

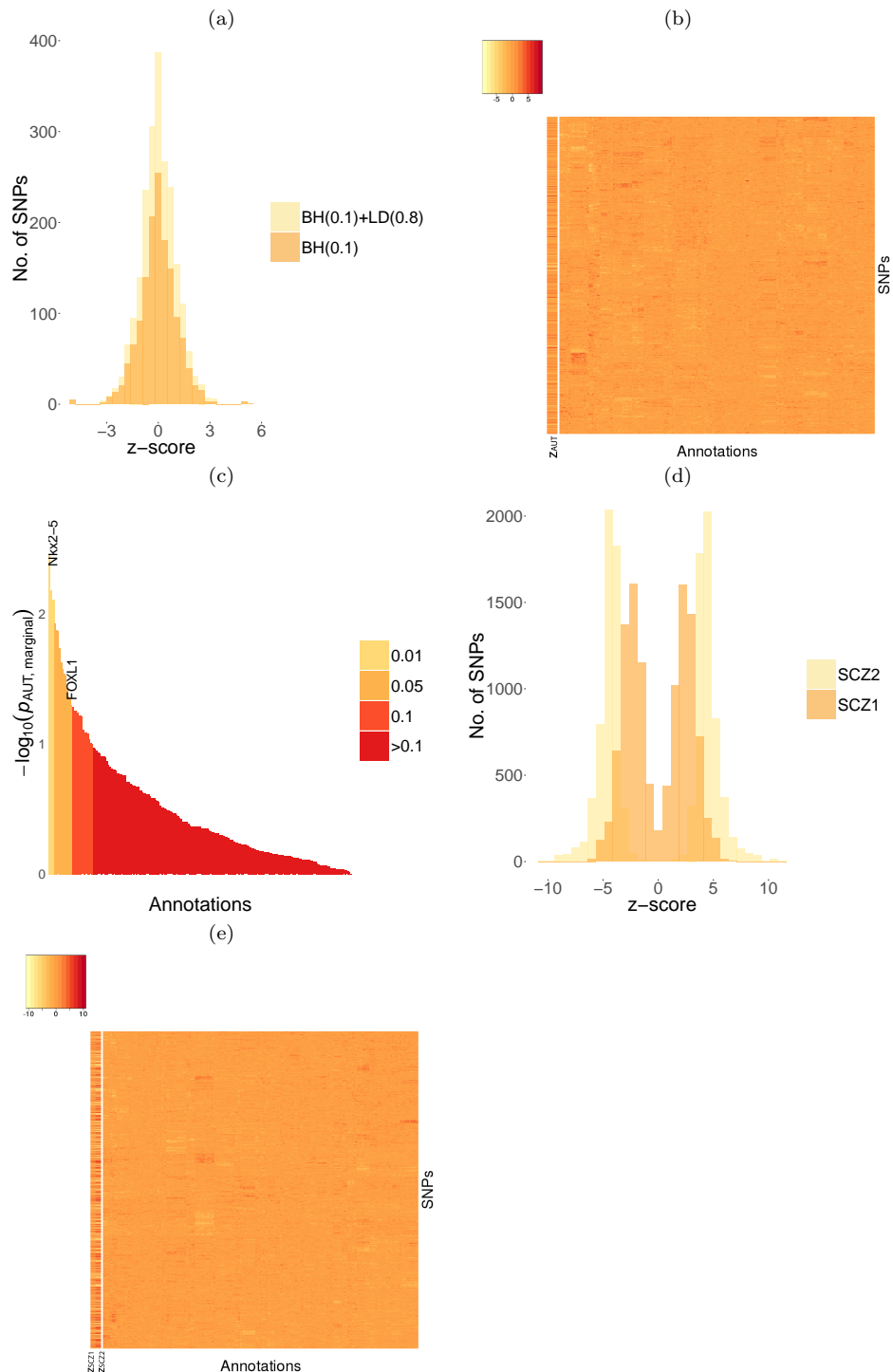
Supplementary Materials

Supplementary Table 1. Genomic characteristics of 44 *ARoG SNPs* from SCZ2 analysis.

