# Supplementary Information: Elucidating the genetic basis of an oligogenic birth defect using whole genome sequence data in a non-model organism, *Bubalus bubalis*

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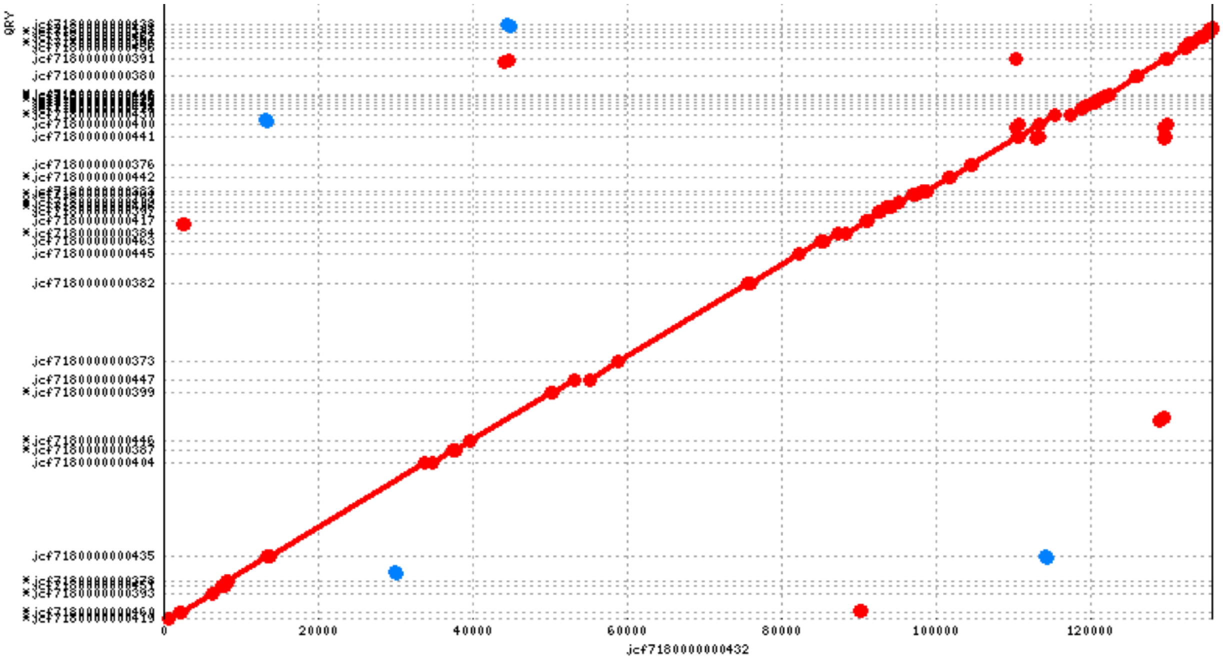

**Figure S1.** Dot plot of multiple contigs comprising the *SMARCA4* gene region in controls *versus* a single contig comprising the *SMARCA4* gene region in cases indicates increased homozygosity in *SMARCA4* in affected animals.

