Supplementary Material

Genetic control of gene expression in whole blood and lymphoblastoid cell lines is largely independent

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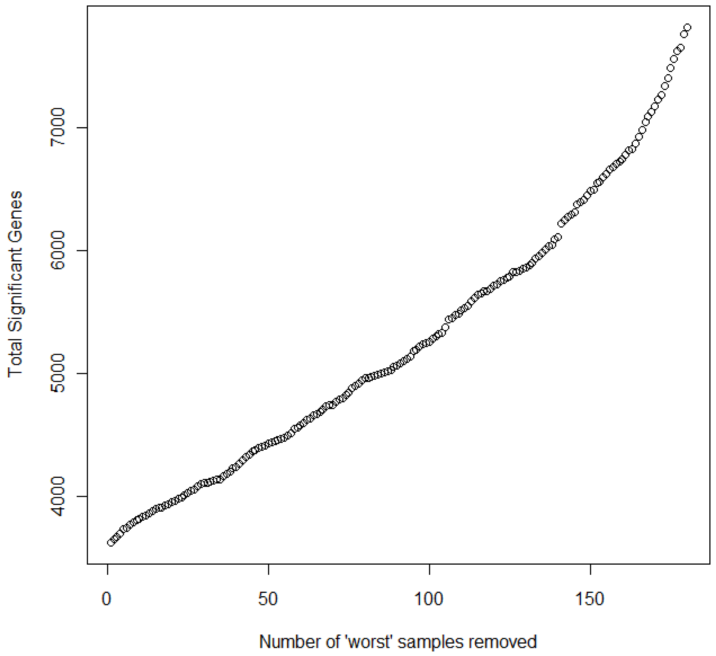
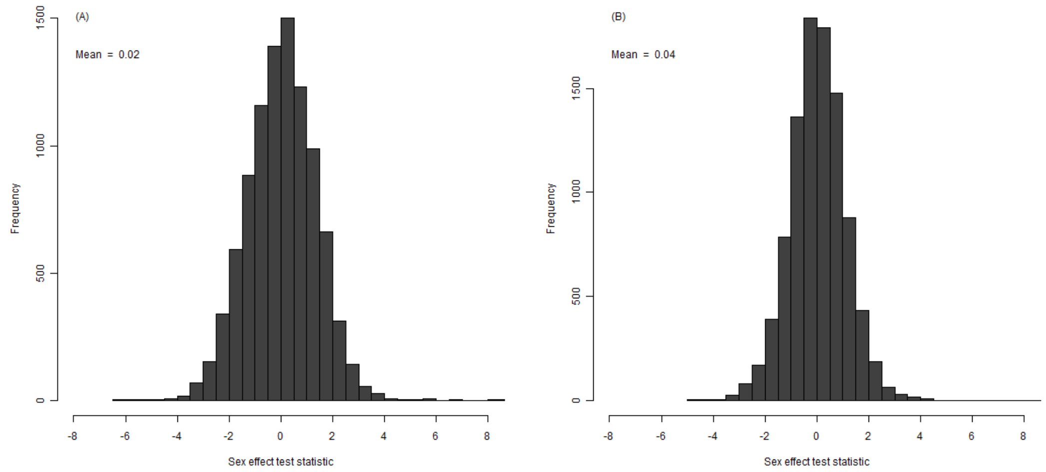
Supplementary Figure 1



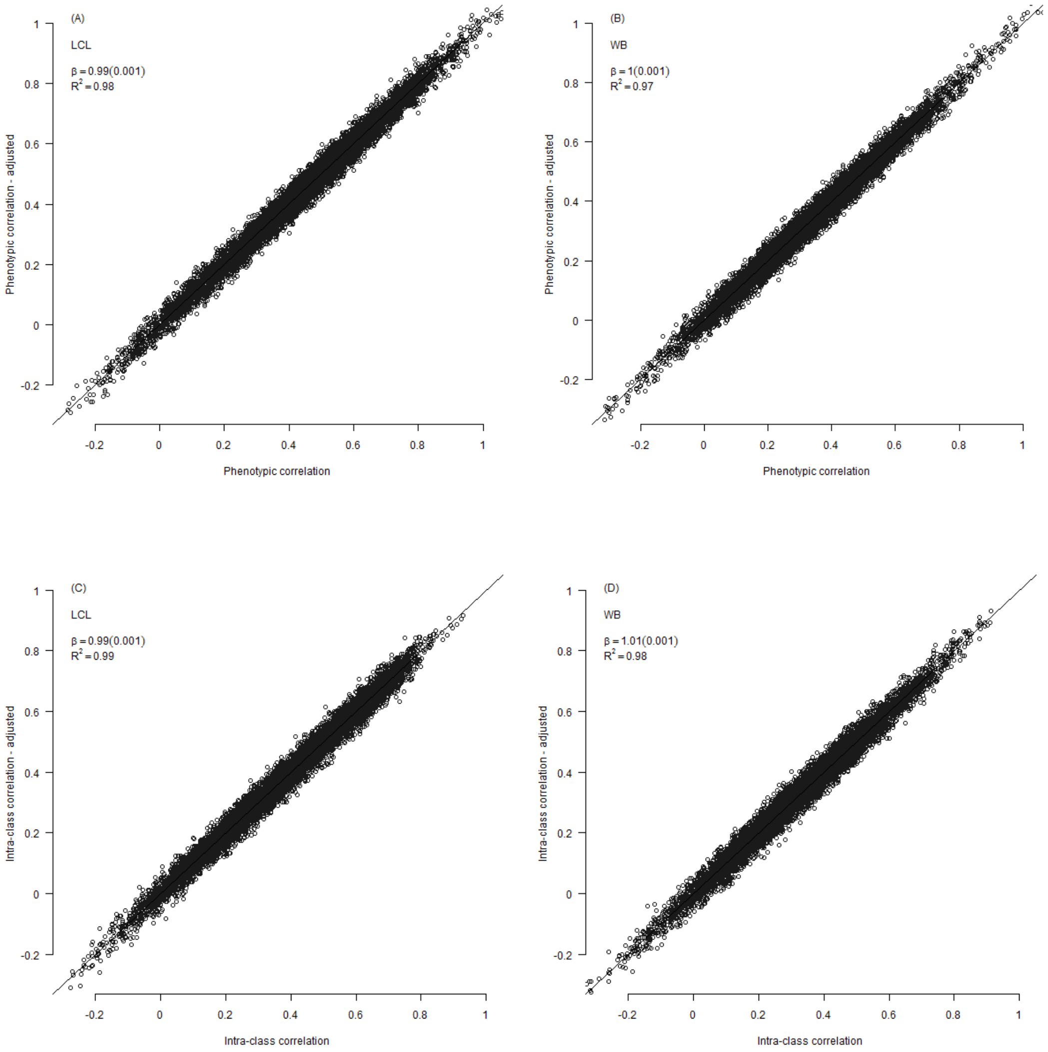
Number of genes expressed in samples. Total number of significant genes in the whole dataset when the samples with the lowest number of genes significantly expressed are removed. As the number of genes expressed in all samples is a function of the total sample size, larger sample sizes would be expected to result in fewer genes passing this quality control threshold. To determine whether a particular sample, or group of samples, caused a large drop in the number of genes expressed in all samples, each sample was ranked on the number of genes significantly expressed within that sample. The sample with the lowest number of significant genes was removed and the total number of genes significantly expressed in all the remaining samples was calculated. This process was repeated by successively removing samples with the lowest number of genes significantly expressed and recalculating the number of genes expressed in all the remaining samples. The lack of gaps in the number of genes significantly expressed as samples are removed implies no large influence of a single sample or chip on reducing the number of genes shown to be expressed in all samples.