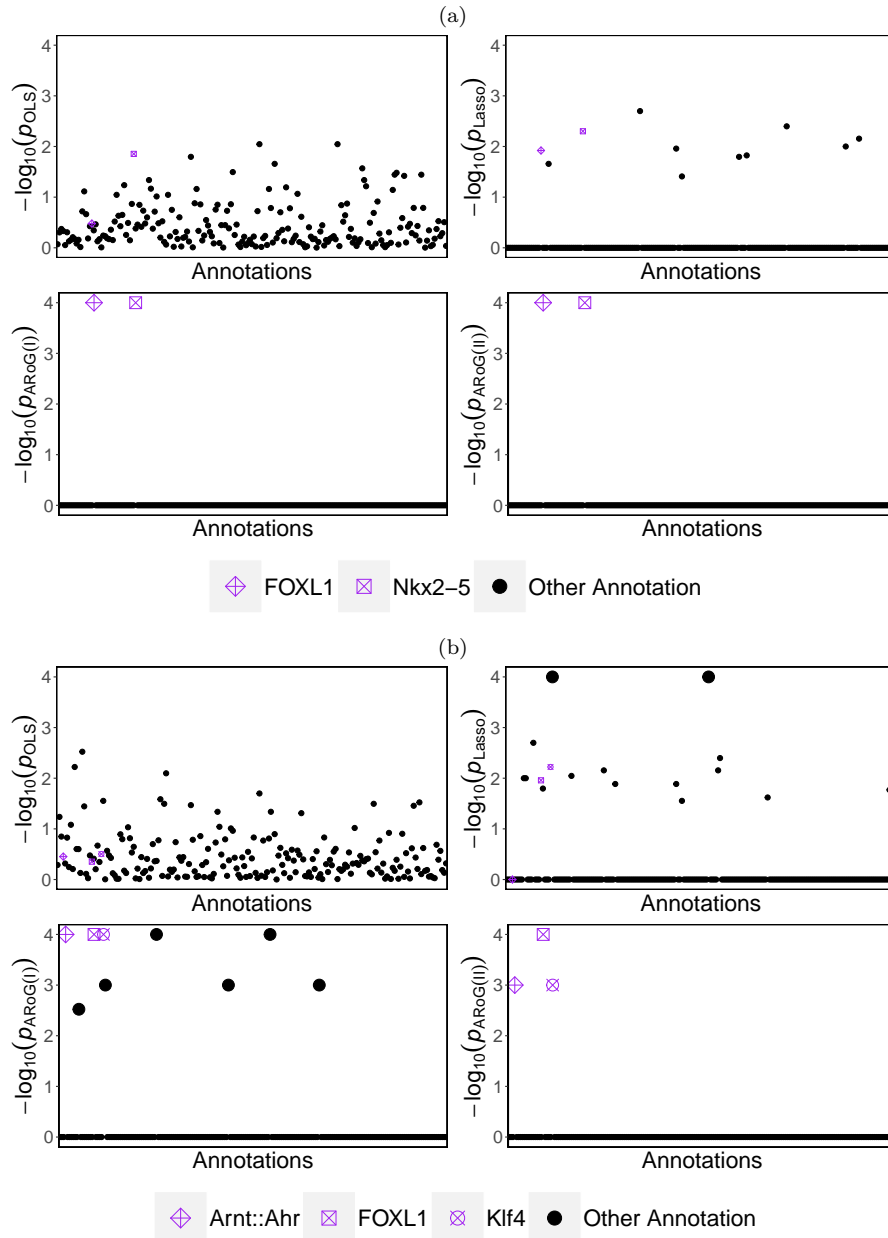
RSID	Chr	Position	p_{SCZ2}	p_{SCZ1}	ARoG Cluster	Regulome DB score
rs10224497	chr7	2149967	$4.70 \cdot 10^{-11}$	$6.48 \cdot 10^{-7}$	6	1b
rs10744560	chr12	2387099	$1.80 \cdot 10^{-16}$	$2.02 \cdot 10^{-6}$	6	7
rs10773921	chr12	123541606	$2.03 \cdot 10^{-11}$	$6.56 \cdot 10^{-3}$	5	7
rs10791097	chr11	130718630	$2.88 \cdot 10^{-12}$	$2.17 \cdot 10^{-4}$	6	5
rs10848428	chr12	123572495	$1.87 \cdot 10^{-11}$	$5.83 \cdot 10^{-3}$	5	7
rs11191425	chr10	104625970	$2.04 \cdot 10^{-12}$	$3.96 \cdot 10^{-5}$	5	7
rs11191580	chr10	104906211	$7.07 \cdot 10^{-16}$	$2.23 \cdot 10^{-8}$	6	1f
rs1124131	chr6	28380248	$9.31 \cdot 10^{-13}$	$2.59 \cdot 10^{-7}$	6	6
rs1150754	chr6	32050758	$5.15 \cdot 10^{-12}$	$1.95 \cdot 10^{-4}$	5	1f
rs12221064	chr10	104677126	$1.52 \cdot 10^{-14}$	$1.38 \cdot 10^{-7}$	5	2b
rs13190754	chr6	26587406	$5.15 \cdot 10^{-16}$	$1.04 \cdot 10^{-3}$	5	6
rs13219354	chr6	27185664	$2.77 \cdot 10^{-19}$	$1.00 \cdot 10^{-6}$	6	6
rs1361385	chr6	28358320	$7.05 \cdot 10^{-13}$	$2.23 \cdot 10^{-7}$	6	7
