# SUPPORTING INFORMATION

for

## Database-assisted screening of autism spectrum disorder related gene set

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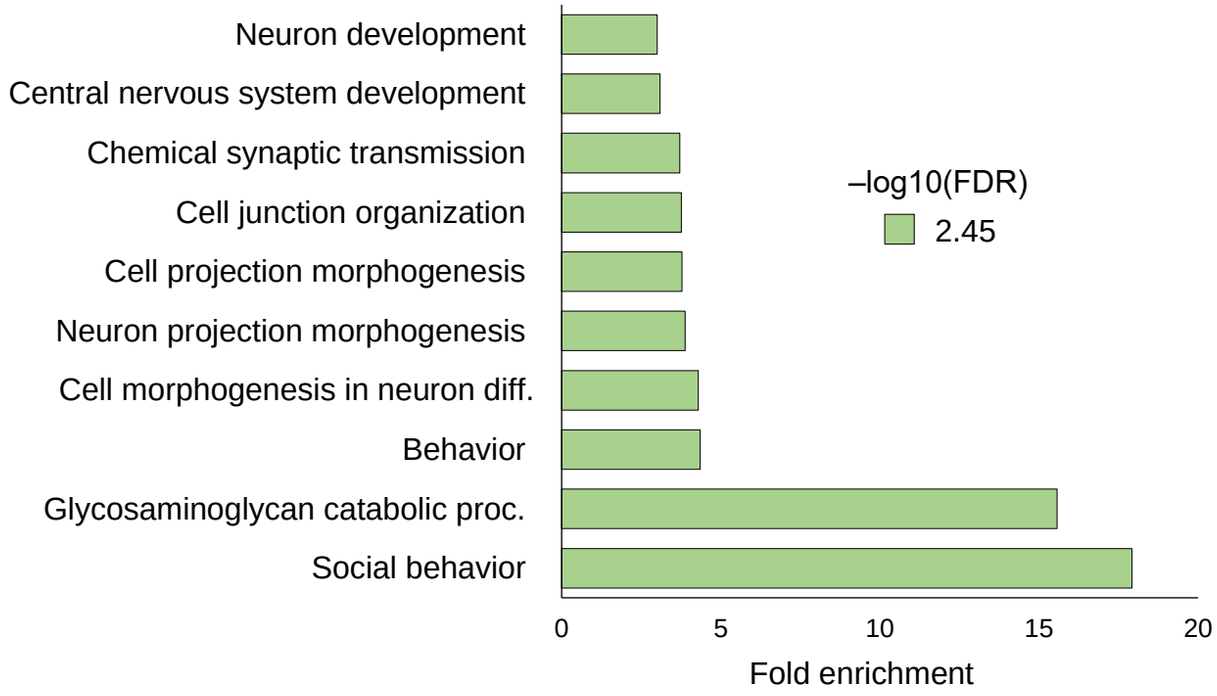
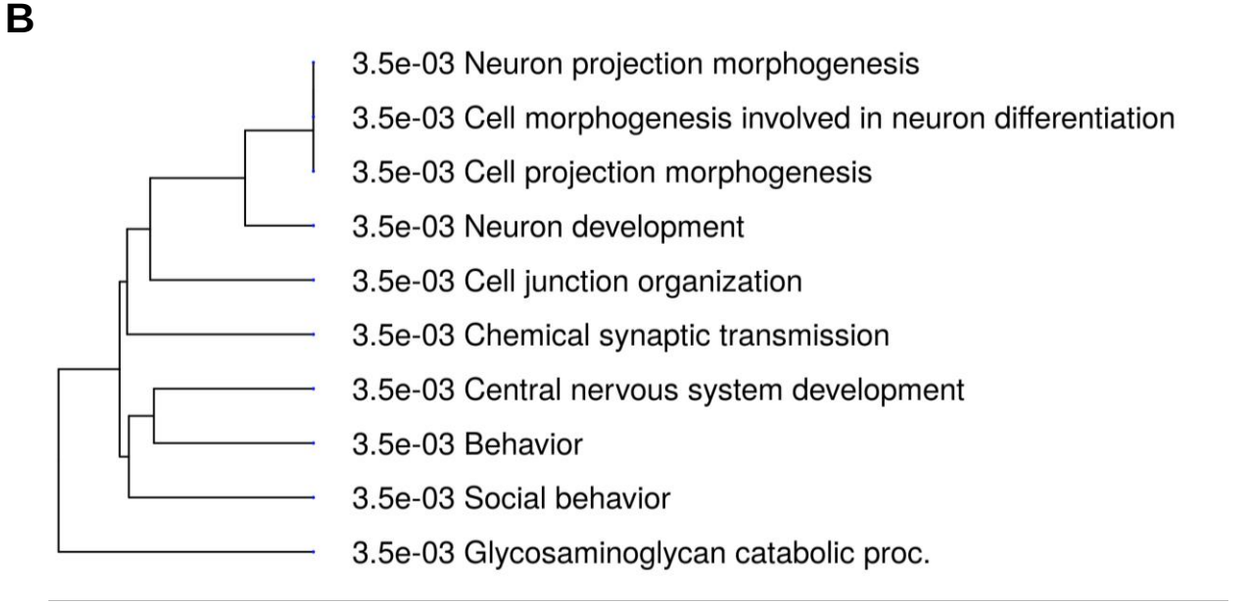
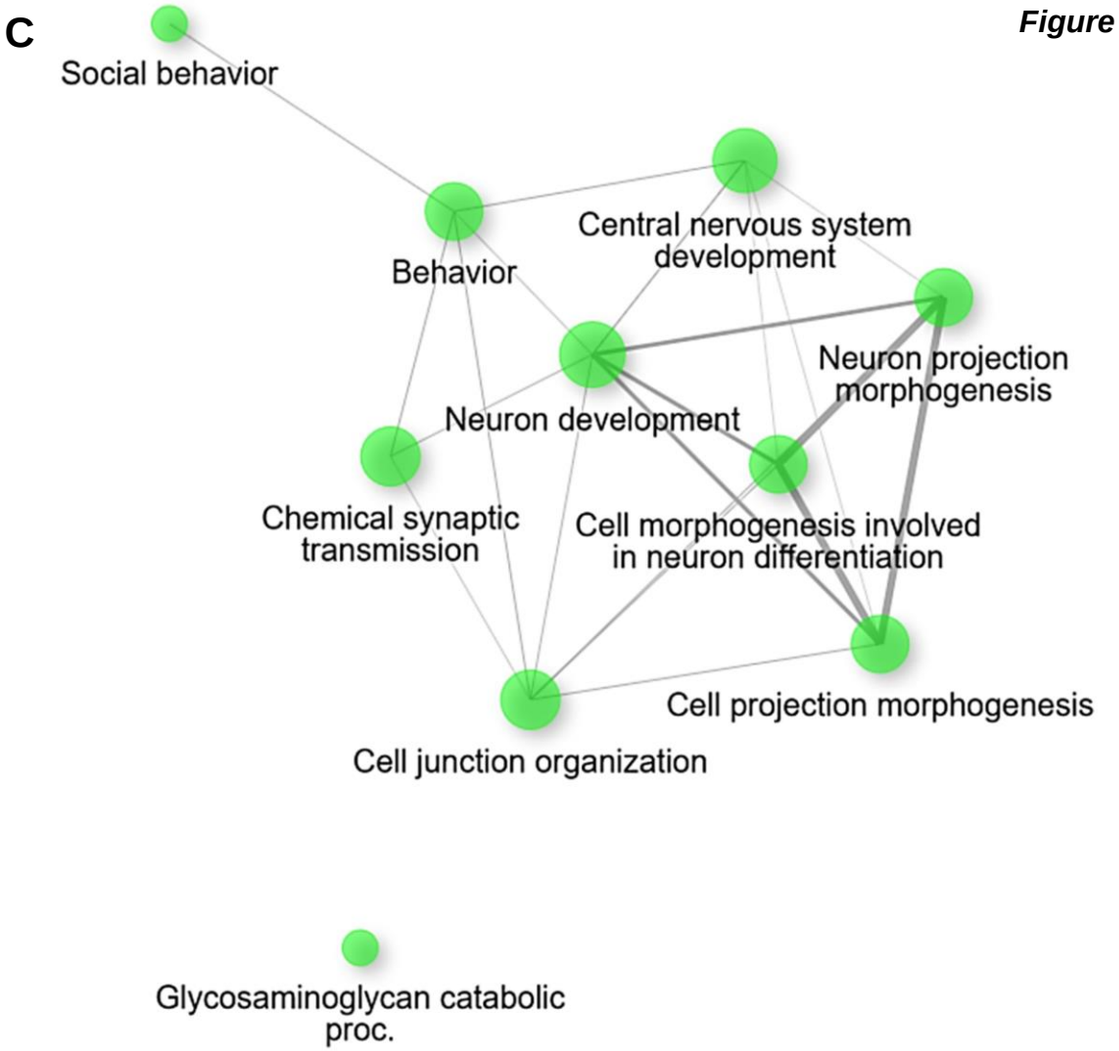
*Figure S1*