Supplementary Figure 2



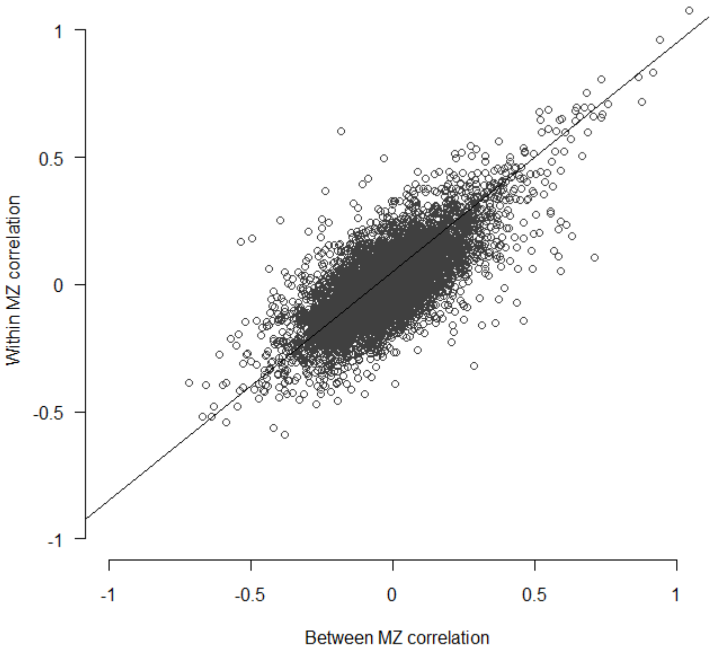
Effect of sex on gene expression. Distributions of test statistics for the effect of sex on expression levels for 9555 genes. Figures **a** and **b** show the distributions for LCL and WB samples respectively. As expected when performing a large number of tests on genes that will, in the majority of cases, not be differentially expressed between the sexes, the central portions of the distributions closely match the expected normal distribution.

Supplementary Figure 3



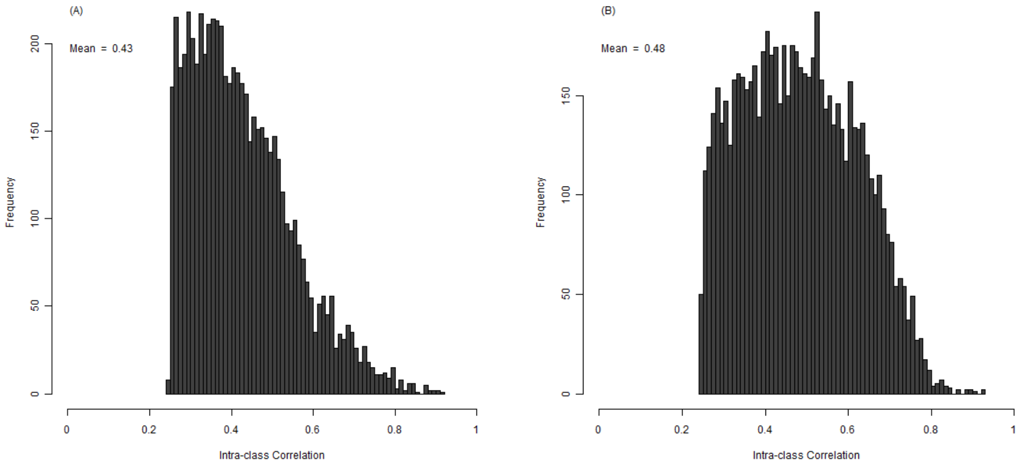
Effect of inclusion of blood components and cell type counts on the between MZ twin phenotypic correlations and $\widehat{H}^2$. The following blood components and cell type counts were included as covariates in eq. 1 to calculate the normalised transcript values for each individual; Haemoglobin levels, red blood cell, platelet, white blood cell, lymphoblast, monocyte, eosinophil count, CD3, CD4, CD8, CD19, CD56 levels, Cd4/CD8 ratio and blood pressure. Figures **a** and **b** show the relationship of between MZ twin phenotypic correlations calculated using expression levels unadjusted (*x*-axis) and adjusted (*y*-axis) for blood and cell count covariates for LCL and WB samples respectively. Figures **c** and **d** show the corresponding $\widehat{H}^2$ estimates. High correlation coefficients (shown on figures) indicate little influence of the additional covariates on expression variability.

Supplementary Figure 4



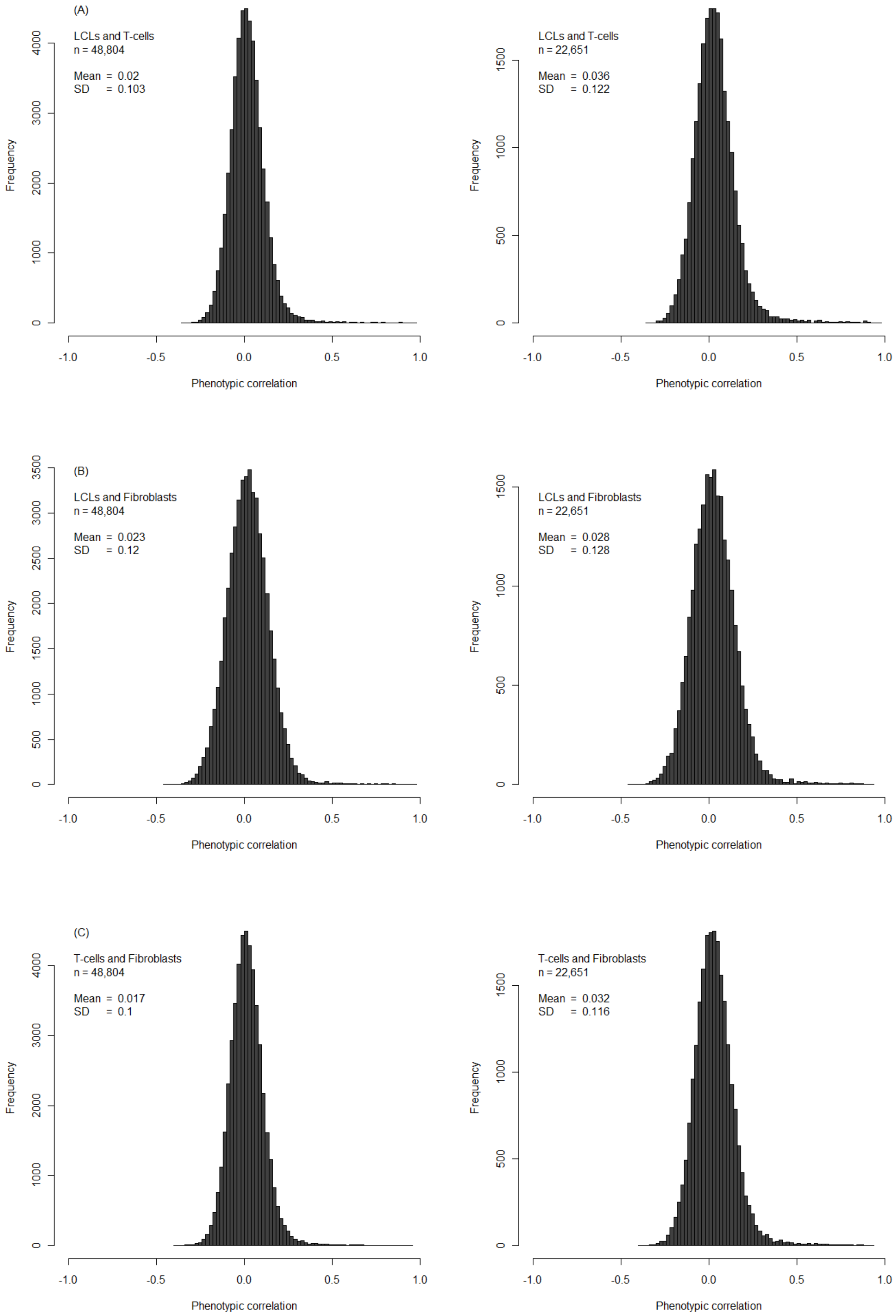
Mean within individual (r_{p_within}) and between ($r_{p\_between}$) MZ phenotypic correlations (see main text Figure 1 for details). Correlation of correlation coefficients calculated from the normalised expression values for the 9555 genes. Regression coefficient = 0.92 with SE=0.012 and correlation coefficient = 0.61.