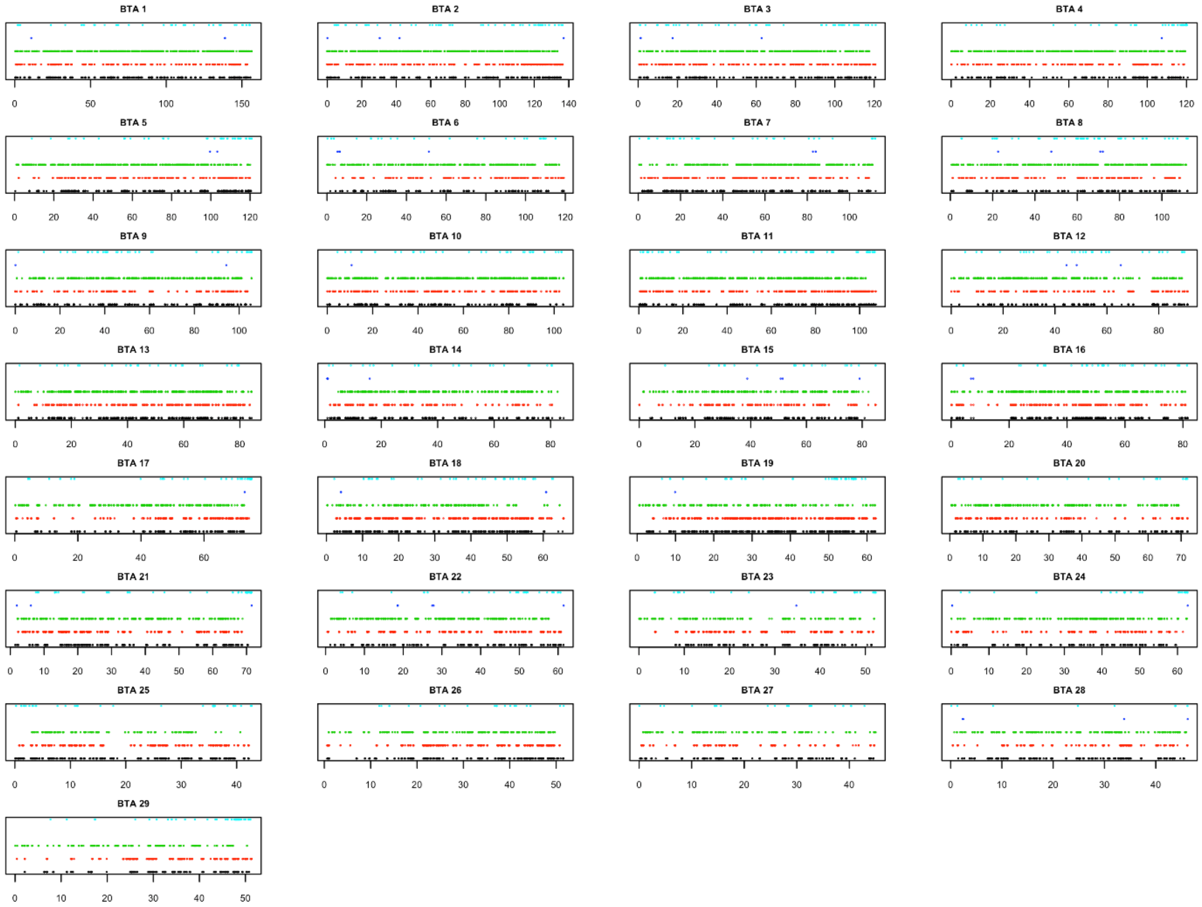

**Figure S2.** Mapping of regions significantly associated with TH to the *Bos taurus* UMD3.1 reference assembly from bilaterally affected case homozygosity mapping (black), unilaterally affected case homozygosity mapping (red), control homozygosity mapping (green), GWAS (dark blue), and SNP concordance analysis (light blue).

