

Supplement
Table S1. TWAS results.

| Gene | Z-score | p-value | Significant |
|---------------------------|-----------|----------|-------------|
| Amigdala | | | |
| PTPN22 | -3.910881 | 0.000092 | yes |
| ADAM33 | 3.667582 | 0.000245 | no |
| PEX13 | 3.535061 | 0.000408 | no |
| PHTF1 | 3.514200 | 0.000441 | no |
| ACER2 | -3.487440 | 0.000488 | no |
| Anterior cingulate cortex | | | |
| LRRC25 | -4.236971 | 0.000040 | yes |
| PRB2 | 3.698503 | 0.000217 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| CSF2RB | 3.397982 | 0.000679 | no |
| FAM120AOS | -3.394392 | 0.000688 | no |
| Caudate basal ganglia | | | |
| PHTF1 | 3.837777 | 0.000124 | no |
| CPNE7 | -3.802630 | 0.000143 | no |
| PSMG3 | -3.690272 | 0.000224 | no |
| PEX13 | 3.638209 | 0.000275 | no |
| DLX6 | 3.553400 | 0.000380 | no |
| Cerebellar Hemisphere | | | |
| HSPBP1 | 3.695897 | 0.000219 | no |
| PSMG3 | -3.636988 | 0.000276 | no |
| SH2D7 | -3.622768 | 0.000291 | no |
| PHTF1 | 3.514200 | 0.000441 | no |
| SH3BP5L | -3.509282 | 0.000449 | no |
| Cerebellum | | | |
| LRRC25 | -4.215465 | 0.000032 | yes |
| PHTF1 | 3.514200 | 0.000441 | no |
| RP11-560J1.2 | -3.473626 | 0.000513 | no |
| CPSF2 | -3.370074 | 0.000751 | no |

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|---------------------------------|-----------|----------|-----|
| SHF | 3.348304 | 0.000813 | no |
| Cortex | | | |
| LRRC25 | -4.117557 | 0.000038 | yes |
| SHF | -3.668321 | 0.000244 | no |
| DUOX1 | -3.647572 | 0.000265 | no |
| PEX13 | 3.638209 | 0.000275 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| Frontal Cortex | | | |
| TMEM14A | 3.622834 | 0.000291 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| PEX13 | 3.535061 | 0.000408 | no |
| RP11-560J1.2 | -3.466095 | 0.000528 | no |
| LINC00390 | -3.386918 | 0.000707 | no |
| Hippocampus | | | |
| AP1S3 | -3.551922 | 0.000382 | no |
| PHTF1 | 3.514200 | 0.000441 | no |
| PRB2 | 3.489408 | 0.000484 | no |
| DUOX1 | -3.342924 | 0.000829 | no |
| ADAM33 | 3.250358 | 0.001153 | no |
| Hypothalamus | | | |
| LRRC25 | -4.001752 | 0.000055 | yes |
| PRB2 | 3.792066 | 0.000149 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| PEX13 | 3.535061 | 0.000408 | no |
| ELANE | -3.523711 | 0.000426 | no |
| Nucleus accumbens basal ganglia | | | |
| DUSP26 | 3.657454 | 0.000255 | no |
| PEX13 | 3.638209 | 0.000275 | no |
| AC016995.3 | -3.615122 | 0.000300 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| TMEM14A | 3.516764 | 0.000437 | no |
| Putamen basal ganglia | | | |

| | | | |
|--------------------------|-----------|----------|-----|
| RASA1 | -3.847408 | 0.000119 | no |
| PSMG3 | -3.732257 | 0.000190 | no |
| DLX6 | 3.582232 | 0.000341 | no |
| NUPR2 | 3.538227 | 0.000403 | no |
| PEX13 | 3.535061 | 0.000408 | no |
| Spinal cord cervical c-1 | | | |
| LRRC25 | -4.116764 | 0.000061 | yes |
| PHTF1 | 3.837777 | 0.000124 | no |
| PSMG3 | -3.700981 | 0.000215 | no |
| ALKBH1 | 3.671495 | 0.000241 | no |
| SH3BP5L | -3.504508 | 0.000457 | no |
| Substantia nigra | | | |
| LRRC25 | -4.102217 | 0.000092 | yes |
| SH2D7 | -3.705672 | 0.000211 | no |
| PHTF1 | 3.514200 | 0.000441 | no |
| C1orf123 | 3.417137 | 0.000633 | no |
| RP11-560J1.2 | -3.392242 | 0.000693 | no |

Note: Table presents 5 most significant genes in each brain part. Z-score>0 reflects upregulation of the gene and Z-score<0 reflects downregulation. The gene is significantly associated with cognitive impairment when $p\text{-value}<10^{-4}$.