Supplementary Figure 5



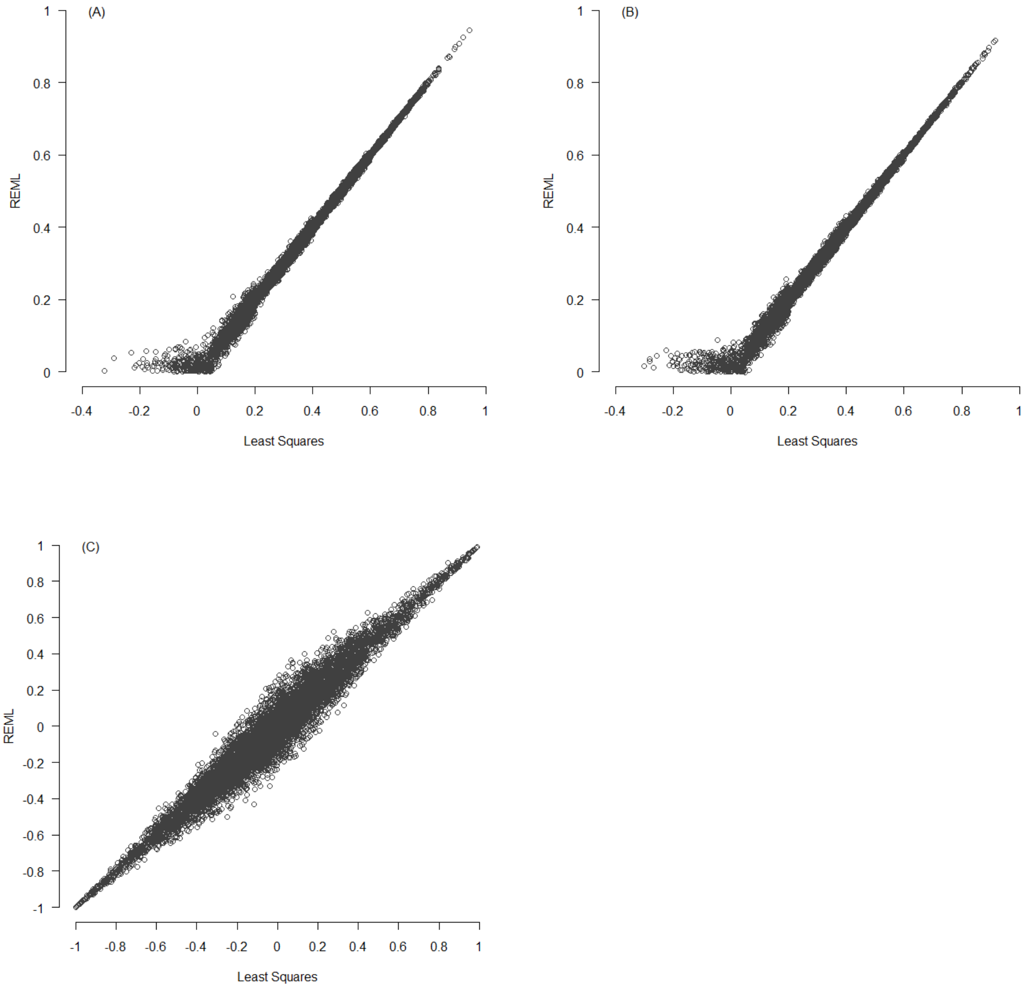
Distributions of significant Intra-class correlations ($\widehat{H}^2$) for **a)** WB and **b)** LCL samples. Using an FDR rate of 0.05. 6184 genes in WB and 7039 in LCL were determined significantly heritable. A total of 4721 genes were significantly heritable in both WB and LCL samples.

Supplementary Figure 6



Publically available gene expression levels measured in LCLs, T-cells and Fibroblasts were downloaded from NCBI's Gene Expression Omnibus (accession number GSE17080) (Dimas et al. 2009). Data was normalised following Dimas et al. (2009) and correlations calculated between a genes' expression in each of the three pairwise combinations of cell types. Distributions of these correlation coefficients are given for; **A**) LCLs and T-cells, **B**) LCLs and Fibroblasts and **C**) T-cells and Fibroblasts. Distributions are shown are given for all transcripts (*n*=48,804) and those transcripts passing quality control of Dimas et al. (2009) (*n*=22,651).

Supplementary Figure 7



Comparison of least squares and REML estimates of $\widehat{H}^2$ and $\hat{r}_G$, calculated using variance components (eq. 2 and 3) estimated using least squares and restricted maximum likelihood (REML) methods. Figures **a** and **b** give the $\widehat{H}^2$ for LCL and WB samples respectively whilst **c** shows the$\hat{r}_G$.

Supplementary Table 1

A list of genes with the highest ($+\hat{r}_G$) and lowest ($-\hat{r}_G$) two percent $\hat{r}_G$, corresponding to genes with $\hat{r}_G > 0.62$ and < -0.56, respectively. *p*-values for $\widehat{H}^2$ estimates are also provided along with r_p_within and r_p_between denoting the mean within MZ and between MZ (see Figure 1) correlations. We also provide phenotypic correlations between the three pair-wise combinations of tissues for genes also present in the Dimas et al (2009) dataset and heritability estimates reported by Dixon et al (2007) in LCLs.

To determine *p* values for $\hat{r}_G$, a series of permutation analyses was performed. For each gene, we permuted the expression levels in one tissue of a twin pair relative to the expression levels in the other tissue. From these permuted data, a $\hat{r}_G$ was calculated using least squares under the null hypothesis of no phenotypic covariance between tissues. For each gene 10,000 permutation cycles were run, providing the empirical null distribution from which *p* values were determined for the observed $\hat{r}_G$ value.

Missing phenotypic correlations and heritability estimates are marked with '/'.