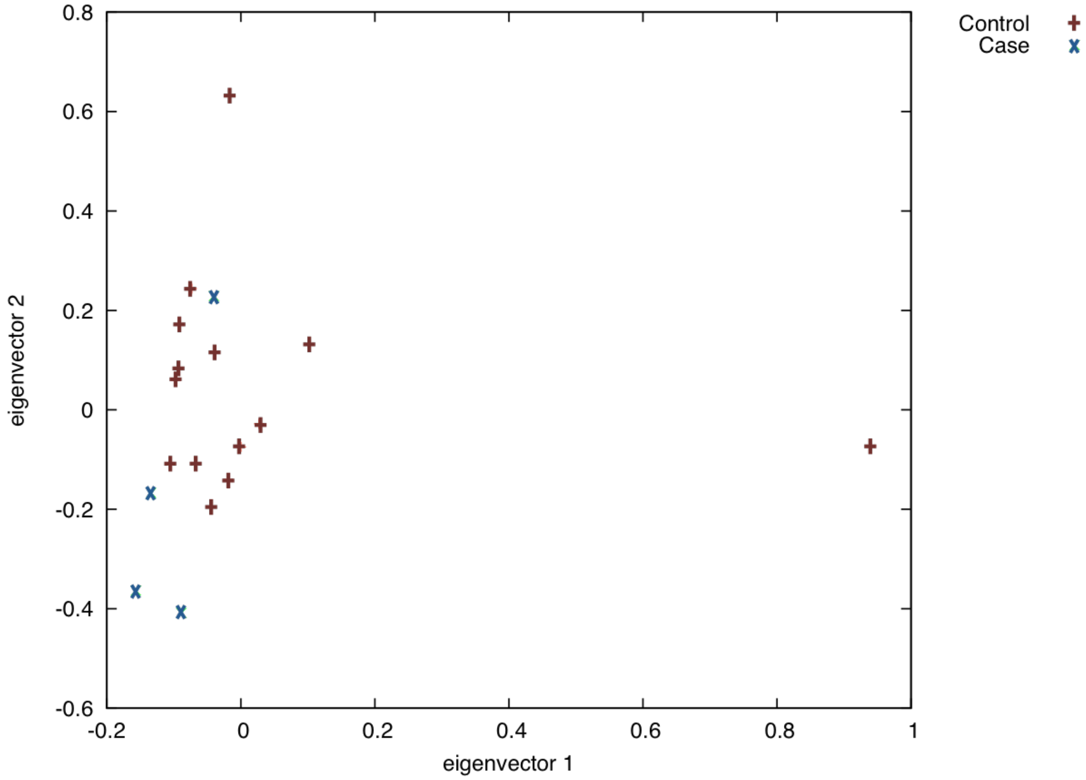

**Figure S3.** Principal component analysis of genotypes for 11 TH affected cases and 14 controls.

**Table S1.** Phenotypes and genome sequencing statistics from 11 TH affected cases and 14 unaffected controls.

| Sample ID | Total Reads* | Percent Reads Mapped | Percent Mapped with Proper Pairing | Average Genome Coverage | TH Phenotype | TH Phenotype Score | SRA Sample Accession | SRA Experiment Accession | SRA Run Accession |
|---|---|---|---|---|---|---|---|---|---|
| 189 | 472,339,399 | 99.47 | 96.08 | 15.66 | Unilateral case (left hindlimb at tarsus) | 7 | SRS1766349 | SRX2281272 | SRR4477894 |
| 190 | 249,980,539 | 98.80 | 94.47 | 9.86 | Unilateral case (left hindlimb at tarsus) | 7 | SRS1766350 | SRX2281273 | SRR4477895 |
| 196 | 395,803,651 | 99.24 | 94.74 | 14.74 | Unilateral case (left hindlimb at tarsus) | 7 | SRS1766351 | SRX2281274 | SRR4477896 |
| 246 | 269,083,067 | 98.74 | 94.44 | 10.44 | Unilateral case (left hindlimb at tarsus) | 7 | SRS1766352 | SRX2281275 | SRR4477897 |
| 337 | 318,870,658 | 98.76 | 94.85 | 11.44 | Bilateral case (both hindlimbs amputated) | 0 | SRS1766370 | SRX2281293 | SRR4477890 |
| 581 | 291,440,073 | 98.96 | 94.09 | 11.23 | Unilateral case (left hindlimb at metatarsus) | 8 | SRS1766353 | SRX2281276 | SRR4477898 |
| 583 | 348,139,255 | 98.78 | 94.49 | 11.56 | Bilateral case (both hindlimbs at fetlock) | 8 | SRS1766371 | SRX2281294 | SRR4477891 |
| 662 | 372,645,970 | 99.26 | 95.09 | 14.35 | Unilateral case (left hindlimb) | 5 | SRS1766354 | SRX2281277 | SRR4477899 |
| 701 | 339,444,712 | 98.51 | 94.59 | 12.37 | Bilateral case (both hindlimbs at stifle) | 2 | SRS1766372 | SRX2281295 | SRR4477892 |
| 850 | 330,371,536 | 98.78 | 94.98 | 12.32 | Bilateral case (both hindlimbs amputated) | 0 | SRS1766373 | SRX2281296 | SRR4477893 |
| 1095 | 192,273,051 | 98.85 | 94.80 | 7.63 | Unilateral case (left hindlimb at metatarsus) | 8 | SRS1766355 | SRX2281278 | SRR4477900 |
| 92764 | 237,146,401 | 99.53 | 96.45 | 7.34 | Control | 10 | SRS1766356 | SRX2281279 | SRR4477876 |
| 92765 | 293,097,788 | 99.50 | 96.40 | 8.11 | Control | 10 | SRS1766357 | SRX2281280 | SRR4477877 |
| 92766 | 278,841,904 | 99.51 | 96.37 | 7.92 | Control | 10 | SRS1766358 | SRX2281281 | SRR4477878 |
| 92767 | 302,482,388 | 99.56 | 96.98 | 8.86 | Control | 10 | SRS1766359 | SRX2281282 | SRR4477879 |
| 92768 | 235,770,765 | 99.57 | 95.60 | 7.43 | Control | 10 | SRS1766360 | SRX2281283 | SRR4477880 |
| 92769 | 198,150,064 | 98.38 | 95.11 | 3.28 | Control | 10 | SRS1766361 | SRX2281284 | SRR4477881 |
| 92770 | 290,662,225 | 99.61 | 97.35 | 9.02 | Control | 10 | SRS1766362 | SRX2281285 | SRR4477882 |
| 92771 | 252,165,270 | 99.62 | 97.36 | 8.45 | Control | 10 | SRS1766363 | SRX2281286 | SRR4477883 |
| 92774 | 328,856,248 | 99.44 | 90.37 | 6.66 | Control | 10 | SRS1766364 | SRX2281287 | SRR4477884 |

|  |  |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|
| 92775 | 339,570,423 | 99.14 | 87.01 | 6.63 | Control | 10 | SRS1766365 | SRX2281288 | SRR4477885 |
| 92776 | 326,975,621 | 99.36 | 90.76 | 6.54 | Control | 10 | SRS1766366 | SRX2281289 | SRR4477886 |
| 92777 | 281,036,266 | 98.72 | 85.69 | 4.57 | Control | 10 | SRS1766367 | SRX2281290 | SRR4477887 |
| 92778 | 326,105,820 | 99.53 | 93.71 | 7.47 | Control | 10 | SRS1766368 | SRX2281291 | SRR4477888 |
| 92795 | 151,865,510 | 99.54 | 84.69 | 4.80 | Control | 10 | SRS1766369 | SRX2281292 | SRR4477889 |
| Average | 296,924,744 | 99.17 | 93.86 | 9.15 |  |  |  |  |  |