rs16891725	chr6	26479150	$1.28 \cdot 10^{-19}$	$2.82 \cdot 10^{-7}$	5	1f
rs17379561	chr1	98340139	$3.33 \cdot 10^{-12}$	$3.90 \cdot 10^{-5}$	6	6
rs1778508	chr6	28229881	$5.56 \cdot 10^{-17}$	$5.03 \cdot 10^{-9}$	6	1d
rs1790121	chr12	123604492	$7.30 \cdot 10^{-11}$	$5.92 \cdot 10^{-3}$	5	4
rs1892252	chr6	25772639	$1.83 \cdot 10^{-12}$	$9.65 \cdot 10^{-6}$	6	6
rs200953	chr6	27837267	$1.22 \cdot 10^{-18}$	$2.89 \cdot 10^{-7}$	6	5
rs200973	chr6	27858421	$2.00 \cdot 10^{-12}$	$1.77 \cdot 10^{-4}$	6	1b
rs2142730	chr6	28266149	$1.00 \cdot 10^{-10}$	$7.99 \cdot 10^{-6}$	6	6
rs2232423	chr6	28366151	$4.32 \cdot 10^{-28}$	$1.98 \cdot 10^{-9}$	6	5
rs2283288	chr12	2299048	$3.39 \cdot 10^{-14}$	$2.46 \cdot 10^{-4}$	6	5
rs2747054	chr6	27783359	$2.36 \cdot 10^{-19}$	$3.87 \cdot 10^{-7}$	6	3a
rs2747429	chr6	29648377	$2.89 \cdot 10^{-11}$	$9.35 \cdot 10^{-3}$	6	1b
rs3734528	chr6	26022244	$8.50 \cdot 10^{-16}$	$6.92 \cdot 10^{-6}$	6	1f
rs3734544	chr6	26468660	$5.01 \cdot 10^{-19}$	$2.07 \cdot 10^{-6}$	5	1f
rs3757188	chr6	28107357	$1.95 \cdot 10^{-17}$	$8.52 \cdot 10^{-8}$	6	7
rs3857546	chr6	26157762	$2.11 \cdot 10^{-22}$	$1.46 \cdot 10^{-9}$	5	1f