A
Neuron development
Central nervous system development
Chemical synaptic transmission
Cell junction organization
Cell projection morphogenesis
Neuron projection morphogenesis
Cell morphogenesis in neuron diff.
Behavior
Glycosaminoglycan catabolic proc.
Social behavior
–log10(FDR)
2.45
0
5
10
15
20
Fold enrichment


B
3.5e-03 Neuron projection morphogenesis
3.5e-03 Cell morphogenesis involved in neuron differentiation
3.5e-03 Cell projection morphogenesis
3.5e-03 Neuron development
3.5e-03 Cell junction organization
3.5e-03 Chemical synaptic transmission
3.5e-03 Central nervous system development
3.5e-03 Behavior
3.5e-03 Social behavior
3.5e-03 Glycosaminoglycan catabolic proc.


C
Social behavior
Behavior
Central nervous system development
Neuron projection morphogenesis
Neuron development
Chemical synaptic transmission
Cell morphogenesis involved in neuron differentiation
Cell projection morphogenesis
Cell junction organization
Glycosaminoglycan catabolic proc.

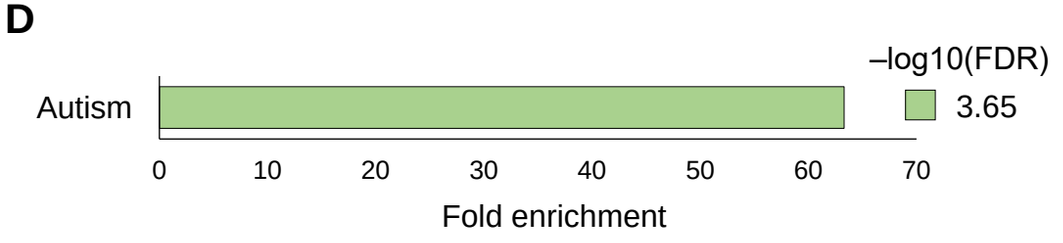

D
Autism
