

a

1

Supplementary Tables

Table S1. Predictive comparison of CorShrink, Robocov and sample correlation estimators for a GTEx gene. We report Mean Absolute Deviation (MAD) and Root Mean Squared Deviation (RMSE) metrics between an estimator (e.g., sample correlation matrix, CorShrink and Robocov) computed on the gene expression data (GTEx project) for half of the individuals (training set) and the sample correlation matrix computed from other half (testing set) of all individuals. Results are averaged over 30 such different training/testing data-splits with the standard errors reported in brackets.

Method	MAD	RMSE
Sample-Est	0.30 (0.01)	0.47 (0.02)
CorShrink	0.24 (0.01)	0.35 (0.01)
Robocov	0.25 (0.01)	0.36 (0.01)

Table S2. Pathway enrichment analysis of Robospan, pRobospan and Corspan genes. Pathway enrichment is performed using the ConsensusPathDB database[28]. Only the top 5 non-redundant and statistically significant (q-value < 0.05) pathways for a gene set are reported.

Gene Set	Top pathways
Robospan	Interferon signaling (1.1e-18), Immune system (3.1e-08), HSF1 activation (1.1e-07), Antigen processing and presentation (2.4e-07), Allograft rejection (1.5e-06)
pRobospan	Immune system (2.7e-21), Interferon signaling (3.4e-15), Innate immune system (5.1e-12), TNF signaling pathway (7.9e-11), Neutrophil degranulation (2.0e-10)
Corspan	Interferon signaling (1.1e-17), Immune system (1.6e-07), Antigen processing and presentation (1.2e-05), HSF1 activation (4.1e-05), Neutrophil degranulation (1e-04),

Table S3. List of 11 blood and autoimmune traits (5 blood traits and 6 autoimmune traits) analyzed in this paper.

Annotation	Traits
Blood traits	Red blood Cell Distribution Width (UKBB[38]), Red blood Cell Count (UKBB[38]), White blood Cell Count (UKBB[38]), Platelet Count (UKBB[38]), Eosinophil Count (UKBB[38])
Immune traits	Ulcerative Colitis[39], Rheumatoid Arthritis[40], Celiac[41], Lupus[42], Crohn’s disease[39], Auto Immune and Inflammatory traits

Table S4. S-LDSC results for SNP annotations corresponding to Robospan, pRobospan, Corspan and SEG-Blood gene sets for blood and autoimmune traits. Standardized Effect sizes ( $\tau^*$ ) and Enrichment (E) of 8 SNP annotations corresponding to 4 gene sets (Robospan, pRobospan, Corspan and SEG-Blood[29]) and 2 SNP annotations corresponding to 5kb and 100kb window based SNP-to-gene linking strategies for each gene set. Results for all annotations are conditional on 86 baselineLD-v2.1 annotations. Reports are meta-analyzed across 11 Blood and Autoimmune traits.

Robospan						
	$\tau^*$	se( $\tau^*$ )	p( $\tau^*$ )	E	se(E)	p(E)
5kb (2.6%)	0.086	0.024	0.00048	2.7	0.16	1.5e-07
100kb (10%)	0.12	0.03	7.9e-05	2.3	0.12	2e-09
pRobospan						
	$\tau^*$	se( $\tau^*$ )	p( $\tau^*$ )	E	se(E)	p(E)
5kb (2.3%)	0.096	0.028	0.00057	3.2	0.22	9.3e-08
100kb (9.9%)	0.11	0.034	0.0011	2.4	0.12	5.5e-09
Corspan						
	$\tau^*$	se( $\tau^*$ )	p( $\tau^*$ )	E	se(E)	p(E)
5kb (2.5%)	0.04	0.024	0.093	2.4	0.15	4.8e-07
100kb (9.8%)	0.038	0.02	0.059	2.1	0.1	1.7e-08
SEG-Blood						
	$\tau^*$	se( $\tau^*$ )	p( $\tau^*$ )	E	se(E)	p(E)
5kb (2.7%)	0.24	0.036	7.6e-11	3.6	0.26	8.7e-10
100kb (10.1%)	0.21	0.029	1.3e-13	2.4	0.095	2.2e-10

a

3

Table S5. **S-LDSC results for SNP annotations corresponding to Robospan, pRobospan, Corspan and SEG-Blood gene sets for 6 autoimmune traits. Standardized Effect sizes ( $\tau^*$ ) and Enrichment (E) of 8 SNP annotations corresponding to 4 gene sets (Robospan, pRobospan, Corspan and SEG-Blood[29]) and 2 SNP annotations corresponding to 5kb and 100kb window based SNP-to-gene linking strategies for each gene set. Results for all annotations are conditional on 86 baselineLD-v2.1 annotations. Reports are meta-analyzed across 6 Autoimmune traits.**

Robospan						
	$\tau^*$	$se(\tau^*)$	$p(\tau^*)$	$E$	$se(E)$	$p(E)$
5kb (2.6%)	0.12	0.036	7e-04	2.7	0.25	5e-05
100kb (10%)	0.14	0.049	0.0051	2.3	0.19	2e-06
pRobospan						
	$\tau^*$	$se(\tau^*)$	$p(\tau^*)$	$E$	$se(E)$	$p(E)$
5kb (2.3%)	0.1	0.043	0.016	3.3	0.39	1e-04
100kb (9.9%)	0.11	0.059	0.061	2.5	0.24	1e-05
Corspan						
	$\tau^*$	$se(\tau^*)$	$p(\tau^*)$	$E$	$se(E)$	$p(E)$
5kb (2.5%)	0.08	0.035	0.021	2.5	0.23	1e-04
100kb (9.8%)	0.037	0.035	0.28	2	0.15	8e-06
SEG-Blood						
	$\tau^*$	$se(\tau^*)$	$p(\tau^*)$	$E$	$se(E)$	$p(E)$
5kb (2.7%)	0.33	0.042	5e-15	4.2	0.25	8e-06
100kb (10.1%)	0.3	0.036	9e-17	2.7	0.11	7e-06

Table S6. **Joint S-LDSC results for annotations corresponding to Robospan, pRobospan, Corspan and SEG-Blood gene sets.: Standardized Effect sizes ( $\tau^*$ ) and Enrichment (E) of SNP annotations that are significant when all annotations from Table S4 are modeled jointly and subjected to forward stepwise elimination. 2 annotations survive in the resulting joint model. The analysis is conditional on 86 baselineLD-v2.1 annotations. Reports are meta-analyzed across 11 Blood and Autoimmune traits.**

	$\tau^*$	$se(\tau^*)$	$p(\tau^*)$	$E$	$se(E)$	$p(E)$
Robospan(100kb)	0.1	0.03	1e-04	2.3	0.1	2e-09
SEG-Blood(100kb)	0.2	0.03	2e-13	2.4	0.09	2e-10