TABLES

Tag SNP	$\hat{\beta}_0$	ASE *P*	Gene Symbol	GWAS *P*	Phenotype
rs950169	-0.413	$< 1 \times 10^{-10}$	*ADAMTSL3*	6×10^{-23} 2×10^{-11}	height schizophrenia
rs72705102	-0.813	$< 1 \times 10^{-10}$	*CEP72*	4×10^{-11}	cystic fibrosis lung function
rs3765107	-0.428	$< 1 \times 10^{-10}$	*SLC15A4*	2×10^{-11}	systemic lupus erythematosus
rs5744258	0.474	1.89×10^{-9}	*IL18*	1×10^{-8}	IL18 levels
rs61854810	-1.504	0.00264		2×10^{-10}	optic disc size
rs2235371	-0.146	0.0127	*IRF6*	1×10^{-14}	cleft lip
rs10418340	-0.103	0.0212	*CEP89*	5×10^{-11}	serum creatinine levels
rs35370743	-0.120	7.17×10^{-6}	*INTS12*	1×10^{-16}	pulmonary function (interaction with smoking)

Table 1. Neanderthal-introgressed haplotypes are associated with modern human phenotypes. Negative values of $\hat{\beta}_0$ indicate downregulation of Neanderthal alleles, while positive values indicate upregulation.

SUPPLEMENTAL FIGURE LEGENDS

Figure S1. Minor allele frequencies of expressed Neanderthal-introgressed haplotype-tagging SNPs on and off of called introgressed haplotypes. Related to STAR Methods. SNPs defining significant *S** Neanderthal haplotypes and matching the Altai Neanderthal allele were further filtered based on the criteria that the Neanderthal allele be observed at >90% frequency on Neanderthal haplotypes and <10% frequency off of these haplotypes or vice versa (European samples in the 1000 Genomes Project Phase 3 dataset).

Figure S2. Proportion of Neanderthal SNPs with significant ASE as a function of FDR threshold. Related to Figure 2. The gray dashed line indicates the FDR ≤ 10% threshold.

Figure S3. Enrichment of SNPs showing significant ASE for directionally-concordant single-tissue eQTL. Related to STAR Methods. Error bars indicate 95% confidence intervals. Blue points indicate introgressed SNPs, while green points indicate non-introgressed SNPs. Enrichment was evaluated within 5% European minor allele frequency bins using a 2 x 2 Fisher's Exact Test, comparing tested SNPs with significant ASE to tested SNPs without significant ASE.

Figure S4. Model estimates of the proportion of reads supporting the Neanderthal allele per tissue, subsetting data into relevant groups. Related to Figure 5. Error bars indicate 95% confidence intervals. **(a**) The full dataset of introgressed SNPs, equivalent to figure 5a. This panel sets the order for the remaining panels. (**b**) Rare

introgressed variants with European derived allele frequency less than or equal to 5%. (**c**) Common introgressed variants with European derived allele frequency greater than 5%. (**d**) The subset of introgressed SNPs that show significant single-tissue eQTL effects for the same gene based on published GTEx data.

Figure S5. Model estimates of the proportion of reads supporting the Neanderthal allele per tissue. Related to Figure 5. Analogous to Fig. 5a, but including Neanderthal-modern human sequence divergence per gene as a covariate in the GLMM.

Figure S6. Per-tissue rate of modern human-Neanderthal sequence divergence. Related to Figure 5. Error bars indicate 2.5% and 97.5% empirical quantiles of bootstrap distributions.

Figure S7. Proportions of significantly up- and downregulated SNPs per tissue. Related to Figure 5. One SNP is sampled per gene to account for correlation among linked SNPs. Brain and testis tissues are enriched for downregulated compared to upregulated SNPs.

STAR METHODS

Contact for Reagent and Resource Sharing

Further information and requests for resources should be directed to and will be fulfilled by the Lead Contact, Joshua Akey (akeyj@uw.edu).

Experimental Model and Subject Details

All analyses were performed using published RNA-seq data obtained from GTEx Consortium (v6; phs000424.v6.p1), which derive from 53 tissues from 544 deceased individuals, 449 of whom were also genotyped to facilitate eQTL analysis. Information about the donors (gender, ethnicity, age, cause of death) can be found at http://www.gtexportal.org/home/tissueSummaryPage#donorInfo. The donor enrollment,