rs4254981	chr6	28371402	$7.95 \cdot 10^{-13}$	$2.73 \cdot 10^{-7}$	6	7
rs4523552	chr1	98328093	$3.41 \cdot 10^{-10}$	$3.47 \cdot 10^{-5}$	5	5
rs4917994	chr10	104811699	$9.19 \cdot 10^{-15}$	$5.07 \cdot 10^{-7}$	5	7
rs6922111	chr6	28325308	$1.95 \cdot 10^{-20}$	$7.09 \cdot 10^{-8}$	5	1f
rs6938200	chr6	27231150	$1.70 \cdot 10^{-17}$	$1.69 \cdot 10^{-6}$	6	6
rs7092200	chr10	104844872	$3.87 \cdot 10^{-13}$	$1.44 \cdot 10^{-6}$	6	5
rs7148456	chr14	104028270	$2.30 \cdot 10^{-12}$	$3.36 \cdot 10^{-3}$	5	1f
rs732998	chr10	104897901	$1.60 \cdot 10^{-15}$	$9.50 \cdot 10^{-8}$	6	6
rs742047	chr6	27739380	$6.81 \cdot 10^{-11}$	$7.38 \cdot 10^{-6}$	6	1f
rs7526108	chr1	98305394	$3.02 \cdot 10^{-11}$	$1.36 \cdot 10^{-5}$	6	7
rs7822538	chr8	143323109	$3.73 \cdot 10^{-11}$	$9.50 \cdot 10^{-4}$	6	5
rs9283880	chr6	27715243	$8.26 \cdot 10^{-11}$	$2.78 \cdot 10^{-6}$	6	6
rs9295661	chr6	25450026	$2.01 \cdot 10^{-16}$	$2.10 \cdot 10^{-5}$	6	1f
rs9393708	chr6	26362643	$8.80 \cdot 10^{-19}$	$1.19 \cdot 10^{-6}$	6	1f
rs943036	chr10	104836047	$5.06 \cdot 10^{-15}$	$2.59 \cdot 10^{-7}$	6	5