Table S2. TWAS results for genes in the HALLMARK_PEROXISOME functional pathway.

| Gene | Z-score |
|--------|------------------|
| PEX13 | 3.63820886611938 |
| CLN6 | 2.67555570602417 |
| PRDX1 | 2.1304612159729 |
| CAT | 2.0485897064209 |
| FABP6 | 1.98931562900543 |
| FADS1 | 1.97097682952881 |
| ACSL1 | 1.73572699102896 |
| SEMA3C | 1.72525085686867 |
| LONP2 | 1.47963955172447 |

| | |
|---------|--------------------|
| IDE | 1.45531608775552 |
| ALDH9A1 | 1.44688725471497 |
| CRABP1 | 1.44518518447876 |
| NR1I2 | 1.4104517698288 |
| ECI2 | 1.31663165681787 |
| CTPS1 | 1.30026899642072 |
| YWHAH | 1.18796241283417 |
| PEX6 | 1.18560476630797 |
| MVP | 1.17668211460114 |
| ABCB1 | 1.12266480922699 |
| DLG4 | 0.959067106246948 |
| ATXN1 | 0.95817244052887 |
| PEX5 | 0.914699076559399 |
| ABCD2 | 0.888072848320007 |
| ABCC5 | 0.869463324546814 |
| HRAS | 0.839134971993951 |
| CTBP1 | 0.819535734044322 |
| TSPO | 0.639193713665009 |
| ACSL5 | 0.630192832736629 |
| IDH2 | 0.59225117554574 |
| EPHX2 | 0.58408540903497 |
| NUDT19 | 0.491290356768309 |
| CACNA1B | 0.491262867277656 |
| ALB | 0.463138925188247 |
| VPS4B | 0.431010156869888 |
| TTR | 0.399503260850906 |
| SULT2B1 | 0.231715073335768 |
| CLN8 | 0.131551551428588 |
| RDH11 | 0.102856811678627 |
| ACOX1 | 0.0733462043704366 |

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|----------|----------------------|
| PEX11B | 0.070492334663868 |
| SLC25A4 | 0.0358498468995094 |
| SLC25A17 | 0.0358004282490421 |
| HSD17B11 | 0.0162292336331964 |
| BCL10 | -0.00241431292544185 |
| ABCD3 | -0.039922684431076 |
| HMGCL | -0.0734709141387598 |
| CDK7 | -0.0790873616933823 |
| SCP2 | -0.102061940059026 |
| GNPAT | -0.10984994218952 |
| DHRS3 | -0.120071083307266 |
| CRABP2 | -0.192239640746695 |
| HSD3B7 | -0.192381531000137 |
| ISOC1 | -0.194867442135236 |
| PRDX5 | -0.257052481174469 |
| PEX11A | -0.318717662768062 |
| ABCB4 | -0.321846929709755 |
| MLYCD | -0.329452773788221 |
| ERCC3 | -0.362680524587631 |
| HSD17B4 | -0.408148258924484 |
| ECH1 | -0.411122857250775 |
| ELOVL5 | -0.498216636857585 |
| SLC35B2 | -0.645164489746094 |
| SMARCC1 | -0.671024193154455 |
| IDH1 | -0.672808706760406 |
| ABCC8 | -0.815831466189483 |
| ITGB1BP1 | -0.926862321708576 |
| CNBP | -0.961186528205872 |
| ACOT8 | -1.05210288126392 |
| SLC27A2 | -1.05491077479041 |

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|-------|-------------------|
| SOD1 | -1.09255468845367 |
| PEX2 | -1.18128180503845 |
| ABCB9 | -1.27028942108154 |
| ACAA1 | -1.64269626140594 |
| FIS1 | -1.64325511455536 |
| CRAT | -1.89146685600281 |