$+\hat{r}_G$ gene list													
		This study								Dimas *et al* 2009 - r_p			Dixon *et al* 2007
Gene	Chr	$\hat{r}_G$	$\hat{r}_G$ *p*-value	$\widehat{H}^2$ WB	$\widehat{H}^2$ WB *p*-value	$\widehat{H}^2$ LCL	$\widehat{H}^2$ LCL *p*-value	r_p_within	r_p_between	LCL & T-cells	LCL & Fibroblasts	T-cells & Fibroblasts	$\widehat{H}^2$
ACTA2	10	0.66	< 1e-04	0.42	0.002352	0.56	0.000461	0.21	0.23	-0.02	-0.1	0.01	0.04
AHI1	6	0.76	< 1e-04	0.3	4.66E-05	0.32	2.85E-07	0.14	0.18	0.04	-0.15	0.03	0.83
AMFR	16	0.73	< 1e-04	0.77	7.62E-05	0.7	6.62E-05	0.57	0.63	0.64	0.72	-0.6	0.75
ANKDD1A	15	0.89	< 1e-04	0.63	0.000282	0.89	9.49E-05	0.63	0.68	-0.03	-0.05	-0.16	/
ARHGEF5L	7	0.69	0.000452	0.67	0.000488	0.85	4.25E-05	0.54	0.59	/	/	/	/
ARL17P1	17	0.81	< 1e-04	0.65	5.58E-05	0.66	2.21E-05	0.37	0.34	-0.05	0.16	-0.02	/
BTN3A2	6	0.84	< 1e-04	0.91	0.000399	0.83	0.001972	0.82	0.87	0.02	-0.01	0.09	0.71
C13ORF18	13	0.77	< 1e-04	0.42	7.60E-05	0.26	0.000176	0.33	0.28	-0.3	-0.22	0.39	0.41
C17ORF97	17	0.93	< 1e-04	0.82	0.002666	0.67	0.000307	0.74	0.75	/	/	/	/
C1ORF115	1	0.96	< 1e-04	0.26	0.001136	0.54	0.000895	0.73	0.4	-0.16	0.03	-0.06	0.75
C3ORF14	3	0.81	< 1e-04	0.36	0.000398	0.31	0.000356	0.25	0.29	-0.73	-0.62	-0.77	0.46
CAMLG	5	0.65	0.000146	0.26	0.000155	0.47	0.00018	0.13	0.34	-0.5	-0.45	-0.4	0.15
CCL4L1	17	0.78	0.000478	0.78	7.62E-05	0.68	0.000773	0.56	0.62	-0.69	0.77	-0.67	0.57
CD151	11	0.72	0.000289	0.54	0.009055	0.53	0.000945	0.39	0.39	0.52	-0.54	-0.37	0.55
CDC34	19	0.75	< 1e-04	0.28	0.001337	0.52	3.51E-05	0.28	0.3	-0.13	-0.11	0.1	0.14
CHPT1	12	0.72	< 1e-04	0.44	0.000111	0.43	9.00E-06	0.31	0.36	-0.38	-0.52	-0.39	0.58
CHURC1	14	0.87	< 1e-04	0.65	0.000103	0.81	0.000448	0.77	0.7	0.01	0.03	-0.02	0.6

CNN3	1	0.84	< 1e-04	0.44	0.00025	0.5	0.004083	0.35	0.37	-0.07	-0.13	0.14	0.29
DENND1A	9	0.63	< 1e-04	0.27	0.00403	0.39	4.93E-05	0.19	0.29	0.36	0.55	0.43	0.11
DENND5B	12	0.68	< 1e-04	0.25	0.000275	0.5	0.000905	0.3	0.21	/	/	/	/
DGKQ	4	0.62	0.00139	0.72	0.000144	0.58	0.001497	0.36	0.36	-0.01	0.03	0	0.25
DHX32	10	0.97	< 1e-04	0.53	0.00011	0.4	0.000176	0.38	0.42	0.02	0.17	0.03	0.27
DNAJB12	10	0.7	< 1e-04	0.36	0.003903	0.6	0.001312	0.14	0.11	-0.15	-0.4	-0.18	0.28
DUSP18	22	0.72	< 1e-04	0.26	0.001051	0.27	0.012979	0.16	0.34	0	0.1	0	0.28
ELL3	15	0.68	< 1e-04	0.27	0.000119	0.25	8.99E-06	0.15	0.08	-0.04	0.03	-0.05	0.33
ERAP2	5	0.81	0.000107	0.82	3.69E-05	0.84	7.06E-06	0.6	0.6	/	/	/	/
FAM118A	22	0.93	< 1e-04	0.72	0.008379	0.83	6.22E-06	0.7	0.71	/	/	/	/
GK5	3	0.72	0.000616	0.43	0.000138	0.61	0.000792	0.43	0.37	/	/	/	/
GM2A	5	0.62	< 1e-04	0.57	2.64E-05	0.39	7.03E-07	0.19	0.22	0.07	-0.04	0.09	0.23
GSTM1	1	0.87	0.00012	0.67	3.30E-06	0.78	0.000336	0.69	0.66	0.87	0.79	0.66	0.83
GSTM2	1	0.83	0.000146	0.68	0.002358	0.7	3.50E-05	0.71	0.66	0.75	0.65	0.61	0.82
GSTM4	1	0.83	0.000123	0.27	4.54E-05	0.39	7.97E-06	0.2	0.13	-0.16	-0.31	-0.12	0.44
GSTT1	22	0.88	< 1e-04	0.88	0.004087	0.91	0.000551	0.58	0.31	-0.09	0.16	0	0.84
GUSBL1	6	0.67	0.000147	0.45	0.003272	0.33	0.000294	0.34	0.33	-0.1	-0.05	0.04	0.55
HBP1	7	0.65	0.000107	0.29	0.003935	0.33	4.44E-05	0.21	0.18	-0.38	-0.23	-0.31	0.06
HIST1H4K	6	0.63	0.001668	0.26	2.32E-06	0.47	3.03E-05	0.15	0.15	-0.02	-0.06	-0.09	/
HLA-A29.1	6	0.92	< 1e-04	0.9	1.09E-05	0.89	0.0001	0.68	0.67	/	/	/	0.58
HLA-C	6	0.84	< 1e-04	0.71	0.000135	0.63	1.35E-05	0.55	0.5	0.58	0.62	0.56	0.42
HLA-DPB1	6	0.94	< 1e-04	0.58	3.62E-05	0.67	5.41E-05	0.67	0.62	0.14	-0.04	-0.14	0.42
HLA-DQB1	6	0.91	< 1e-04	0.88	0.000189	0.93	9.59E-05	0.31	0.34	-0.04	0.08	0.07	0.89
HLA-DRB1	6	0.9	< 1e-04	0.79	7.54E-05	0.9	0.000323	0.67	0.69	-0.12	0.02	-0.04	0.63
HLA-DRB5	6	0.78	0.000117	0.66	0.000179	0.8	1.86E-06	0.65	0.6	-0.17	-0.01	0.08	0.35
HLA-DRB6	6	0.65	0.001031	0.81	4.35E-05	0.74	0.000174	0.49	0.56	0.58	0.51	0.67	0.33
HMBOX1	8	0.9	< 1e-04	0.58	0.000303	0.52	0.000201	0.31	0.26	-0.07	0.15	-0.07	/
HOXB2	17	0.73	< 1e-04	0.62	0.000395	0.35	2.28E-05	0.29	0.27	0.09	-0.11	-0.12	0.77
HS.145307	12	0.68	0.000133	0.41	0.00279	0.46	0.003199	0.27	0.29	0.07	-0.13	-0.12	/
HS.20255	2	0.7	< 1e-04	0.36	3.82E-05	0.32	9.75E-05	0.17	0.2	0.02	-0.06	0.07	/
HS.279842	1	0.69	< 1e-04	0.61	0.000354	0.6	4.61E-05	0.58	0.67	0.08	-0.09	-0.11	/
HS.385749	2	0.66	< 1e-04	0.4	3.91E-06	0.38	9.08E-05	0.23	0.17	-0.01	-0.09	-0.04	/
HS.551815	1	0.65	0.000333	0.8	0.000144	0.66	3.54E-06	0.3	0.33	0.1	-0.08	-0.06	/
IPO8	12	0.89	< 1e-04	0.64	0.000188	0.67	2.23E-06	0.74	0.71	-0.02	0.04	0.07	0.27
IRF5	7	0.92	< 1e-04	0.65	3.49E-05	0.79	0.001065	0.66	0.66	0.79	0.97	0.93	0.26