*After quality filtering

**Table S2.** Variant call rates for cases and controls.

| Sample ID | Missing Genotypes | Total Genotypes | Frequency of Missing |
|---|---|---|---|
| 1095 | 705,137 | 19,829,264 | 0.0356 |
| 189 | 318,869 | 19,829,264 | 0.0161 |
| 190 | 483,836 | 19,829,264 | 0.0244 |
| 196 | 320,074 | 19,829,264 | 0.0161 |
| 246 | 428,965 | 19,829,264 | 0.0216 |
| 337 | 361,217 | 19,829,264 | 0.0182 |
| 581 | 385,264 | 19,829,264 | 0.0194 |
| 583 | 341,047 | 19,829,264 | 0.0172 |
| 662 | 287,239 | 19,829,264 | 0.0145 |
| 701 | 329,280 | 19,829,264 | 0.0166 |
| 850 | 347,345 | 19,829,264 | 0.0175 |
| 92764 | 1,293,640 | 19,829,264 | 0.0652 |
| 92765 | 1,318,679 | 19,829,264 | 0.0665 |
| 92766 | 1,204,282 | 19,829,264 | 0.0607 |
| 92767 | 943,547 | 19,829,264 | 0.0476 |
| 92768 | 1,161,960 | 19,829,264 | 0.0586 |
| 92769 | 5,517,056 | 19,829,264 | 0.2782 |
| 92770 | 945,464 | 19,829,264 | 0.0477 |
| 92771 | 883,420 | 19,829,264 | 0.0446 |
| 92774 | 1,726,724 | 19,829,264 | 0.0871 |
| 92775 | 1,787,533 | 19,829,264 | 0.0902 |
| 92776 | 1,793,981 | 19,829,264 | 0.0905 |
| 92777 | 2,860,236 | 19,829,264 | 0.1442 |
| 92778 | 1,388,107 | 19,829,264 | 0.0700 |
| 92795 | 2,196,779 | 19,829,264 | 0.1108 |
| Case Mean | | | 0.0198 |
| Control Mean | | | 0.0901 |
| Total Mean | | | 0.0592 |

**Table S3.** *De novo* assembly statistics from pools of genome sequence data for four individuals.

| Sample Group | Pooled Coverage | Total Bases in Scaffolds | Number of Scaffolds | Scaffold N50 |
|---|---|---|---|---|
| Bilateral cases | 47.69 | 2,645,914,807 | 218,053 | 36,594 |
| Unilateral cases | 50.70 | 2,641,090,365 | 221,020 | 34,411 |
| Control | 31.96 | 2,563,943,329 | 541,203 | 8,898 |

**Table S4**. Significant GWAS associations under the binary phenotype model.

| Contig | Position | P-value | *Candidate gene(s)* |
|---|---|---|---|
| gi\|551741020\|ref\|NW_005765473.1\| | 1041 | 4.18E-10 | -- |
| gi\|551733415\|ref\|NW_005773077.1\| | 1806 | 1.76E-11 | -- |
| gi\|551732811\|ref\|NW_005773470.1\| | 858 | 2.88E-20 | -- |
| gi\|551731300\|ref\|NW_005774981.1\| | 6595 | 8.05E-11 | -- |
| gi\|551730022\|ref\|NW_005776259.1\| | 1637 | 8.16E-14 | -- |
| gi\|551729656\|ref\|NW_005776625.1\| | 4632 | 1.35E-08 | -- |
| gi\|551723571\|ref\|NW_005782710.1\| | 3036 | 1.63E-11 | -- |
| gi\|551721651\|ref\|NW_005784628.1\| | 324709 | 5.55E-19 | *LOC102406836* |
| gi\|551720955\|ref\|NW_005785322.1\| | 62402 | 1.09E-09 | *LOC102402736, LOC102402095* |
| gi\|551720771\|ref\|NW_005785506.1\| | 71732 | 3.45E-10 | -- |
| gi\|551720570\|ref\|NW_005785701.1\| | 458656 | 1.54E-10 | *CHAMP1* |
| gi\|552101018\|ref\|NW_005438356.1\| | 524 | 1.39E-08 | -- |
| gi\|552093047\|ref\|NW_005445879.1\| | 2664 | 2.80E-10 | -- |
| gi\|552029652\|ref\|NW_005499085.1\| | 592 | 3.56E-12 | -- |
| gi\|552021103\|ref\|NW_005507230.1\| | 1062 | 3.32E-12 | -- |
| gi\|551818273\|ref\|NW_005688295.1\| | 6134 | 3.32E-12 | -- |
| gi\|551818114\|ref\|NW_005688454.1\| | 2244 | 5.55E-19 | -- |
| gi\|551814314\|ref\|NW_005692254.1\| | 522 | 1.91E-11 | -- |

**Table S5**. Significant GWAS associations under the semi-quantitative phenotype model.

| Contig | Position | P-value | Candidate gene(s) |
|---|---|---|---|
| gi\|551723235\|ref\|NW_005783046.1\| | 2615 | 2.75E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1032062 | 4.23E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1032137 | 6.23E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1044302 | 2.75E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1050027 | 6.23E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1078885 | 4.68E-10 | -- |
| gi\|551722604\|ref\|NW_005783677.1\| | 1079152 | 2.09E-10 | -- |
| gi\|551722330\|ref\|NW_005783951.1\| | 288101 | 1.54E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 311320 | 4.84E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 323554 | 4.68E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 326651 | 4.23E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 337775 | 1.54E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 340646 | 2.09E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 356823 | 4.45E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 358391 | 6.23E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 358393 | 6.23E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 358958 | 2.09E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 359017 | 4.26E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 359399 | 2.09E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 361386 | 4.64E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 362978 | 4.68E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 363061 | 4.93E-10 | *ADAMTS16* |
| gi\|551722330\|ref\|NW_005783951.1\| | 363067 | 4.93E-10 | *ADAMTS16* |
| gi\|551721677\|ref\|NW_005784602.1\| | 9999 | 2.09E-10 | -- |
| gi\|551721677\|ref\|NW_005784602.1\| | 59585 | 1.54E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 59586 | 1.54E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 59627 | 6.23E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 76344 | 6.23E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 83868 | 4.68E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 84207 | 2.75E-10 | *PEX5L* |