Supplementary Table 2. Simulation setting with the annotation predictor matrix from the PGC autism GWAS analysis.

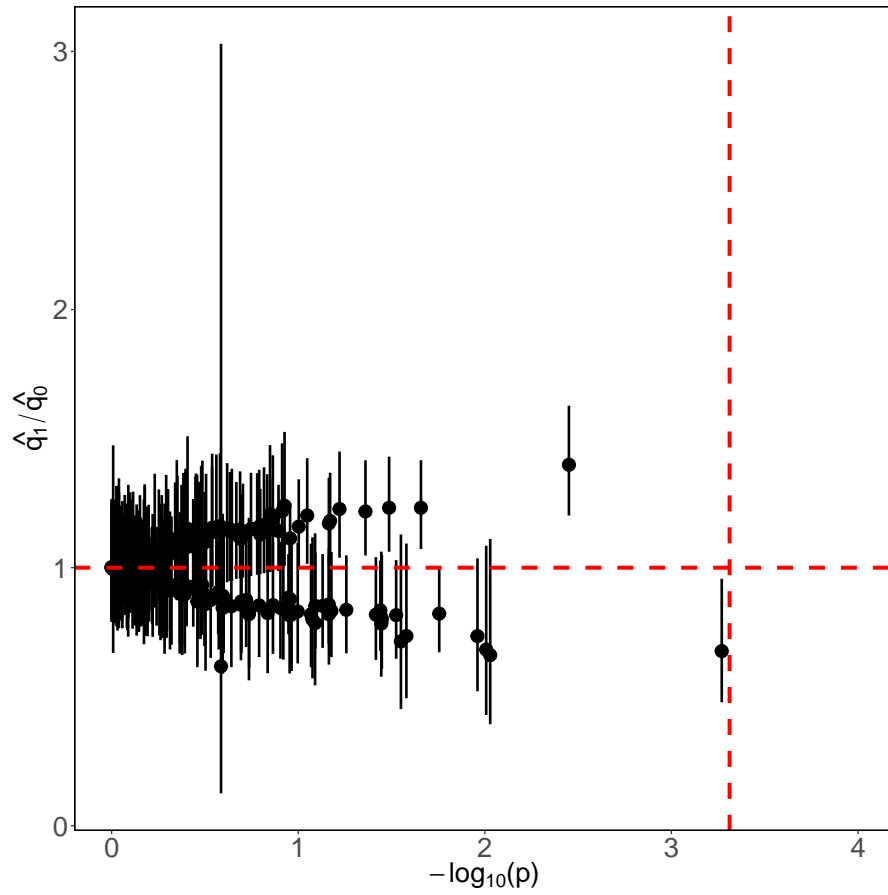
Cluster	β	σ	π
1	$(0, 0.5, -0.5, 0, 0, 1, \underbrace{0, \dots, 0}_{200 \text{ repetitions}})$	0.2	0.1
2	$(0, 0, 0, -0.5, -1, 0, \underbrace{0, \dots, 0}_{200 \text{ repetitions}})$	0.2	0.1
3	$(\underbrace{0, \dots, 0}_{206 \text{ repetitions}})$	0.8	0.8



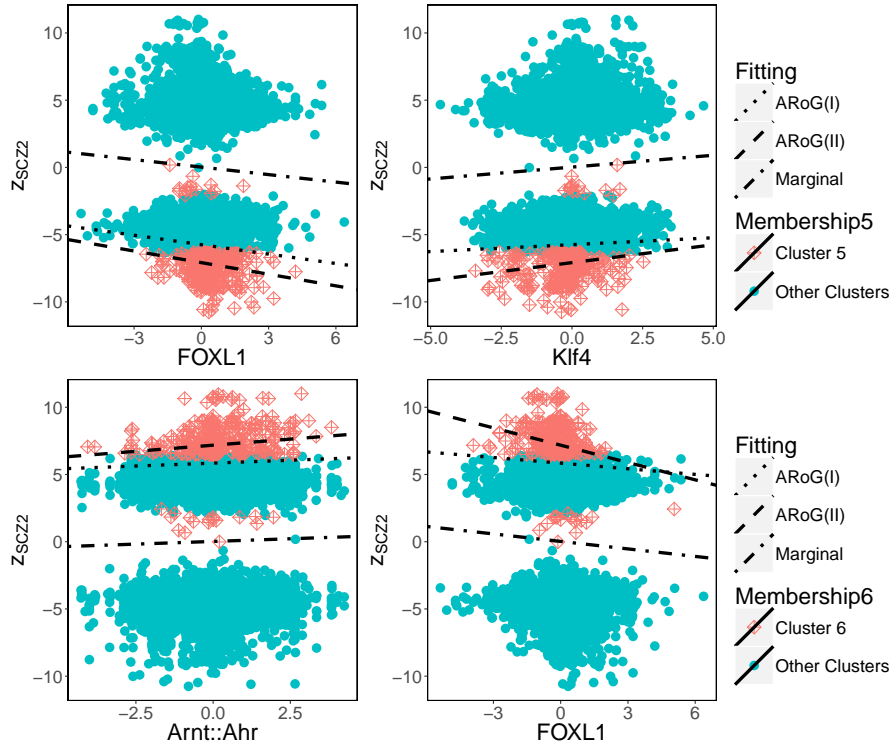
Supplementary Figure 1. (a) Histogram of autism z-scores for SNPs with BH adjusted p-values smaller than equal to 0.1 and their LD partners ($r^2 \geq 0.8$). (b) Heatmap of annotation scores with autism z-scores (leftmost column). (c) Ranking of TFs based on marginal regressions of autism z-scores on annotations scores for each TF. Nkx2-5 and FOXL1 TFs that are identified as associated with the z-scores by AROG in Section 4.1 are labeled. (d) Histogram of the z-scores of all 11,386 SNPs from both SCZ1 and SCZ2 studies. (e) Heatmap of annotation scores with schizophrenia z-scores from SCZ1 and SCZ2 (leftmost two columns).