KCTD10	12	0.77	0.000164	0.69	0.000101	0.68	0.000567	0.37	0.35	-0.08	-0.02	-0.08	0.34
KIAA0748	12	0.66	< 1e-04	0.56	0.000315	0.31	0.000101	0.25	0.32	-0.01	-0.14	0.06	0.57
LAPTM4B	8	0.71	< 1e-04	0.58	0.002516	0.51	0.00055	0.8	0.6	0.81	0.68	0.56	0.84
LASS5	12	0.89	< 1e-04	0.5	0.000452	0.42	2.13E-06	0.55	0.37	-0.04	0.11	-0.11	0.16
LOC100132288	21	0.81	< 1e-04	0.41	0.000608	0.73	0.000205	0.37	0.46	/	/	/	/
LOC113386	19	0.79	< 1e-04	0.49	0.000225	0.51	0.000141	0.5	0.45	0.03	0.01	0.07	0.58
LOC220686	22	0.74	0.000398	0.32	0.000143	0.38	0.00052	0.34	0.23	-0.06	0.01	0.09	0.51
LOC401233	6	0.73	< 1e-04	0.55	0.000169	0.46	0.003564	0.43	0.43	-0.22	-0.2	-0.13	0.53
LOC440993	3	0.68	< 1e-04	0.69	0.000896	0.37	0.018333	0.23	0.22	-0.07	0.24	0.11	0.53
LOC644330	19	0.84	< 1e-04	0.62	1.11E-05	0.26	0.000334	0.17	0.12	0.28	0.19	0.24	/
LOC644670	X	0.7	0.000138	0.43	0.003828	0.63	8.02E-05	0.36	0.45	-0.09	-0.02	-0.1	/
LOC653610	1	0.64	0.000161	0.38	7.21E-05	0.64	5.84E-05	0.22	0.27	0.07	-0.03	-0.05	/
MED4	13	0.63	0.000471	0.49	2.67E-05	0.83	6.27E-05	0.39	0.36	0	0.03	0.04	0.28
MRI1	19	0.95	0.000111	0.88	5.01E-05	0.88	0.000158	1.12	1.11	/	/	/	/
MT1E	16	0.87	0.000167	0.41	0.005671	0.3	0.001926	0.26	0.34	0.29	0.49	0.44	0.54
NAAA	4	0.97	< 1e-04	0.35	0.000723	0.4	0.000193	0.3	0.38	/	/	/	/
NAPRT1	8	0.82	0.000547	0.63	0.000235	0.87	0.000545	0.97	0.96	-0.11	-0.06	-0.1	0.71
NLRP2	19	0.77	0.000132	0.59	0.000221	0.63	0.000426	0.43	0.42	/	/	/	/
NMT2	10	0.62	0.001026	0.53	0.000901	0.37	6.18E-06	0.24	0.46	-0.62	-0.56	-0.45	/
PDE6B	4	0.7	0.000112	0.27	2.08E-05	0.43	8.37E-06	0.24	0.29	-0.07	0.2	-0.09	0.01
PEX6	6	0.74	< 1e-04	0.6	4.97E-05	0.83	1.13E-06	0.43	0.37	0.16	-0.04	-0.04	0.78
PHACS	11	0.76	< 1e-04	0.42	0.000175	0.56	0.000405	0.33	0.38	0.04	0.22	-0.08	0.73
PI4KAP1	22	0.65	< 1e-04	0.34	0.002756	0.39	0.001383	0.34	0.25	/	/	/	/
PI4KAP2	22	0.75	0.000105	0.29	0.00019	0.43	0.000193	0.26	0.15	/	/	/	/
PLA2G4C	19	0.74	< 1e-04	0.45	9.37E-05	0.68	0.002083	0.42	0.46	0.05	-0.08	0	0.07
PLCXD1	X	0.9	0.000259	0.51	0.002895	0.63	0.000223	0.55	0.47	-0.22	-0.23	0.01	0.38
PPIL3	2	0.75	0.000152	0.26	0.00116	0.51	0.000827	0.15	0.19	0.32	0.3	0.19	0.56
PQLC1	18	0.73	< 1e-04	0.39	0.000635	0.47	4.39E-05	0.46	0.33	0.04	0	0.1	0.32
PREB	2	0.64	< 1e-04	0.43	4.90E-05	0.61	0.000187	0.32	0.45	-0.08	0.11	-0.06	0.51
PRPF31	19	0.78	< 1e-04	0.65	0.04701	0.52	0.011672	0.55	0.47	0.08	0.06	-0.14	0.35
PXMP4	20	0.63	0.000129	0.3	0.000203	0.29	0.00026	0.31	0.11	-0.18	-0.18	-0.14	0.39
PYGB	20	0.86	< 1e-04	0.28	0.008177	0.49	0.000626	0.23	0.25	0	-0.06	-0.09	0.62
RAP1A	1	0.76	< 1e-04	0.28	0.000269	0.29	0.010473	0.18	0.07	-0.12	-0.25	-0.17	0
RFP	6	0.64	< 1e-04	0.55	2.04E-05	0.28	1.57E-05	0.11	0.13	-0.2	-0.09	-0.21	0.42
RPS23	5	0.95	< 1e-04	0.91	5.26E-05	0.92	1.08E-06	1.08	1.04	-0.07	0.2	0.05	0.24

RPS26L	13	0.82	0.000171	0.85	0.000155	0.78	5.06E-05	0.43	0.42	-0.08	-0.02	-0.22	0.76
RRP7A	22	0.75	< 1e-04	0.43	0.04068	0.77	0.000764	0.5	0.41	/	/	/	/
SH2B2	7	0.71	< 1e-04	0.26	0.000587	0.35	2.45E-05	0.31	0.17	/	/	/	/
SNHG5	6	0.78	0.000195	0.61	4.57E-05	0.82	1.33E-05	0.44	0.4	0.14	0.21	-0.07	/
SPATA20	17	0.63	0.000164	0.79	0.000156	0.68	6.27E-05	0.4	0.33	0.07	0.05	0.18	0.49
SRXN1	20	0.88	< 1e-04	0.41	0.000667	0.56	0.001894	0.61	0.59	-0.06	0.04	-0.12	0.87
STAT6	12	0.64	< 1e-04	0.48	8.04E-05	0.35	0.000465	0.26	0.23	0.11	0.03	-0.09	0.47
TFG	3	0.63	0.001201	0.65	0.000366	0.56	0.005536	0.46	0.44	0.36	0.41	0.51	0.23
TGFBRAP1	2	0.82	< 1e-04	0.42	0.000847	0.33	0.000995	0.2	0.22	0.02	-0.21	0.02	0.46
THG1L	5	0.89	< 1e-04	0.26	0.001509	0.39	0.003076	0.13	0.14	-0.06	0.03	0.08	/
THRAP5	19	0.64	0.000169	0.56	3.80E-06	0.3	7.22E-06	0.29	0.23	0.31	0.4	0.34	0.14
TIMM10	11	0.77	< 1e-04	0.53	0.022614	0.7	0.000783	0.34	0.41	-0.04	0.06	-0.09	0.67
TUBB6	18	0.66	< 1e-04	0.26	4.93E-05	0.45	8.83E-05	0.13	0.06	-0.1	-0.12	-0.1	0.58
WDR41	5	0.89	< 1e-04	0.55	0.000334	0.74	0.000655	0.43	0.41	0	-0.1	-0.07	0.34
ZNF234	19	0.66	< 1e-04	0.49	0.000279	0.52	0.000123	0.32	0.46	0.63	0.59	0.43	/
ZNF431	19	0.62	< 1e-04	0.3	4.38E-05	0.41	0.000752	0.25	0.11	-0.03	-0.04	0.05	0.21
ZP3	7	0.7	< 1e-04	0.59	0.001978	0.72	0.000461	0.59	0.56	0.71	0.67	0.81	0.75