–log10(FDR)
3.65
0
10
20
30
40
50
60
70
Fold enrichment

*Figure S2*

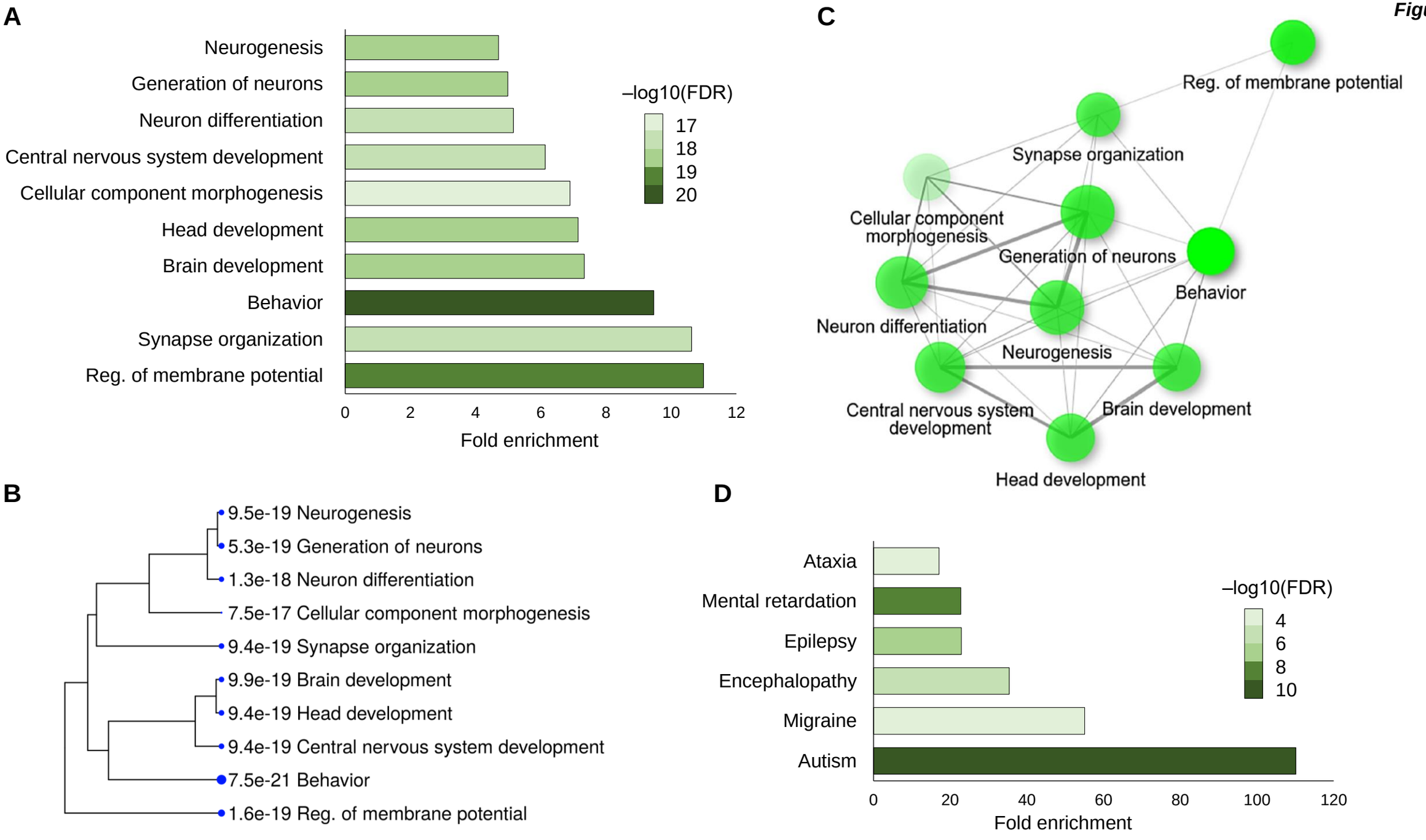

A
Neurogenesis
Generation of neurons
Neuron differentiation
Central nervous system development
Cellular component morphogenesis
Head development
Brain development
Behavior
Synapse organization
Reg. of membrane potential
–log10(FDR)
17
18
19
20
0
2
4
6
8
10
12
Fold enrichment
C
Reg. of membrane potential
Synapse organization
Cellular component morphogenesis
Generation of neurons
Behavior
Neuron differentiation
Neurogenesis
Central nervous system development
Brain development
Head development
B
9.5e-19 Neurogenesis
5.3e-19 Generation of neurons
1.3e-18 Neuron differentiation
7.5e-17 Cellular component morphogenesis
9.4e-19 Synapse organization
9.9e-19 Brain development
9.4e-19 Head development
9.4e-19 Central nervous system development
7.5e-21 Behavior
1.6e-19 Reg. of membrane potential
D
Ataxia
Mental retardation
Epilepsy
Encephalopathy
Migraine
Autism
–log10(FDR)
4
6
8
10
0
20
40
60
80
100
120
Fold enrichment