|  |  |  |  |
|---|---|---|---|
| gi\|551721677\|ref\|NW_005784602.1\| | 92660 | 5.01E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 94269 | 4.93E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 94588 | 6.23E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 94796 | 4.93E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 94970 | 5.04E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 95368 | 6.23E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 95504 | 6.23E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 95648 | 2.75E-10 | *PEX5L* |
| gi\|551721677\|ref\|NW_005784602.1\| | 95764 | 2.75E-10 | *PEX5L* |
| gi\|551721597\|ref\|NW_005784682.1\| | 930485 | 1.16E-08 | -- |
| gi\|551721597\|ref\|NW_005784682.1\| | 944705 | 1.16E-08 | -- |
| gi\|551721575\|ref\|NW_005784704.1\| | 540038 | 4.68E-10 | *MIER3* |
| gi\|551721575\|ref\|NW_005784704.1\| | 547826 | 4.68E-10 | *MIER3* |
| gi\|551721575\|ref\|NW_005784704.1\| | 551466 | 4.68E-10 | *MIER3* |
| gi\|551721575\|ref\|NW_005784704.1\| | 553129 | 4.68E-10 | *MIER3* |
| gi\|551721575\|ref\|NW_005784704.1\| | 1161864 | 6.23E-10 | *ANKRD55* |
| gi\|551721575\|ref\|NW_005784704.1\| | 1161916 | 6.23E-10 | *ANKRD55* |
| gi\|551721409\|ref\|NW_005784868.1\| | 68605 | 1.54E-10 | -- |
| gi\|551721409\|ref\|NW_005784868.1\| | 96621 | 1.54E-10 | -- |
| gi\|551721409\|ref\|NW_005784868.1\| | 107282 | 1.54E-10 | -- |
| gi\|551721409\|ref\|NW_005784868.1\| | 107294 | 1.54E-10 | -- |
| gi\|551721409\|ref\|NW_005784868.1\| | 130154 | 1.54E-10 | -- |
| gi\|551721409\|ref\|NW_005784868.1\| | 163189 | 1.54E-10 | -- |
| gi\|551721329\|ref\|NW_005784948.1\| | 2011086 | 1.15E-08 | *MIOS* |
| gi\|551721209\|ref\|NW_005785068.1\| | 5901500 | 4.36E-10 | *ASCC1* |
| gi\|551721209\|ref\|NW_005785068.1\| | 5901586 | 1.15E-09 | *ASSC1* |
| gi\|551720917\|ref\|NW_005785360.1\| | 27661 | 4.40E-10 | *LOC102400491* |
| gi\|551720904\|ref\|NW_005785373.1\| | 6985 | 2.25E-11 | *FZD4* |
| gi\|551720904\|ref\|NW_005785373.1\| | 572932 | 4.95E-10 | *TMEM135, FZD4* |
| gi\|551720881\|ref\|NW_005785396.1\| | 1623273 | 6.23E-10 | *FGFR1* |
| gi\|551720789\|ref\|NW_005785488.1\| | 1398022 | 4.80E-10 | *CCSER2* |
| gi\|551720688\|ref\|NW_005785589.1\| | 1335886 | 4.26E-10 | *SKAP1* |
| gi\|551720649\|ref\|NW_005785623.1\| | 1084940 | 4.23E-10 | *GRM5* |

| | | | |
|---|---|---|---|
| gi\|551720521\|ref\|NW_005785747.1\| | 19920 | 1.66E-08 | *LOC102412685* |
| gi\|551720521\|ref\|NW_005785747.1\| | 427178 | 1.15E-09 | *DDIT4* |
| gi\|551767899\|ref\|NW_005738669.1\| | 1277 | 2.75E-10 | -- |

**Table S6.** Model statistics from binary and semi-quantitative GWAS.

| | **Binary Phenotype** | **Quantitative Phenotype** |
|---|---:|---:|
| Total SNPs | 19,829,264 | 19,829,264 |
| Analyzed SNPs | 2,990,419 | 2,990,419 |
| REMLE log-likelihood | -16.769 | -61.328 |
| MLE log-likelihood | -11.789 | -57.888 |
| pve estimate | 1.000 | 1.000E-05 |
| se(pve) | 0.005 | -nan |
| vg estimate | 0.767 | 9.707E-05 |
| ve estimate | 7.674E-06 | 9.707 |
| beta estimate | 0.440 | 7.960 |
| se(beta) | 0.001 | 0.623 |