$-\hat{r}_G$ gene list													
		This study								Dimas *et al* 2009 - R_p			Dixon *et al* 2007
Gene	Chr	$\hat{r}_G$	$\hat{r}_G$ *p*-value	$\widehat{H}^2$ WB	$\widehat{H}^2$ WB *p*-value	$\widehat{H}^2$ LCL	$\widehat{H}^2$ LCL *p*-value	r_p_within	r_p_between	LCL & T-cells	LCL & Fibroblasts	T-cells & Fibroblasts	$\widehat{H}^2$
AARS2	6	-0.56	0.000154	0.25	0.000164	0.63	3.46E-05	-0.18	-0.15	/	/	/	/
ABCA1	9	-0.71	< 1e-04	0.49	0.001702	0.26	0.000307	-0.27	-0.28	0.04	-0.25	0.01	0.12
ABCB1	7	-0.61	0.00024	0.49	6.39E-05	0.32	0.001074	-0.38	-0.27	0.16	0.22	0.23	0.14
ADCY7	16	-0.57	0.001198	0.42	0.002052	0.28	0.003098	-0.14	-0.22	0.12	0.1	0.09	0.25
AKAP3	12	-0.68	< 1e-04	0.35	0.016784	0.36	6.26E-05	-0.21	-0.15	-0.32	-0.03	-0.09	0.2
ARID5A	2	-0.57	0.000157	0.33	3.51E-05	0.25	0.000165	-0.11	-0.09	0.02	-0.03	0.04	0.11
ATP5D	19	-0.77	< 1e-04	0.56	0.002299	0.26	0.003758	-0.15	-0.21	0.19	0.15	0.19	0.22
ATP6V0E2	7	-0.6	0.000649	0.31	0.007064	0.39	0.001732	-0.32	-0.27	/	/	/	/
ATPBD1B	1	-0.58	0.000425	0.49	0.001758	0.45	0.000589	-0.41	-0.44	-0.36	-0.57	-0.42	0.54
BAZ1A	14	-0.57	0.000115	0.38	0.000109	0.6	0.00238	-0.2	-0.19	0.15	0.05	0.15	0.34
BCCIP	10	-0.71	0.000136	0.36	0.002837	0.42	0.003065	-0.09	-0.2	0.14	-0.01	0.02	0.37

BUD13	11	-0.87	< 1e-04	0.25	0.004683	0.52	0.000298	-0.22	-0.24	/	/	/	/
C12ORF65	12	-0.59	< 1e-04	0.3	0.003513	0.51	0.003582	-0.14	-0.18	/	/	/	/
C14ORF135	14	-0.66	0.000183	0.27	0.000187	0.69	1.22E-06	-0.25	-0.34	-0.28	-0.25	-0.35	0.14
C16ORF35	16	-0.59	0.001253	0.45	4.61E-06	0.52	0.000124	-0.19	-0.22	0.17	0.08	0.11	0.22
C17ORF71	17	-0.57	< 1e-04	0.5	0.00161	0.28	0.00311	-0.13	-0.09	0.03	-0.16	0.07	/
C21ORF33	21	-0.67	0.000102	0.29	0.000609	0.6	2.64E-05	-0.46	-0.28	0.2	0.22	0.31	0.13
C6ORF153	6	-0.6	0.000149	0.55	9.93E-05	0.34	0.000241	-0.19	-0.17	-0.07	0.19	-0.04	0.2
C9ORF86	9	-0.75	0.000321	0.51	0.000297	0.27	0.010421	-0.21	-0.2	0.08	0.01	0.05	0.41
CALML4	15	-0.62	< 1e-04	0.37	0.000991	0.42	0.000446	-0.15	-0.2	0.16	0.11	0.06	0.15
CHUK	10	-0.68	0.000173	0.31	0.013448	0.5	8.03E-05	-0.2	-0.2	-0.03	0.01	0.01	0.25
CISD1	10	-0.64	< 1e-04	0.25	0.000234	0.52	1.08E-05	-0.2	-0.48	/	/	/	/
COL14A1	8	-0.75	< 1e-04	0.39	0.00022	0.29	0.001704	-0.25	-0.27	-0.65	-0.66	-0.58	0.11
CREB3L2	7	-0.56	0.000473	0.28	0.000699	0.41	9.61E-06	-0.32	-0.19	-0.01	-0.1	-0.05	0.47
CSAD	12	-0.6	< 1e-04	0.46	0.011805	0.51	4.64E-05	-0.23	-0.19	0.1	0.05	0.13	0.05
CSPP1	8	-0.64	< 1e-04	0.28	0.000123	0.39	0.00204	-0.29	-0.19	0.06	-0.01	-0.04	0.24
DECR1	8	-0.71	0.000201	0.69	0.001317	0.36	0.001391	-0.33	-0.26	0	-0.2	0	0.55
DYNC1I2	2	-0.65	< 1e-04	0.29	0.000286	0.54	0.000486	-0.19	-0.3	-0.04	0.18	0.21	/
EML4	2	-0.57	< 1e-04	0.33	0.003001	0.3	0.003892	-0.16	-0.23	0.16	0.07	0.14	0
ENO1	1	-0.64	0.00013	0.31	0.001901	0.36	0.000953	-0.09	-0.17	0.1	-0.1	-0.07	0.24
FLJ22795	15	-0.85	0.000397	0.3	0.000244	0.56	0.000709	-0.19	-0.32	0	-0.02	0.09	0.18
FLJ41423	11	-0.67	< 1e-04	0.42	0.000788	0.63	1.22E-05	-0.38	-0.59	-0.12	-0.12	-0.02	/
GCLM	1	-0.56	< 1e-04	0.4	0.014913	0.42	0.000336	-0.27	-0.35	0.41	0.24	0.33	0.33
GK2	4	-0.79	0.000357	0.31	0.000269	0.27	0.002549	-0.35	-0.11	0.06	-0.11	0.01	0.04
GOLGA5	14	-0.57	< 1e-04	0.35	0.000377	0.36	2.68E-05	-0.16	-0.19	-0.05	0.03	-0.02	0.52
GPATCH4	1	-0.9	< 1e-04	0.58	0.001677	0.54	0.000321	-0.38	-0.32	-0.25	0.22	0.18	/
GTF3C5	9	-0.64	0.000269	0.57	0.008974	0.27	0.004837	-0.28	-0.26	0.02	0.13	-0.14	0.17
HELB	12	-0.75	0.000489	0.31	0.000371	0.35	4.19E-05	-0.12	-0.17	-0.18	-0.15	-0.26	0.67
HIST1H2BJ	6	-0.61	0.000163	0.38	0.002806	0.45	0.000451	-0.16	-0.25	-0.05	-0.27	0.02	0.35
HSPH1	13	-0.64	< 1e-04	0.5	0.000263	0.38	2.37E-05	-0.39	-0.47	-0.18	-0.08	-0.13	0.51
IDH1	2	-0.77	0.000146	0.33	0.00025	0.58	6.27E-06	-0.52	-0.61	0.51	0.63	0.58	0.21
IFI44L	1	-0.89	0.000281	0.35	0.000421	0.29	0.010303	-0.16	-0.29	0.15	0.19	-0.07	0.41
IFIT2	10	-0.62	0.000181	0.28	0.004326	0.32	0.003617	-0.24	-0.25	-0.34	-0.13	-0.23	0.19
IQCK	16	-0.8	< 1e-04	0.33	0.024225	0.29	0.004763	-0.2	-0.15	0.11	-0.04	-0.06	
IRF3	19	-0.84	< 1e-04	0.29	0.002405	0.54	2.90E-05	-0.3	-0.42	-0.02	-0.1	-0.08	0.41
JUNB	19	-0.88	< 1e-04	0.39	0.000286	0.46	5.98E-05	-0.26	-0.29	0.07	0.02	0.04	0.09