*Figure S3*

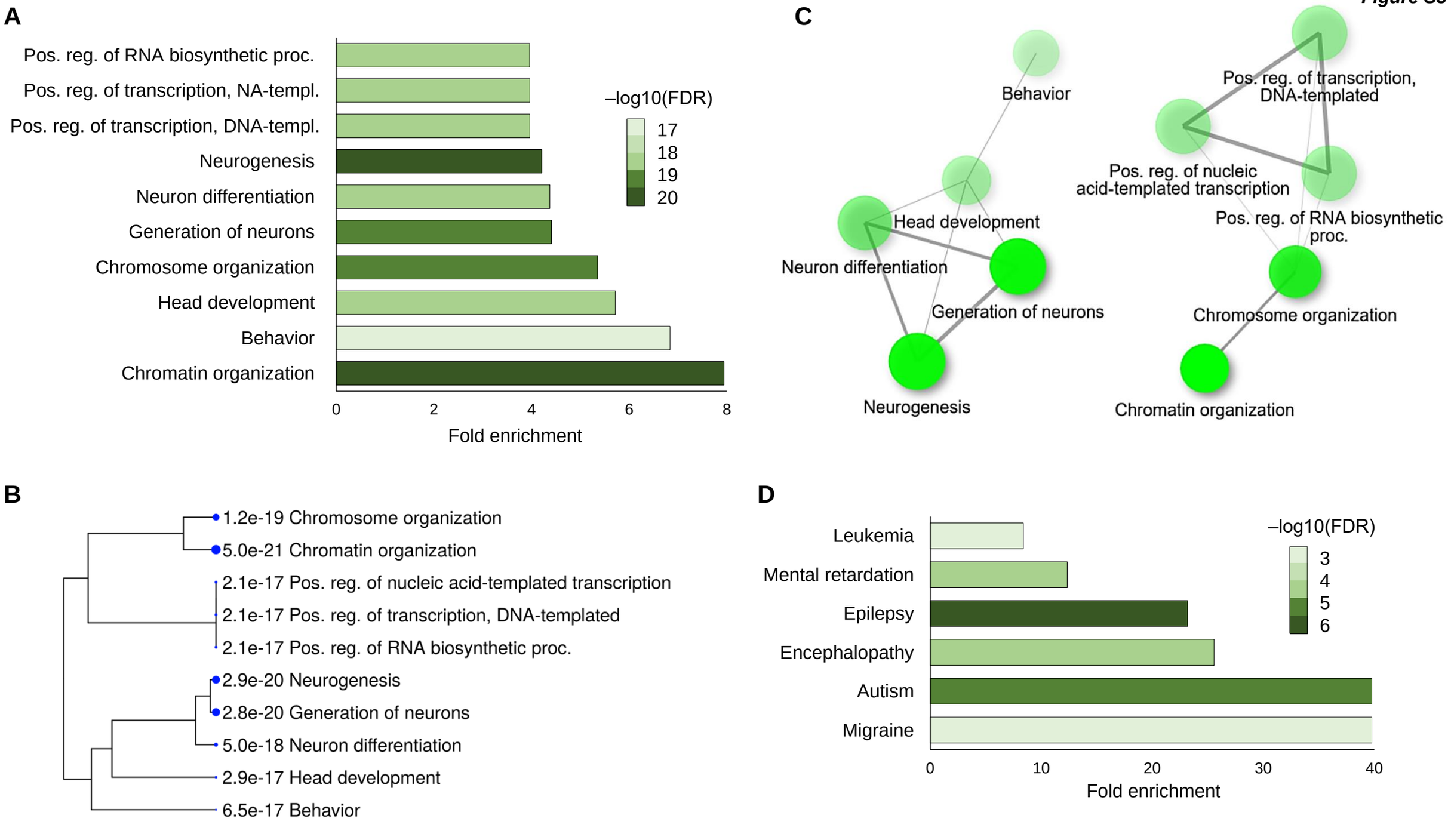

A
Pos. reg. of RNA biosynthetic proc.
Pos. reg. of transcription, NA-templ.
Pos. reg. of transcription, DNA-templ.
Neurogenesis
Neuron differentiation
Generation of neurons
Chromosome organization
Head development
Behavior
Chromatin organization
–log10(FDR)
17
18
19
20
0
2
4
6
8
Fold enrichment
C
Behavior
Pos. reg. of transcription, DNA-templated
Pos. reg. of nucleic acid-templated transcription
Head development
Pos. reg. of RNA biosynthetic proc.
Neuron differentiation
Generation of neurons
Chromosome organization
Neurogenesis
Chromatin organization
B
1.2e-19 Chromosome organization
5.0e-21 Chromatin organization
2.1e-17 Pos. reg. of nucleic acid-templated transcription
2.1e-17 Pos. reg. of transcription, DNA-templated
2.1e-17 Pos. reg. of RNA biosynthetic proc.
2.9e-20 Neurogenesis
2.8e-20 Generation of neurons
5.0e-18 Neuron differentiation
2.9e-17 Head development
6.5e-17 Behavior
D
Leukemia
Mental retardation
Epilepsy
Encephalopathy
Autism
Migraine
–log10(FDR)
3
4
5
6
0
10
20
30
40
Fold enrichment

**Figure S1:** GOBP and OMIM Disease GSEA of ASD-related genes selected exclusively from the ClinVar database, and hierarchical clustering and network analysis of enriched GOBPs. GSEA of the 168 ASD genes identified in ClinVar for GOBPs (**A**), and their hierarchical clustering (**B**) and network analysis (**C**). The hierarchical clustering tree summarizes the correlation among significant pathways. In network analysis two nodes are connected if they share 20% or more genes. Darker nodes are more significantly enriched gene sets. Bigger nodes represent larger gene sets. Thicker edges represent more overlapped genes. **D** GSEA of the 168 ASD genes identified in ClinVar for OMIM Disease database. For each GSEA performed, the FDR threshold was reduced to 0.01, and only the first 10 significant hits selected by the FDR and sorted by FE were considered.

**Figure S2:** GOBP and OMIM Disease GSEA of ASD-related genes selected exclusively from the SFARI Gene database, and hierarchical clustering and network analysis of enriched GOBPs. GSEA of the 146 ASD genes identified in SFARI Gene for GOBPs (**A**), and their hierarchical clustering (**B**) and network analysis (**C**). The hierarchical clustering tree summarizes the correlation among significant pathways. In network analysis two nodes are connected if they share 20% or more genes. Darker nodes are more significantly enriched gene sets. Bigger nodes represent larger gene sets. Thicker edges represent more overlapped genes. **D** GSEA of the 146 ASD genes identified in SFARI Gene for OMIM Disease database. For each GSEA performed, the FDR threshold was reduced to 0.01, and only the first 10 significant hits selected by the FDR and sorted by FE were considered.