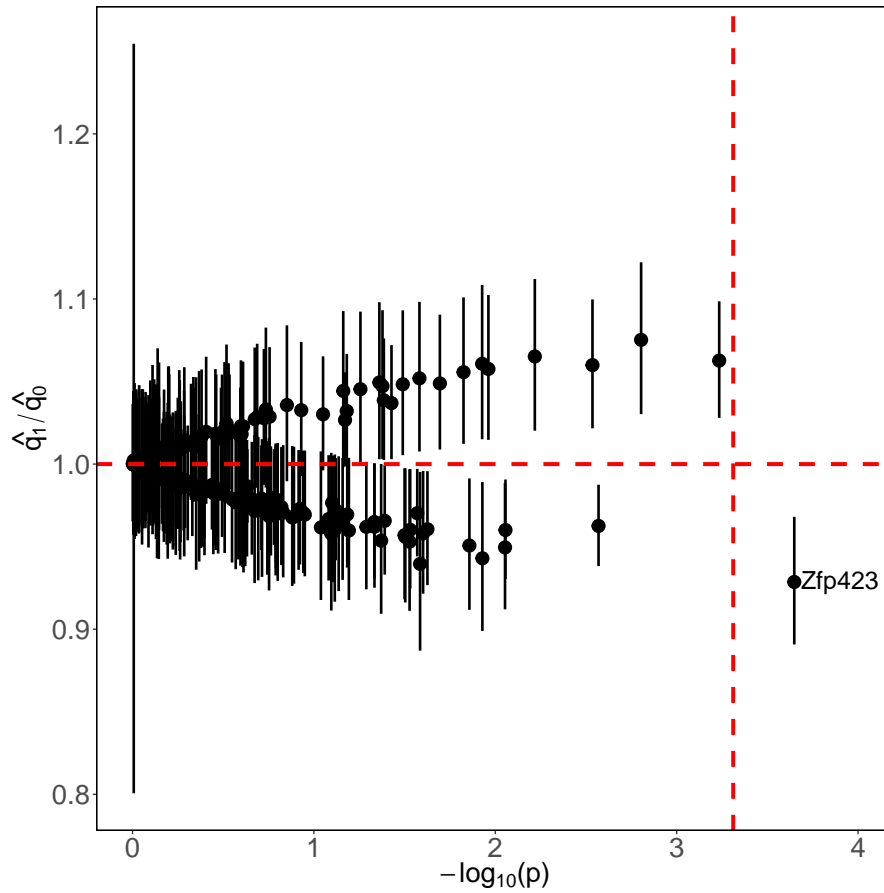
Supplementary Figure 2. (a) Permutation p-values of the 205 annotations in the autism application. Annotations reaching BH adjusted p-values at level 0.1 are depicted with enlarged plotting symbols. (b) Permutation p-values of the 205 annotations in the SCZ2 application. Annotations reaching BH adjusted p-values at level 0.1 are depicted with enlarged plotting symbols. In both panels, permutation p-values of 0 are depicted as negative log p-values of 4.



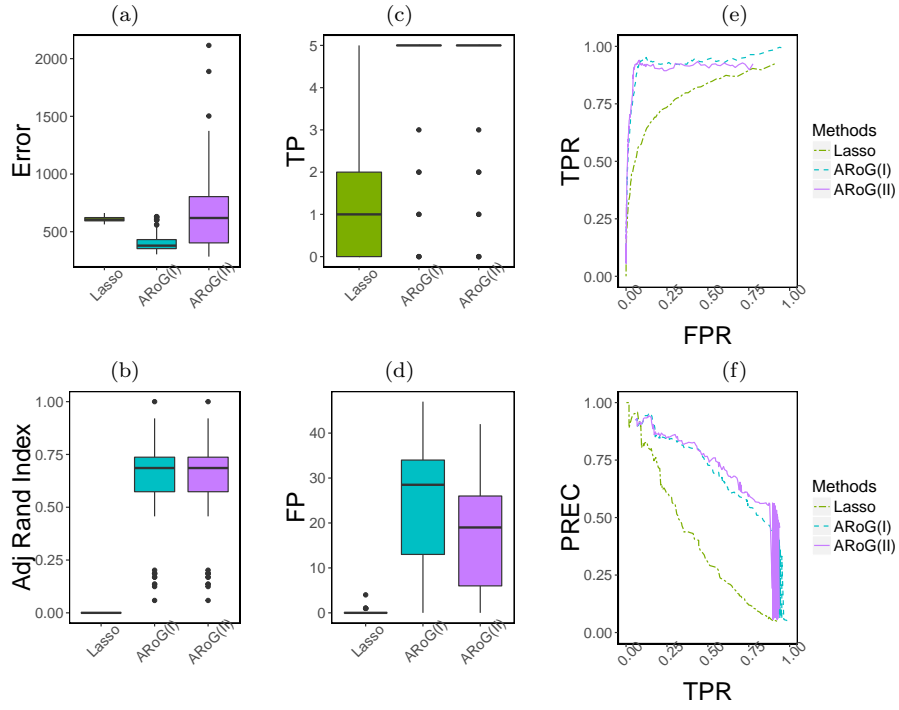
Supplementary Figure 3. Application of GPA [9] to the autism dataset. The plot depicts $-\log_{10}(\text{p-values})$ from the enrichment test vs. the estimated enrichment ratio $\hat{q}_{1j}/\hat{q}_{0j}$, $j = 1, \dots, 205$, where \hat{q}_{1j} and \hat{q}_{0j} denote the estimated proportions of non-null and null SNPs with the j -th annotation, respectively. The 95% confidence intervals are depicted with vertical lines for each individual annotation. The red dashed vertical line corresponds to Bonferroni cut-off at significance level of 0.1 and the red dashed horizontal line corresponds to the equal enrichment of annotations in the estimated null and non-null GWAS SNP sets.