KHDRBS1	1	-0.56	0.000124	0.4	0.002583	0.27	3.67E-05	-0.19	-0.29	0.01	-0.14	0.14	0.27
KIAA0240	6	-0.58	0.000172	0.4	0.004274	0.33	0.003028	-0.2	-0.1	-0.08	0	-0.09	0.26
KIAA0528	12	-0.69	0.000143	0.36	0.000516	0.35	0.000665	-0.17	-0.21	-0.04	-0.15	0	0.08
KPNA4	3	-0.6	0.000111	0.43	0.001599	0.69	0.000209	-0.45	-0.41	0.03	0.01	0.1	0.19
LASS6	2	-0.6	0.000189	0.52	0.000847	0.63	3.33E-05	-0.54	-0.66	-0.12	-0.04	0.04	0.54
LOC285900	7	-0.84	< 1e-04	0.3	0.006388	0.32	0.000889	-0.07	-0.27	0.05	0.05	0.02	/
LOC387841	12	-0.57	0.000265	0.3	0.000729	0.26	0.017953	-0.12	-0.13	-0.02	-0.06	0.08	/
LOC389901	X	-0.63	0.00013	0.33	7.02E-05	0.46	5.04E-05	-0.07	-0.04	0.05	0.03	0.01	/
LOC441032	4	-0.61	0.000154	0.46	7.89E-06	0.58	0.001013	-0.32	-0.5	0.02	0.02	-0.01	/
LOC643872	14	-0.7	< 1e-04	0.64	0.001545	0.37	0.000437	-0.35	-0.45	/	/	/	/
LOC644117	10	-0.75	< 1e-04	0.29	0.000417	0.27	0.000346	-0.29	-0.11	-0.08	-0.09	-0.15	/
LOC646483	7	-0.66	< 1e-04	0.31	0.000772	0.39	0.001811	-0.11	-0.24	-0.11	0	0.05	/
LOC727866	X	-0.69	0.000586	0.36	0.000269	0.3	0.002516	-0.32	-0.24	/	/	/	/
LRBA	4	-0.62	< 1e-04	0.53	0.000277	0.54	0.00195	-0.32	-0.38	0.37	0.37	0.33	0.48
MAD2L2	1	-0.58	< 1e-04	0.39	0.024391	0.48	0.001404	-0.38	-0.23	0.16	0.07	0.1	0.14
MAFG	17	-0.6	0.00024	0.27	0.000208	0.64	0.000352	-0.16	-0.18	0.13	0.06	0.16	0.39
MAN2B2	4	-0.6	0.005345	0.65	0.000216	0.34	0.001811	-0.24	-0.18	-0.14	-0.03	-0.02	0.66
MAP3K14	17	-0.57	< 1e-04	0.34	0.000221	0.49	4.00E-05	-0.12	-0.18	-0.73	-0.49	-0.39	0.11
MCTP2	15	-0.85	0.000219	0.3	0.000992	0.3	0.003719	-0.28	-0.42	-0.16	-0.16	-0.12	0.13
MGAT2	14	-0.63	< 1e-04	0.43	0.01784	0.36	0.00369	-0.21	-0.29	0.24	0.13	0.17	0.39
MON2	12	-0.63	< 1e-04	0.25	0.00066	0.33	0.002577	-0.2	-0.14	-0.04	-0.03	0.09	/
MRPL21	11	-0.6	< 1e-04	0.37	0.000649	0.31	0.001419	-0.07	-0.2	0.16	0.24	0.08	0.28
MRPS7	17	-0.57	0.000417	0.43	7.71E-05	0.6	0.000267	-0.24	-0.28	-0.08	-0.11	-0.04	0.26
MTPN	7	-0.57	< 1e-04	0.79	0.002263	0.26	0.000288	-0.23	-0.22	0.19	0.05	0.14	0.37
MTRF1	13	-0.85	0.000469	0.35	0.005778	0.25	0.002049	-0.23	-0.06	-0.35	-0.03	-0.23	0.55
NECAP1	12	-0.65	0.00012	0.31	0.001856	0.4	0.00226	-0.18	-0.14	0.01	-0.11	-0.08	0
NFKB2	10	-0.58	0.000286	0.27	0.003209	0.37	0.00091	-0.19	-0.27	0.21	0.14	0.19	0.21
NLRC5	16	-0.61	< 1e-04	0.37	0.000681	0.34	0.004669	-0.16	-0.23	/	/	/	/
NRD1	1	-0.59	< 1e-04	0.49	0.007598	0.28	0.001827	-0.18	-0.17	0.15	0.06	-0.17	0.32
NUDT16L1	16	-0.62	< 1e-04	0.33	0.000136	0.36	0.003948	-0.27	-0.39	0	-0.07	-0.01	0.17
OXCT1	5	-0.71	< 1e-04	0.26	0.001615	0.33	0.001179	-0.13	-0.19	0.04	0	-0.04	0.44
PCYOX1	2	-0.58	0.003563	0.51	0.001593	0.44	0.00198	-0.4	-0.47	-0.42	-0.42	-0.38	0.24
PIK3R1	5	-0.66	0.000141	0.53	7.30E-05	0.4	0.000594	-0.26	-0.21	0.05	-0.07	0.07	0.3
PLEK	2	-0.67	0.000134	0.49	0.005011	0.27	0.006051	-0.23	-0.17	-0.13	0.17	0.1	0.49
PNRC2	1	-0.85	< 1e-04	0.3	0.000435	0.27	0.002652	-0.18	-0.26	0.27	-0.28	-0.32	0.12