**Table S11.** Significant results from gene ontology enrichment analysis with gProfileR.

| GO Term | GO ID | P-value |
|---|---|---|
| protein binding | GO:0005515 | 6.75E-14 |
| intracellular part | GO:0044424 | 7.64E-13 |
| intracellular | GO:0005622 | 3.58E-12 |
| system development | GO:0048731 | 8.54E-12 |
| cytoplasm | GO:0005737 | 1.59E-11 |
| single-organism process | GO:0044699 | 7.74E-11 |
| multicellular organism development | GO:0007275 | 9.95E-11 |
| positive regulation of biological process | GO:0048518 | 1.70E-10 |
| positive regulation of cellular process | GO:0048522 | 1.78E-10 |
| cellular process | GO:0009987 | 5.93E-10 |
| single-organism cellular process | GO:0044763 | 6.86E-10 |
| positive regulation of metabolic process | GO:0009893 | 1.44E-09 |
| anatomical structure development | GO:0048856 | 1.57E-09 |
| cytosol | GO:0005829 | 1.59E-09 |
| cellular component organization or biogenesis | GO:0071840 | 2.44E-09 |
| nervous system development | GO:0007399 | 4.67E-09 |
| positive regulation of gene expression | GO:0010628 | 5.11E-09 |
| cell differentiation | GO:0030154 | 6.94E-09 |
| developmental process | GO:0032502 | 7.04E-09 |
| single-organism developmental process | GO:0044767 | 7.67E-09 |
| animal organ development | GO:0048513 | 9.89E-09 |
| binding | GO:0005488 | 1.09E-08 |
| cellular component organization | GO:0016043 | 1.17E-08 |
| positive regulation of macromolecule metabolic process | GO:0010604 | 1.19E-08 |
| cytoplasmic part | GO:0044444 | 2.10E-08 |
| neurogenesis | GO:0022008 | 2.22E-08 |
| organelle | GO:0043226 | 2.45E-08 |
| negative regulation of biological process | GO:0048519 | 2.58E-08 |
| positive regulation of nitrogen compound metabolic process | GO:0051173 | 5.77E-08 |
| regulation of transcription from RNA polymerase II promoter | GO:0006357 | 6.38E-08 |

| | | |
|---|---|---|
| nervous system development | GO:0007399 | 8.45E-08 |
| positive regulation of macromolecule biosynthetic process | GO:0010557 | 8.45E-08 |
| generation of neurons | GO:0048699 | 1.07E-07 |
| negative regulation of cellular process | GO:0048523 | 1.20E-07 |
| regulation of signaling | GO:0023051 | 1.53E-07 |
| single-multicellular organism process | GO:0044707 | 2.38E-07 |
| cellular developmental process | GO:0048869 | 2.39E-07 |
| regulation of cell communication | GO:0010646 | 3.43E-07 |
| programmed cell death | GO:0012501 | 4.15E-07 |
| anatomical structure morphogenesis | GO:0009653 | 4.26E-07 |
| neuron differentiation | GO:0030182 | 5.08E-07 |
| positive regulation of nucleobase-containing compound metabolic process | GO:0045935 | 5.94E-07 |
| positive regulation of RNA metabolic process | GO:0051254 | 7.24E-07 |
| intracellular organelle | GO:0043229 | 7.43E-07 |
| transcription from RNA polymerase II promoter | GO:0006366 | 8.23E-07 |
| organelle part | GO:0044422 | 8.80E-07 |
| positive regulation of cellular metabolic process | GO:0031325 | 9.08E-07 |
| positive regulation of transcription, DNA-templated | GO:0045893 | 1.00E-06 |
| positive regulation of nucleic acid-templated transcription | GO:1903508 | 1.00E-06 |
| positive regulation of biosynthetic process | GO:0009891 | 1.09E-06 |
| positive regulation of RNA biosynthetic process | GO:1902680 | 1.17E-06 |
| membrane-bounded organelle | GO:0043227 | 1.33E-06 |
| intracellular membrane-bounded organelle | GO:0043231 | 1.33E-06 |
| intracellular organelle part | GO:0044446 | 1.64E-06 |
| localization | GO:0051179 | 1.67E-06 |
| regulation of signal transduction | GO:0009966 | 1.80E-06 |
| biological_process | GO:0008150 | 2.32E-06 |
| positive regulation of cellular biosynthetic process | GO:0031328 | 2.36E-06 |
| positive regulation of transcription from RNA polymerase II promoter | GO:0045944 | 2.38E-06 |
| cell death | GO:0008219 | 2.48E-06 |
| apoptotic process | GO:0006915 | 2.71E-06 |
| cellular macromolecule metabolic process | GO:0044260 | 3.84E-06 |
| metabolic process | GO:0008152 | 8.71E-06 |

| | | |
|---|---|---|
| cell | GO:0005623 | 9.74E-06 |
| establishment of localization in cell | GO:0051649 | 1.06E-05 |
| cell development | GO:0048468 | 1.27E-05 |
| nuclear part | GO:0044428 | 1.82E-05 |
| regulation of molecular function | GO:0065009 | 2.17E-05 |
| cell part | GO:0044464 | 2.41E-05 |
| cell morphogenesis involved in differentiation | GO:0000904 | 2.58E-05 |
| establishment of localization | GO:0051234 | 2.84E-05 |
| single-organism localization | GO:1902578 | 2.93E-05 |
| cellular component organization | GO:0016043 | 3.00E-05 |
| localization | GO:0051179 | 3.42E-05 |
| cellular localization | GO:0051641 | 3.48E-05 |
| neuron part | GO:0097458 | 3.48E-05 |
| cellular metabolic process | GO:0044237 | 3.68E-05 |
| anatomical structure development | GO:0048856 | 4.03E-05 |
| regulation of cell death | GO:0010941 | 4.25E-05 |
| cell development | GO:0048468 | 5.26E-05 |
| macromolecule metabolic process | GO:0043170 | 6.37E-05 |
| transcription factor binding | GO:0008134 | 0.000118 |
| regulation of programmed cell death | GO:0043067 | 0.000119 |
| cellular_component | GO:0005575 | 0.000122 |
| multicellular organism development | GO:0007275 | 0.000156 |
| cellular component organization or biogenesis | GO:0071840 | 0.000156 |
| regulation of response to stimulus | GO:0048583 | 0.00018 |
| generation of neurons | GO:0048699 | 0.000189 |
| single-organism transport | GO:0044765 | 0.00021 |
| cellular component assembly | GO:0022607 | 0.000295 |
| cellular protein metabolic process | GO:0044267 | 0.000297 |
| nuclear lumen | GO:0031981 | 0.00034 |
| cell projection | GO:0042995 | 0.000353 |
| nucleoplasm | GO:0005654 | 0.000361 |
| axon development | GO:0061564 | 0.000378 |
| regulation of catalytic activity | GO:0050790 | 0.000391 |