**Figure S3:** GOBP and OMIM Disease GSEA of ASD-related genes selected exclusively from the AutDB database, and hierarchical clustering and network analysis of enriched GOBPs. GSEA of the 201 ASD genes identified in AutDB for GOBPs (**A**), and their hierarchical clustering (**B**) and network analysis (**C**). The hierarchical clustering tree summarizes the correlation among significant pathways. In network analysis two nodes are connected if they share 20% or more genes. Darker nodes are more significantly enriched gene sets. Bigger nodes represent larger gene sets. Thicker edges represent more overlapped genes. **D** GSEA of the 201 ASD genes identified in AutDB for OMIM Disease database. For each GSEA performed, the FDR threshold was reduced to 0.01, and only the first 10 significant hits selected by the FDR and sorted by FE were considered.

| Variation length | | | | | |
|---|---|---|---|---|---|
| **Gene** | **Database** | **Singe gene** | **Multiple genes** | ***p*** | **adj_*p*** |
| *WAC* | ClinVar | 24 | 0 | 1.10E-01 | 2.20E-01 |
| | AutDB | 64 | 7 | | |
| *TRIO* | ClinVar | 23 | 1 | 6.79E-01 | 7.54E-01 |
| | AutDB | 148 | 10 | | |
| *UBE3A* | ClinVar | 14 | 40 | 6.47E-07 | ***4.31E-06*** |
| | AutDB | 38 | 13 | | |
| *CACNA1C* | ClinVar | 46 | 3 | 5.28E-01 | 6.60E-01 |
| | AutDB | 79 | 8 | | |
| *GABRB3* | ClinVar | 0 | 39 | 1.10E-29 | ***1.10E-28*** |
| | AutDB | 142 | 15 | | |
| *AUTS2* | ClinVar | 24 | 8 | 6.40E-04 | ***3.20E-03*** |
| | AutDB | 111 | 6 | | |
| *POGZ* | ClinVar | 40 | 0 | 2.76E-01 | 4.59E-01 |
| | AutDB | 201 | 6 | | |
| *DDX3X* | ClinVar | 74 | 6 | 4.21E-02 | 1.05E-01 |
| | AutDB | 291 | 8 | | |
| *ADNP* | ClinVar | 44 | 0 | 3.68E-01 | 5.25E-01 |
| | AutDB | 162 | 3 | | |
| *PTEN* | ClinVar | 62 | 0 | 2.22E-01 | 4.03E-01 |
| | AutDB | 165 | 4 | | |
| *STXBP1* | ClinVar | 70 | 2 | 6.99E-01 | 7.36E-01 |
| | AutDB | 232 | 9 | | |
| *GRIN2B* | ClinVar | 89 | 6 | 2.58E-02 | 7.37E-02 |
| | AutDB | 308 | 6 | | |
| *TCF4* | ClinVar | 104 | 3 | 2.10E-02 | 7.01E-02 |
| | AutDB | 72 | 9 | | |
| *CHD8* | ClinVar | 44 | 1 | 7.67E-01 | 7.67E-01 |
| | AutDB | 305 | 5 | | |
| *NRXN1* | ClinVar | 33 | 3 | 1.02E-02 | ***4.07E-02*** |
| | AutDB | 356 | 6 | | |
| *DYRK1A* | ClinVar | 98 | 5 | 5.80E-01 | 6.82E-01 |
| | AutDB | 267 | 10 | | |
| *CHD2* | ClinVar | 142 | 3 | 3.33E-01 | 5.12E-01 |
| | AutDB | 197 | 8 | | |
| *SHANK3* | ClinVar | 39 | 39 | 1.08E-39 | ***2.16E-38*** |
| | AutDB | 402 | 8 | | |
| *SYNGAP1* | ClinVar | 172 | 0 | 3.78E-01 | 5.04E-01 |
| | AutDB | 221 | 1 | | |
| *MECP2* | ClinVar | 427 | 8 | 6.13E-02 | 1.36E-01 |
| | AutDB | 249 | 11 | | |

