

**S1 Table. Estimates of cross-tissue and tissue-specific local  $h^2$ .** Expression levels derived by Orthogonal Tissue Decomposition and  $h^2$  estimated using the `--reml-no-constrain` method.

tissue	n	mean $h^2$ (SE)	% $P < 0.05$	num $P < 0.05$	num expressed
Cross-tissue	450	0.062 (0.0008)	35.4	6003	16951
Adipose - Subcutaneous	298	0.017 (0.0004)	10.3	1747	16951
Adrenal Gland	126	0.037 (0.0007)	10.2	1731	16951
Artery - Aorta	198	0.022 (0.0005)	10.2	1733	16951
Artery - Coronary	119	0.048 (0.0008)	12.2	2066	16951
Artery - Tibial	285	0.022 (0.0004)	13.3	2262	16951
Brain - Anterior cingulate cortex (BA24)	72	0.037 (0.0012)	8.6	1451	16951
Brain - Caudate (basal ganglia)	100	0.042 (0.0009)	9.8	1659	16951
Brain - Cerebellar Hemisphere	89	0.046 (0.0011)	10.2	1730	16951
Brain - Cerebellum	103	0.041 (0.0009)	10.8	1825	16951
Brain - Cortex	96	0.053 (0.0010)	10.6	1803	16951
Brain - Frontal Cortex (BA9)	92	0.037 (0.0009)	8.4	1418	16951
Brain - Hippocampus	81	0.033 (0.0010)	7.6	1292	16951
Brain - Hypothalamus	81	0.020 (0.0011)	7.8	1321	16951
Brain - Nucleus accumbens (basal ganglia)	93	0.040 (0.0010)	8.9	1511	16951
Brain - Putamen (basal ganglia)	82	0.033 (0.0010)	7.8	1323	16951
Breast - Mammary Tissue	183	0.020 (0.0005)	7.7	1307	16951
Cells - EBV-transformed lymphocytes	115	0.045 (0.0008)	10.8	1833	16951
Cells - Transformed fibroblasts	272	0.019 (0.0004)	10.6	1805	16951
Colon - Sigmoid	124	0.024 (0.0007)	9.0	1530	16951
Colon - Transverse	170	0.022 (0.0005)	8.6	1462	16951
Esophagus - Gastroesophageal Junction	127	0.029 (0.0007)	8.9	1512	16951
Esophagus - Mucosa	242	0.026 (0.0005)	13.7	2319	16951
Esophagus - Muscularis	219	0.024 (0.0005)	11.0	1871	16951
Heart - Atrial Appendage	159	0.031 (0.0006)	9.4	1601	16951
Heart - Left Ventricle	190	0.025 (0.0005)	11.2	1894	16951
Liver	98	0.036 (0.0009)	8.9	1506	16951
Lung	279	0.018 (0.0004)	10.7	1819	16951
Muscle - Skeletal	361	0.020 (0.0003)	13.1	2223	16951
Nerve - Tibial	256	0.026 (0.0004)	13.3	2250	16951
Ovary	85	0.043 (0.0009)	7.8	1323	16951
Pancreas	150	0.036 (0.0007)	11.6	1969	16951
Pituitary	87	0.044 (0.0010)	9.4	1590	16951
Skin - Not Sun Exposed (Suprapubic)	196	0.041 (0.0005)	19.2	3249	16951
Skin - Sun Exposed (Lower leg)	303	0.027 (0.0004)	17.3	2939	16951
Small Intestine - Terminal Ileum	77	0.046 (0.0011)	7.9	1340	16951
Spleen	89	0.062 (0.0010)	10.7	1820	16951
Stomach	171	0.020 (0.0005)	8.3	1406	16951
Testis	157	0.042 (0.0007)	14.0	2378	16951
Thyroid	279	0.024 (0.0004)	13.3	2250	16951
Whole Blood	339	0.025 (0.0004)	17.7	3004	16951

All tissues are from the GTEx Project. Mean heritability ( $h^2$ ) and the standard error of the mean (SE) are calculated across genes for each tissue. The percentage (%) and number (num) of genes with significant  $h^2$  estimates ( $P < 0.05$ ) and the number of genes expressed in each tissue are also reported.