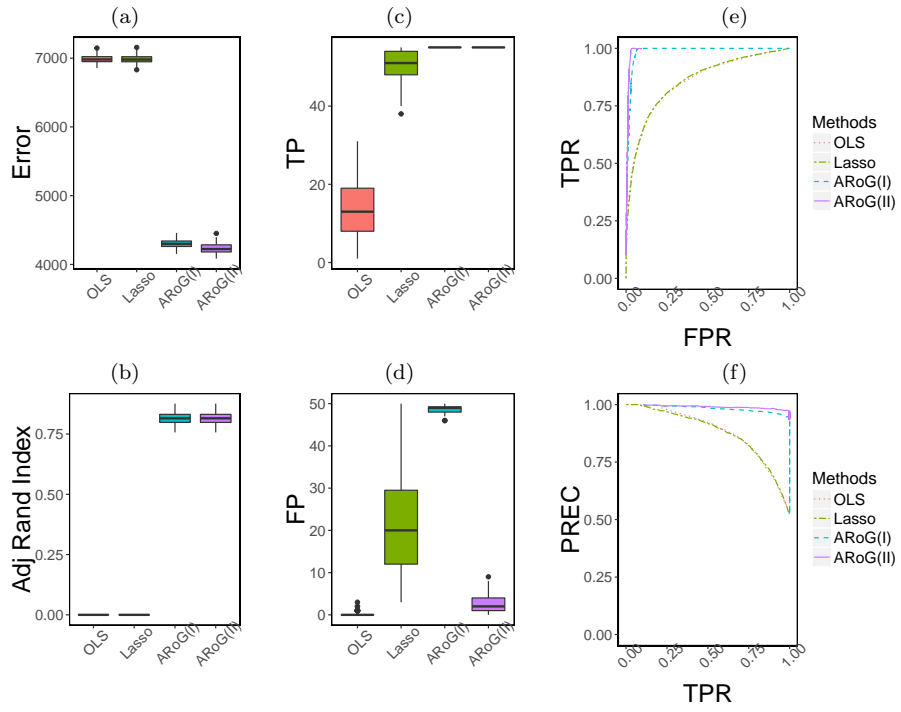
Supplementary Figure 4. SCZ2 z-scores vs. annotation scores of FOXL1, Klf4 TFs selected for cluster 5 and Arnt::Ahr and FOXL1 TFs selected for cluster 6. Both marginal linear regression and ARoG line fits are included.