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|---|---|---|
| regulation of metabolic process | GO:0019222 | 0.000393 |
| regulation of apoptotic process | GO:0042981 | 0.000416 |
| intracellular signal transduction | GO:0035556 | 0.000426 |
| neuron part | GO:0097458 | 0.000456 |
| macromolecular complex binding | GO:0044877 | 0.000476 |
| neurogenesis | GO:0022008 | 0.000477 |
| regulation of cellular component organization | GO:0051128 | 0.000483 |
| transport | GO:0006810 | 0.000485 |
| system development | GO:0048731 | 0.000527 |
| sequence-specific DNA binding | GO:0043565 | 0.00053 |
| cell surface receptor signaling pathway | GO:0007166 | 0.000532 |
| regulation of developmental process | GO:0050793 | 0.000551 |
| organic substance metabolic process | GO:0071704 | 0.000551 |
| protein binding | GO:0005515 | 0.00061 |
| regulation of macromolecule metabolic process | GO:0060255 | 0.000642 |
| intracellular organelle lumen | GO:0070013 | 0.000672 |
| regulation of intracellular signal transduction | GO:1902531 | 0.000787 |
| central nervous system development | GO:0007417 | 0.000838 |
| synapse | GO:0045202 | 0.000866 |
| single-organism cellular process | GO:0044763 | 0.000877 |
| movement of cell or subcellular component | GO:0006928 | 0.000892 |
| axonogenesis | GO:0007409 | 0.000903 |
| regulation of multicellular organismal development | GO:2000026 | 0.000934 |
| synaptic transmission | GO:0007268 | 0.000961 |
| synaptic signaling | GO:0099536 | 0.000961 |
| trans-synaptic signaling | GO:0099537 | 0.000961 |
| cell junction | GO:0030054 | 0.000992 |
| cell morphogenesis | GO:0000902 | 0.001 |
| cell-cell signaling | GO:0007267 | 0.00107 |
| organelle lumen | GO:0043233 | 0.0011 |
| cellular component morphogenesis | GO:0032989 | 0.00113 |
| axon guidance | GO:0007411 | 0.00135 |
| neuron projection guidance | GO:0097485 | 0.00135 |

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|---|---|---|
| positive regulation of biological process | GO:0048518 | 0.0017 |
| neuron development | GO:0048666 | 0.00172 |
| cytoplasm | GO:0005737 | 0.00173 |
| developmental process | GO:0032502 | 0.002 |
| cytoplasmic part | GO:0044444 | 0.00205 |
| cell projection | GO:0042995 | 0.00217 |
| single-organism developmental process | GO:0044767 | 0.00219 |
| neuron differentiation | GO:0030182 | 0.00223 |
| regulation of multicellular organismal process | GO:0051239 | 0.00228 |
| cellular nitrogen compound biosynthetic process | GO:0044271 | 0.00238 |
| regulatory region DNA binding | GO:0000975 | 0.00239 |
| RNA polymerase II transcription factor activity, sequence-specific DNA binding | GO:0000981 | 0.0024 |
| membrane-enclosed lumen | GO:0031974 | 0.00246 |
| neuron development | GO:0048666 | 0.0025 |
| regulatory region nucleic acid binding | GO:0001067 | 0.00256 |
| protein complex | GO:0043234 | 0.00303 |
| transcription regulatory region DNA binding | GO:0044212 | 0.00343 |
| regulation of localization | GO:0032879 | 0.00353 |
| sensory organ development | GO:0007423 | 0.00371 |
| neuron projection | GO:0043005 | 0.00391 |
| regulation of nervous system development | GO:0051960 | 0.00423 |
| binding | GO:0005488 | 0.00435 |
| regulation of cell development | GO:0060284 | 0.00435 |
| response to organic substance | GO:0010033 | 0.00441 |
| nucleus | GO:0005634 | 0.00445 |
| tube morphogenesis | GO:0035239 | 0.00456 |
| single-organism process | GO:0044699 | 0.00479 |
| positive regulation of cellular process | GO:0048522 | 0.00484 |
| movement of cell or subcellular component | GO:0006928 | 0.00507 |
| negative regulation of macromolecule metabolic process | GO:0010605 | 0.0052 |
| vesicle-mediated transport | GO:0016192 | 0.0054 |
| presynaptic process involved in synaptic transmission | GO:0099531 | 0.00554 |
| protein metabolic process | GO:0019538 | 0.00569 |