PPP1R8	1	-0.85	< 1e-04	0.31	6.08E-05	0.25	0.000269	-0.37	-0.26	0.27	0.16	0.24	0.52
PSMC5	17	-0.6	0.000137	0.77	0.000167	0.32	0.001554	-0.23	-0.22	0.06	-0.01	-0.16	0.46
RALBP1	18	-0.56	< 1e-04	0.59	0.001486	0.3	0.002009	-0.13	-0.13	0	-0.17	0.05	0.34
RBED1	2	-0.57	< 1e-04	0.31	0.001227	0.39	0.000748	-0.15	-0.09	-0.01	0.06	0.07	0.61
RBM12	20	-0.69	< 1e-04	0.31	0.000941	0.57	8.32E-05	-0.34	-0.44	-0.41	-0.33	-0.42	0.49
RERE	1	-0.56	0.000494	0.45	0.000117	0.35	0.002206	-0.16	-0.33	0.23	0.17	0.32	0.01
RFWD2	1	-0.68	0.000136	0.58	0.007915	0.31	0.001362	-0.23	-0.19	0.2	0.07	0.11	0.57
RNF149	2	-0.63	0.000143	0.28	0.001216	0.31	0.000822	-0.08	-0.21	-0.11	0.08	0.16	0.34
RPS14	5	-0.7	0.000159	0.26	5.24E-05	0.36	0.001337	-0.08	-0.19	0.11	0.08	0.11	0.21
RPS19	19	-0.61	< 1e-04	0.57	0.000196	0.36	0.000675	-0.26	-0.26	0.13	-0.04	0.01	0.76
SF3B5	6	-0.65	0.000265	0.5	0.014343	0.48	0.005552	-0.27	-0.41	0.04	-0.05	-0.03	0.39
SLC3A2	11	-0.65	0.000328	0.29	0.002887	0.37	0.003532	-0.2	-0.28	-0.28	-0.21	-0.25	0.52
SMARCAD1	4	-0.77	0.000132	0.33	8.25E-05	0.29	1.37E-05	-0.21	-0.14	-0.08	0.09	-0.15	0.25
SNORA7B	3	-0.59	< 1e-04	0.33	0.000203	0.28	0.001315	-0.32	-0.19	/	/	/	/
STAU2	8	-0.74	0.00031	0.37	0.003212	0.58	9.46E-05	-0.28	-0.31	0.01	0.1	0.09	0.24
TCEB2	16	-0.64	0.000103	0.39	0.003529	0.41	0.001579	-0.13	-0.15	0.1	0.03	0.06	0.22
TSR2	X	-0.58	< 1e-04	0.29	0.005188	0.43	0.000162	-0.18	-0.19	/	/	/	/
UBAC2	13	-0.67	< 1e-04	0.33	0.000122	0.53	2.84E-05	-0.25	-0.22	/	/	/	/
USP5	12	-0.71	< 1e-04	0.48	0.000539	0.38	0.000397	-0.27	-0.24	-0.11	-0.08	0.07	0.22
WAS	X	-0.57	< 1e-04	0.33	0.002849	0.5	0.001231	-0.17	-0.27	-0.04	-0.09	-0.01	0.54
WBP2	17	-0.68	< 1e-04	0.34	0.002596	0.58	0.000105	-0.2	-0.2	0.05	-0.06	-0.06	0.23
ZC3H12A	1	-0.63	< 1e-04	0.35	0.002749	0.38	0.001189	-0.31	-0.21	-0.07	0.09	0.02	0.24
ZNF232	17	-0.7	0.000179	0.33	0.000216	0.31	3.17E-05	-0.23	-0.2	-0.06	-0.08	-0.12	0.39
ZNF295	21	-0.58	< 1e-04	0.37	0.007286	0.4	0.000139	-0.17	-0.29	-0.07	0.06	-0.03	0
ZNF655	7	-0.7	0.000114	0.3	0.000123	0.51	0.000225	-0.25	-0.29	-0.33	-0.3	-0.33	0
ZNF800	7	-0.7	< 1e-04	0.39	0.000164	0.39	0.000153	-0.24	-0.31	/	/	/	/

Supplementary Table 2

Gene ontology enrichment analysis of $-\hat{r}_G$ and $+\hat{r}_G$ gene sets. The 10 GO terms with the smallest *p*-values are given for each of the gene sets. A list of probe IDs for the genes listed in the $-\hat{r}_G$ and $+\hat{r}_G$ groups was submitted to the online version of GOEAST (Zheng and Wang 2008). GOEAST identifies statistically over-represented GO terms within a list of genes and uses a hyper-geometric test to determine the significance level of the enrichment. We account for multiple testing by adjusting the *p*-values using a false discovery rate (FDR) of 0.05 (Benjamini and Yekutieli 2001).

$-\hat{\boldsymbol{r}}_G$ Gene enrichment			**$+\hat{\boldsymbol{r}}_G$ Gene enrichment**		
GO ID	**GO Term**	***p*-value**	**GO_ID**	**GO Term**	***p*-value**
GO:0005622	intracellular	2.68E-09	GO:0032395	MHC class II receptor activity	3.58E-05
GO:0005488	binding	3.13E-09	GO:0019882	antigen processing and presentation	6.87E-05
GO:0044424	intracellular part	1.93E-08	GO:0042613	MHC class II protein complex	6.87E-05
GO:0005623	cell	5.38E-06	GO:0042611	MHC protein complex	7.68E-05
GO:0044464	cell part	5.38E-06	GO:0002504	antigen processing via MHC class II	1.85E-04
GO:0043226	organelle	7.77E-06	GO:0004364	glutathione transferase activity	5.12E-04
GO:0043229	intracellular organelle	7.77E-06	GO:0016765	transferase activity	1.08E-03
GO:0043227	membrane-bounded organelle	3.40E-05	GO:0003824	catalytic activity	1.88E-03
GO:0043231	intracellular membrane-bounded organelle	3.40E-05	GO:0005623	cell	5.52E-02
GO:0005737	cytoplasm	5.76E-04	GO:0044424	intracellular part	5.52E-02

Supplementary Table 3

Sampling variance of heritability (H^2). Mean squares and mean cross products were drawn from a Wishart distribution and used to calculate an estimate of heritability ($\widehat{H}^2$). For each combination parameters of sample size and (true) H^2, one hundred thousand replicates were simulated and from these the empirical variance*1 of $\widehat{H}^2$ was calculated. This is compared to the expected sampling variance*2 calculated using eq. 4 (main text) with N = sample size and $H^2 = \overline{H}^2$.

Sample size	H^2	Empirical *var*(H^2)*1	Expected *var*(H^2)*2
48	0.33	0.0168	0.0164
	0.5	0.0125	0.0117
	0.66	0.0068	0.0065
	0.99	3.62e-05	3.58e-05
100	0.33	0.0078	0.0079
	0.5	0.0056	0.0056
	0.66	0.0031	0.0031
	0.99	1.68e-05	1.69e-05
1000	0.33	0.00078	0.00079
	0.5	0.00056	0.00056
	0.66	0.00029	0.00030
	0.99	1.52e-06	1.53e-06

Supplementary Table 4

Sampling variance of genetic correlations (r_G). Mean squares and mean cross products were drawn from a Wishart distribution and used to calculate an estimate of heritability ($\hat{r}_G$). For each combination parameters of sample size and (true) H^2, one hundred thousand replicates were simulated and from these the empirical variance[*1] of $\hat{r}_G$ was calculated. This is compared to the expected sampling variance[*2] calculated using eq. 5 (main text) with N = sample size and $\overline{H}^2_{LCL} = \overline{H}^2_{WB} = \overline{H}^2$. With both $\widehat{H}^2$ and $\hat{r}_G$ empirical and expected variances rapidly asymptote as sample size and H^2 increases.

Sample size	H^2	Empirical *var*($\hat{r}_G$)[*1]	Expected var($\hat{r}_G$)[*2]
48	0.33	0.153	0.104
	0.5	0.058	0.052
	0.66	0.035	0.034
	0.98	0.021	0.021
100	0.33	0.060	0.05
	0.5	0.025	0.025
	0.66	0.016	0.016
	0.98	0.010	0.010
1000	0.33	0.005	0.005
	0.5	0.0025	0.0025
	0.66	0.0016	0.0016
	0.98	0.0010	0.0010
10000	0.33	0.0005	0.0005
	0.5	0.00025	0.00025
	0.66	0.00016	0.00016
	0.98	0.00010	0.00010

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