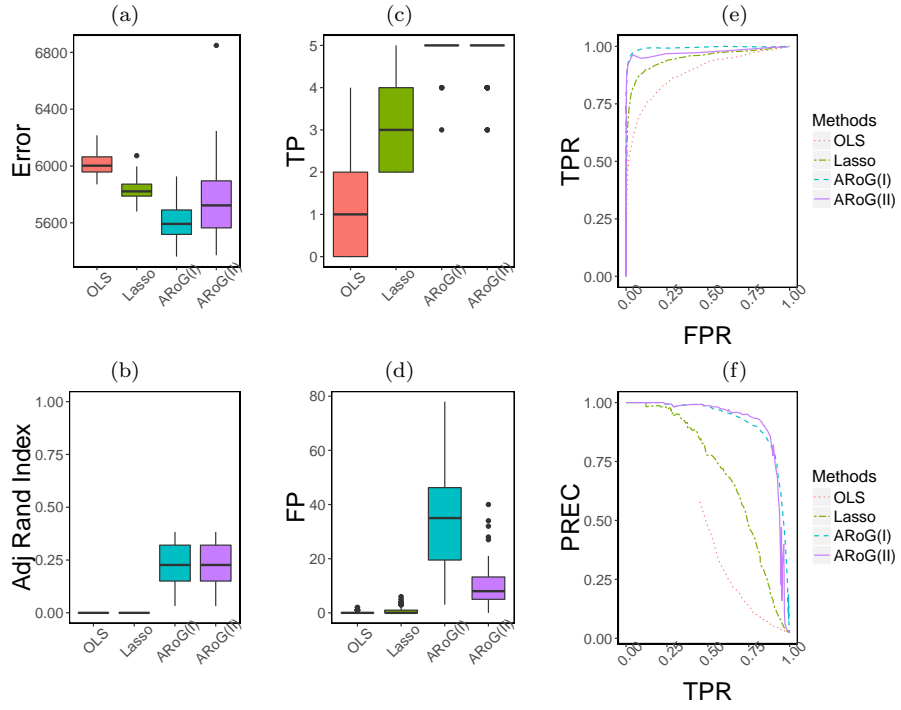
Supplementary Figure 5. Application of GPA [9] to the SCZ2 dataset. The plot depicts $-\log_{10}(\text{p-values})$ from the enrichment test vs. the estimated enrichment ratio $\hat{q}_{1j}/\hat{q}_{0j}$, $j = 1, \dots, 205$, where \hat{q}_{1j} and \hat{q}_{0j} denote the estimated proportions of non-null and null SNPs with the j -th annotation, respectively. The 95% confidence intervals are depicted with vertical lines for each individual annotation. The red dashed vertical line corresponds to Bonferroni cut-off at significance level of 0.1 and the red dashed horizontal line corresponds to the equal enrichment of annotations in the estimated null and non-null GWAS SNP sets.



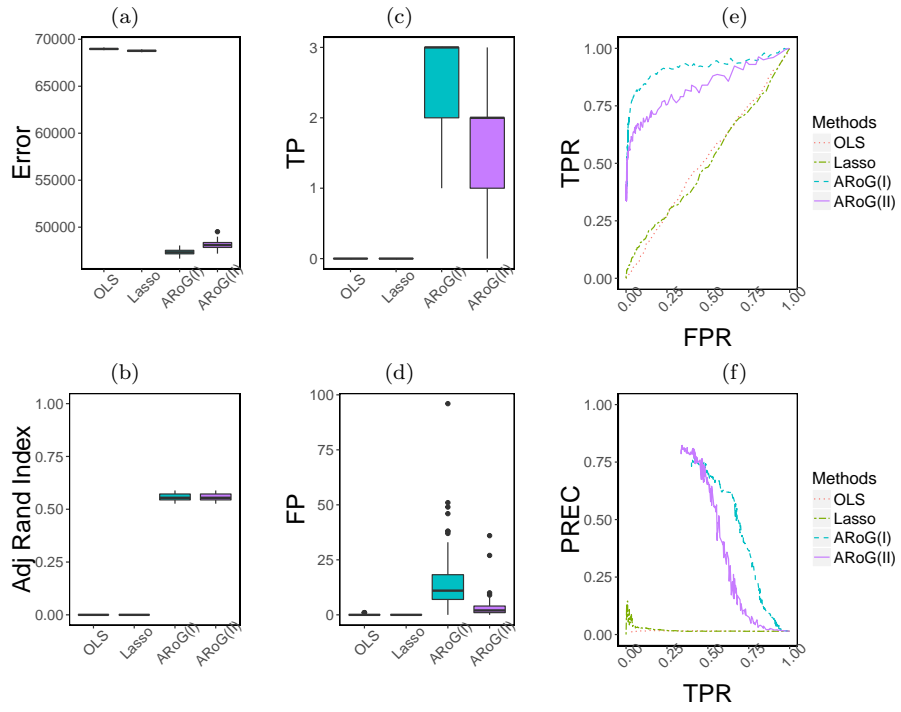
Supplementary Figure 6. Simulation results for Sparse(I) setting of Table 3.



Supplementary Figure 7. Simulation results for Intermediate(I) setting of Table 3.



Supplementary Figure 8. Simulation results from Supplementary Table 2 setting.



Supplementary Figure 9. Simulation results for the SCZ2 data analysis driven setting.