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|---|---|---|
| regulation of cell differentiation | GO:0045595 | 0.00574 |
| regulation of hydrolase activity | GO:0051336 | 0.006 |
| cell morphogenesis involved in neuron differentiation | GO:0048667 | 0.00616 |
| regulation of cell proliferation | GO:0042127 | 0.00631 |
| regulation of transport | GO:0051049 | 0.00647 |
| primary metabolic process | GO:0044238 | 0.00658 |
| tissue development | GO:0009888 | 0.00672 |
| cellular response to organic substance | GO:0071310 | 0.00675 |
| neuron projection morphogenesis | GO:0048812 | 0.00712 |
| double-stranded DNA binding | GO:0003690 | 0.00714 |
| cellular component biogenesis | GO:0044085 | 0.00823 |
| neuron projection development | GO:0031175 | 0.00844 |
| signaling | GO:0023052 | 0.00856 |
| cell projection organization | GO:0030030 | 0.00969 |
| single-multicellular organism process | GO:0044707 | 0.00969 |
| neuron projection | GO:0043005 | 0.00999 |
| endomembrane system organization | GO:0010256 | 0.0102 |
| regulation of cellular protein metabolic process | GO:0032268 | 0.011 |
| intracellular part | GO:0044424 | 0.0113 |
| gene expression | GO:0010467 | 0.0117 |
| actin filament-based process | GO:0030029 | 0.0118 |
| regulation of neurotransmitter levels | GO:0001505 | 0.0121 |
| actin cytoskeleton organization | GO:0030036 | 0.0128 |
| secretion | GO:0046903 | 0.0128 |
| signal release | GO:0023061 | 0.013 |
| single organism signaling | GO:0044700 | 0.013 |
| organ morphogenesis | GO:0009887 | 0.0135 |
| regulation of localization | GO:0032879 | 0.0137 |
| organelle organization | GO:0006996 | 0.0138 |
| positive regulation of cellular component organization | GO:0051130 | 0.0139 |
| regulation of cellular metabolic process | GO:0031323 | 0.0144 |
| cell communication | GO:0007154 | 0.0146 |
| negative regulation of cellular metabolic process | GO:0031324 | 0.0147 |

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|---|---|---|
| organelle localization | GO:0051640 | 0.0147 |
| neurotransmitter transport | GO:0006836 | 0.015 |
| chemotaxis | GO:0006935 | 0.0153 |
| cell proliferation | GO:0008283 | 0.0154 |
| taxis | GO:0042330 | 0.0162 |
| embryo development | GO:0009790 | 0.0163 |
| signal release from synapse | GO:0099643 | 0.0164 |
| neuron projection development | GO:0031175 | 0.0165 |
| neurotransmitter secretion | GO:0007269 | 0.0178 |
| regulation of protein metabolic process | GO:0051246 | 0.0182 |
| multicellular organismal process | GO:0032501 | 0.0188 |
| negative regulation of metabolic process | GO:0009892 | 0.019 |
| tube development | GO:0035295 | 0.0196 |
| cell projection organization | GO:0030030 | 0.0199 |
| positive regulation of molecular function | GO:0044093 | 0.0199 |
| regulation of transmembrane transport | GO:0034762 | 0.0214 |
| negative regulation of signaling | GO:0023057 | 0.0221 |
| cell differentiation | GO:0030154 | 0.0242 |
| sequence-specific double-stranded DNA binding | GO:1990837 | 0.0246 |
| negative regulation of protein modification process | GO:0031400 | 0.0253 |
| synapse part | GO:0044456 | 0.0256 |
| regulation of cellular process | GO:0050794 | 0.0285 |
| transcription regulatory region sequence-specific DNA binding | GO:0000976 | 0.0286 |
| nitrogen compound metabolic process | GO:0006807 | 0.0299 |
| macromolecular complex | GO:0032991 | 0.0303 |
| regulation of anatomical structure morphogenesis | GO:0022603 | 0.0308 |
| macromolecular complex | GO:0032991 | 0.0341 |
| cellular nitrogen compound metabolic process | GO:0034641 | 0.0357 |
| positive regulation of cellular component organization | GO:0051130 | 0.0368 |
| regulation of cellular component organization | GO:0051128 | 0.0382 |
| locomotion | GO:0040011 | 0.0384 |
| cell | GO:0005623 | 0.0406 |
| negative regulation of transcription from RNA polymerase II promoter | GO:0000122 | 0.0418 |

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|---|---|---|
| negative regulation of cell communication | GO:0010648 | 0.0422 |
| regulation of nervous system development | GO:0051960 | 0.0422 |
| cytoskeleton organization | GO:0007010 | 0.0438 |
| regulation of neurogenesis | GO:0050767 | 0.0439 |
| regulation of cell development | GO:0060284 | 0.0449 |
| cellular protein modification process | GO:0006464 | 0.05 |
| peroxisome organization | GO:0007031 | 0.05 |
| protein localization | GO:0008104 | 0.05 |
| protein modification process | GO:0036211 | 0.05 |