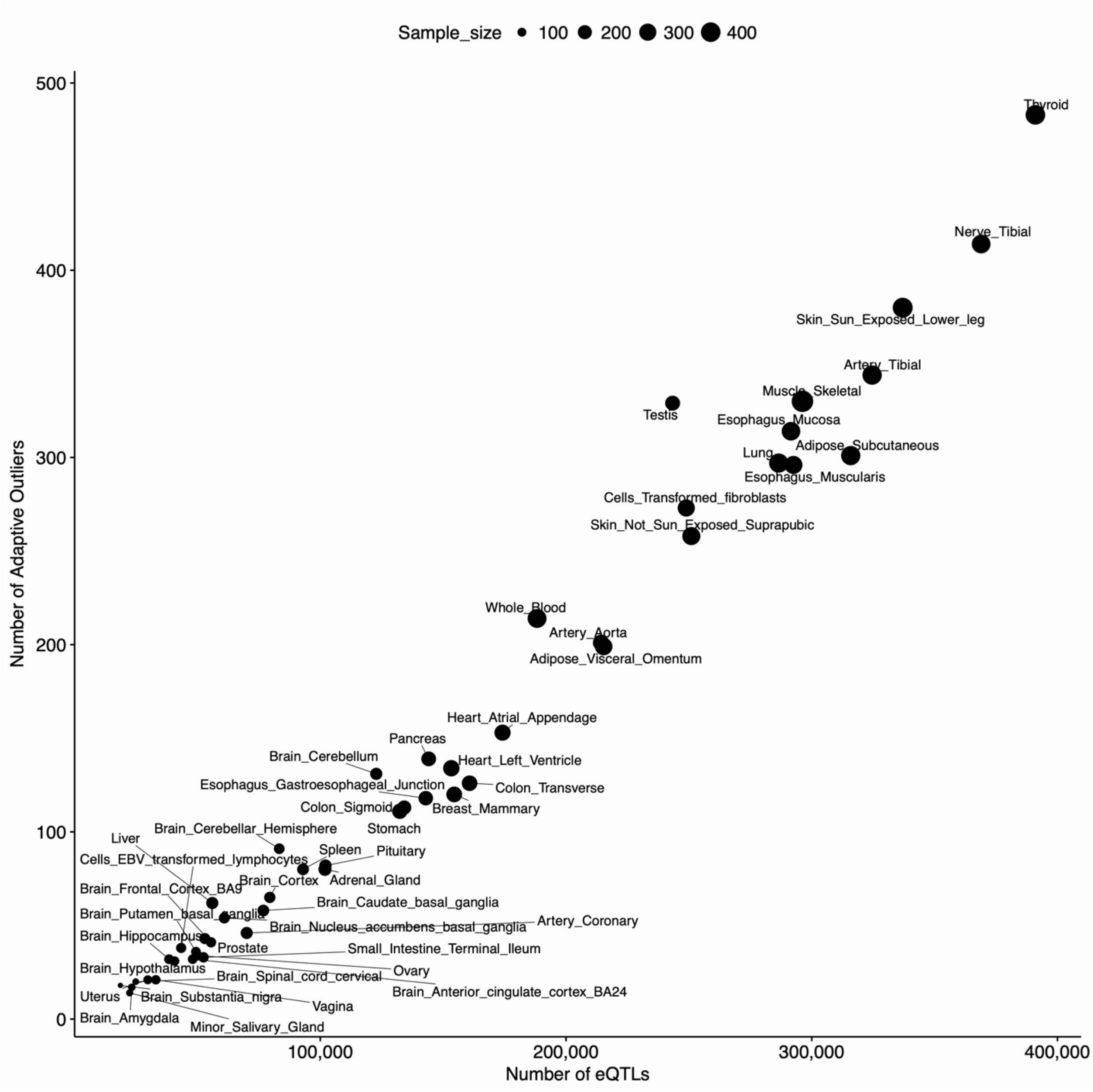

Figure S8. Numbers of adaptive outliers and eQTLs for each tissue. Each point represented a different tissue, with the size of each point indicating sample size (numbers of individuals). Here, adaptive outliers are LD-pruned eQTLs that have PBS scores in the top 1% of all V7 GTEx eQTLs.