| Time of origin | | | | | |
|---|---|---|---|---|---|
| **Gene** | **Database** | **de novo** | **familial/ germline** | ***p*** | **adj_*p*** |
| *WAC* | ClinVar | 15 | 18 | 4.18E-05 | ***6.44E-05*** |
| | AutDB | 39 | 5 | | |
| *TRIO* | ClinVar | 12 | 17 | 1.56E-02 | ***1.83E-02*** |
| | AutDB | 53 | 26 | | |
| *UBE3A* | ClinVar | 8 | 12 | 4.21E-01 | 4.43E-01 |
| | AutDB | 14 | 13 | | |
| *CACNA1C* | ClinVar | 7 | 16 | 1.29E-02 | ***1.61E-02*** |
| | AutDB | 32 | 20 | | |
| *GABRB3* | ClinVar | 8 | 12 | 6.81E-03 | ***9.08E-03*** |
| | AutDB | 70 | 28 | | |
| *AUTS2* | ClinVar | 13 | 13 | 6.86E-02 | 7.63E-02 |
| | AutDB | 49 | 21 | | |
| *POGZ* | ClinVar | 30 | 26 | 2.20E-07 | ***4.40E-07*** |
| | AutDB | 134 | 20 | | |
| *DDX3X* | ClinVar | 51 | 50 | 3.59E-23 | ***1.80E-22*** |
| | AutDB | 249 | 14 | | |
| *ADNP* | ClinVar | 34 | 29 | 3.28E-09 | ***8.21E-09*** |
| | AutDB | 100 | 8 | | |
| *PTEN* | ClinVar | 32 | 58 | 5.19E-08 | ***1.15E-07*** |
| | AutDB | 80 | 28 | | |
| *STXBP1* | ClinVar | 57 | 51 | 1.61E-15 | ***5.36E-15*** |
| | AutDB | 134 | 6 | | |
| *GRIN2B* | ClinVar | 66 | 64 | 1.83E-26 | ***1.22E-25*** |
| | AutDB | 226 | 7 | | |
| *TCF4* | ClinVar | 45 | 84 | 3.36E-11 | ***9.60E-11*** |
| | AutDB | 52 | 8 | | |
| *CHD8* | ClinVar | 28 | 33 | 2.63E-06 | ***4.78E-06*** |
| | AutDB | 146 | 42 | | |
| *NRXN1* | ClinVar | 10 | 17 | 6.28E-01 | 6.28E-01 |
| | AutDB | 68 | 142 | | |
| *DYRK1A* | ClinVar | 54 | 80 | 2.67E-22 | ***1.07E-21*** |
| | AutDB | 162 | 15 | | |
| *CHD2* | ClinVar | 40 | 131 | 1.52E-39 | ***1.52E-38*** |
| | AutDB | 151 | 8 | | |
| *SHANK3* | ClinVar | 32 | 25 | 1.53E-04 | ***2.19E-04*** |
| | AutDB | 166 | 40 | | |
| *SYNGAP1* | ClinVar | 64 | 144 | 3.35E-40 | ***6.71E-39*** |
| | AutDB | 170 | 5 | | |
| *MECP2* | ClinVar | 183 | 153 | 1.29E-05 | ***2.16E-05*** |
| | AutDB | 132 | 46 | | |

| | | Molecular consequence | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Gene** | **Database** | **missense** | **nonsense** | **synonimous** | **frame shift** | **copy number loss** | **copy number gain** | **splice site** | **UTR** | **ncRNA** | ***p*** | **adj_*p*** |
| *WAC* | ClinVar | 1 | 10 | 0 | 12 | 0 | 0 | 2 | 1 | 0 | 1.62E-01 | 1.80E-01 |
| | AutDB | 17 | 13 | 0 | 21 | 2 | 0 | 9 | 0 | 0 | | |
| *TRIO* | ClinVar | 28 | 25 | 0 | 30 | 0 | 0 | 12 | 3 | 30 | 2.33E-19 | ***1.17E-18*** |
| | AutDB | 116 | 12 | 2 | 12 | 1 | 1 | 4 | 0 | 0 | | |
| *UBE3A* | ClinVar | 5 | 3 | 0 | 5 | 0 | 31 | 0 | 3 | 0 | 4.17E-06 | ***9.26E-06*** |
| | AutDB | 20 | 3 | 1 | 10 | 0 | 2 | 0 | 0 | 0 | | |
| *CACNA1C* | ClinVar | 17 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 1.55E-01 | 1.83E-01 |
| | AutDB | 47 | 4 | 7 | 4 | 1 | 0 | 2 | 0 | 0 | | |
| *GABRB3* | ClinVar | 0 | 0 | 0 | 0 | 0 | 31 | 0 | 0 | 0 | 5.68E-21 | ***3.79E-20*** |
| | AutDB | 80 | 7 | 2 | 4 | 1 | 3 | 1 | 0 | 0 | | |
| *AUTS2* | ClinVar | 2 | 7 | 0 | 11 | 5 | 1 | 1 | 0 | 0 | 1.07E-03 | ***1.78E-03*** |
| | AutDB | 11 | 7 | 2 | 10 | 57 | 6 | 2 | 0 | 0 | | |
| *POGZ* | ClinVar | 0 | 16 | 0 | 19 | 0 | 0 | 6 | 0 | 0 | 1.34E-02 | ***1.79E-02*** |
| | AutDB | 49 | 56 | 2 | 80 | 2 | 1 | 8 | 0 | 0 | | |
| *DDX3X* | ClinVar | 26 | 20 | 0 | 20 | 2 | 3 | 5 | 17 | 69 | 6.85E-39 | ***6.85E-38*** |
| | AutDB | 134 | 39 | 0 | 64 | 0 | 0 | 34 | 0 | 0 | | |
| *ADNP* | ClinVar | 1 | 19 | 0 | 23 | 0 | 0 | 1 | 0 | 0 | 2.41E-01 | 2.54E-01 |
| | AutDB | 20 | 46 | 1 | 91 | 2 | 0 | 0 | 0 | 0 | | |
| *PTEN* | ClinVar | 25 | 11 | 0 | 15 | 0 | 0 | 9 | 33 | 0 | 5.14E-08 | ***1.47E-07*** |
| | AutDB | 81 | 31 | 0 | 21 | 2 | 0 | 14 | 6 | 0 | | |
| *STXBP1* | ClinVar | 27 | 25 | 0 | 16 | 4 | 1 | 31 | 1 | 0 | 3.34E-01 | ***6.07E-14*** |
| | AutDB | 134 | 23 | 16 | 17 | 3 | 0 | 7 | 5 | 0 | | |
| *GRIN2B* | ClinVar | 40 | 15 | 0 | 9 | 0 | 1 | 4 | 0 | 0 | 1.52E-14 | 3.34E-01 |
| | AutDB | 161 | 43 | 2 | 37 | 17 | 2 | 37 | 0 | 0 | | |
| *TCF4* | ClinVar | 13 | 21 | 0 | 40 | 5 | 0 | 19 | 4 | 0 | 1.46E-03 | ***2.25E-03*** |
| | AutDB | 25 | 17 | 1 | 9 | 3 | 0 | 10 | 0 | 0 | | |
| *CHD8* | ClinVar | 3 | 22 | 0 | 12 | 1 | 0 | 7 | 0 | 0 | 6.47E-03 | ***9.24E-03*** |
| | AutDB | 109 | 76 | 8 | 64 | 6 | 4 | 33 | 0 | 0 | | |
| *NRXN1* | ClinVar | 0 | 0 | 0 | 2 | 27 | 2 | 0 | 0 | 0 | 4.33E-02 | 5.41E-02 |
| | AutDB | 82 | 9 | 11 | 12 | 222 | 6 | 6 | 2 | 0 | | |
| *DYRK1A* | ClinVar | 8 | 34 | 0 | 39 | 4 | 3 | 8 | 3 | 0 | 3.54E-05 | ***6.44E-05*** |
| | AutDB | 62 | 71 | 1 | 68 | 16 | 0 | 41 | 0 | 0 | | |
| *CHD2* | ClinVar | 9 | 54 | 0 | 53 | 3 | 1 | 6 | 0 | 0 | 3.80E-08 | ***1.27E-07*** |
| | AutDB | 76 | 45 | 0 | 48 | 7 | 0 | 16 | 1 | 0 | | |
| *SHANK3* | ClinVar | 2 | 8 | 0 | 22 | 21 | 2 | 2 | 0 | 0 | 6.49E-06 | ***1.30E-05*** |
| | AutDB | 126 | 16 | 32 | 105 | 84 | 3 | 14 | 1 | 0 | | |
| *SYNGAP1* | ClinVar | 10 | 45 | 0 | 99 | 1 | 0 | 15 | 0 | 0 | 5.54E-07 | ***1.38E-06*** |
| | AutDB | 49 | 62 | 4 | 63 | 8 | 0 | 23 | 0 | 0 | | |
| *MECP2* | ClinVar | 49 | 50 | 0 | 249 | 6 | 5 | 47 | 0 | 0 | 3.62E-44 | ***7.24E-43*** |
| | AutDB | 109 | 59 | 18 | 35 | 3 | 8 | 0 | 3 | 0 | | |

**Table S1:** Case numbers of genetic variation types of the 20 shared genes for the "Variation length" dimension from ClinVar and AutDB, with *p* and adjusted *p*-values for the given genes. Adjusted *p*-values less than 0.05 are highlighted in bold italics.

**Table S2:** Case numbers of genetic variation types of the 20 shared genes for the "Time of origin" dimension from ClinVar and AutDB, with *p* and adjusted *p*-values for the given genes. Adjusted *p*-values less than 0.05 are highlighted in bold italics.

**Table S3:** Case numbers of genetic variation types of the 20 shared genes for the "Molecular Consequence" dimension from ClinVar and AutDB, with *p* and adjusted *p*-values for the given genes. Adjusted *p*-values less than 0.05 are highlighted in bold italics.