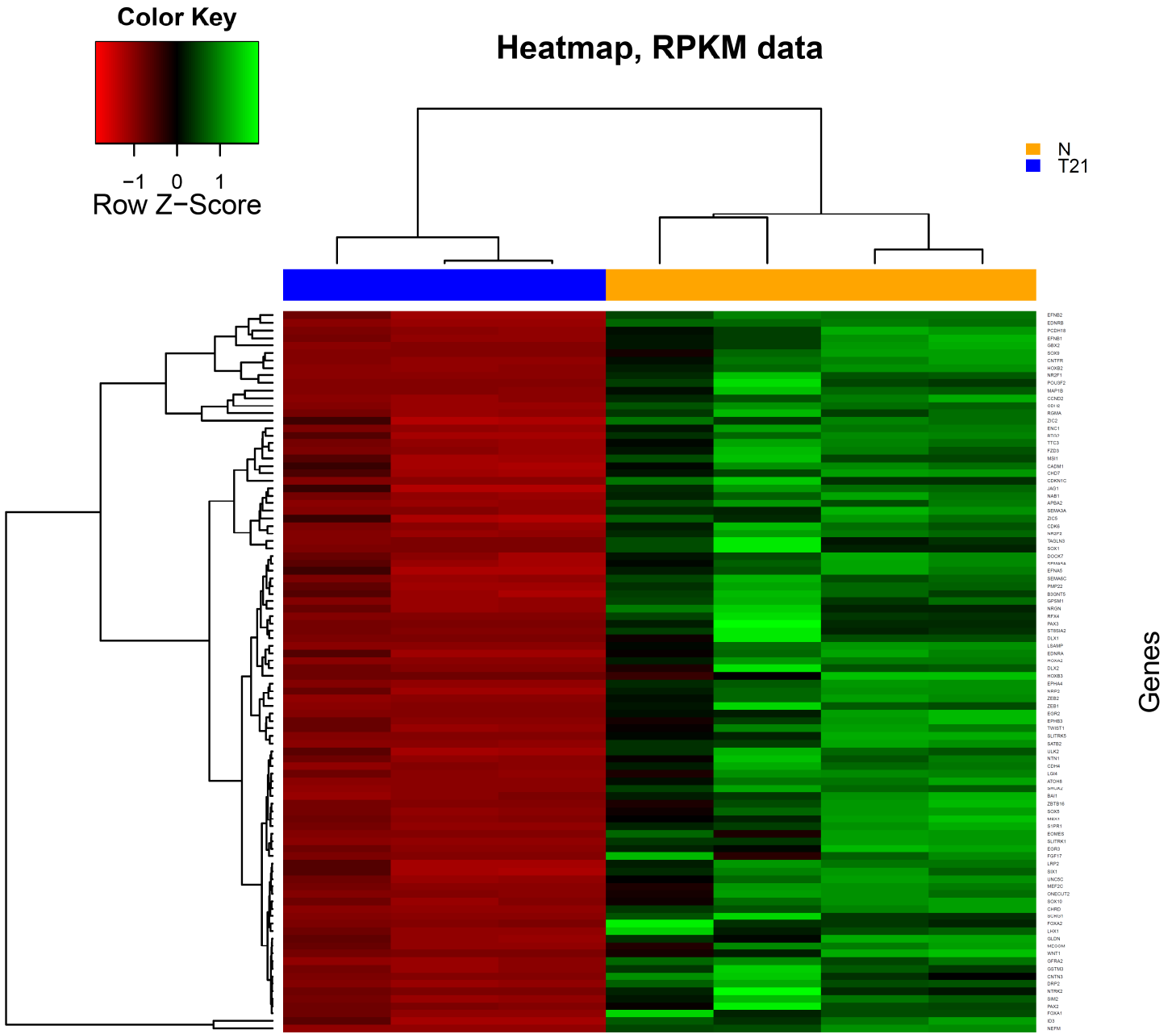


A



B

Categories	Genes in the network	Count	P-value	Benjamini
Nervous system development (GO:0007399)	NRP2, MEF2C, FOXA2, GLDN, CADM1, FGF17, ZEB2, ZEB1, PAX3, JAG1, PAX2, ZIC2, EDNRB, WNT1, GSTM3, S1PR1, SCRG1, LGI4, ATOH8, SEMA3A, UNC5C, NR2F2, NR2F1, TWIST1, SOX10, SATB2, EGR3, EGR2, EFN1, EN1, EFN2, EOMES, CDK6, MECOM, SLITRK1, MSX1, BTG2, CCND2, LSAMP, NAB1, SIX1, EFNA5, CNTN3, NRG1, PMP22, SLITRK5, SOX1, ONECUT2, SOX5, CNTFR, CDH2, ZBTB16, ST8SIA2, EPHB3, TAGLN3, CDH4, TTC3, SEMA5A, RGMA, HOXA2, CHD7, C11ORF9, B3GNT5, LHX1, BAI1, MSI1, GPSM1, GBX2, APBA2, POU3F2, NEFM, SIM2, RFX4, MAP1B, FOXA1, FZD3, DOCK7, NTN1, PCDH18, CDKN1C, SHOX2, HOXB3, EPHA4, DLX2, DLX1, HOXB2, SEMA6C, DRP2, ULK2, ZIC5, NTRK2, ID3, LRP2, CHRD, GFRA2	95	2.30E-21	8.20E-19
Neurogenesis (GO:0022008)	NRP2, FOXA2, JAG1, PAX3, PAX2, WNT1, S1PR1, LGI4, UNC5C, SEMA3A, NR2F2, TWIST1, NR2F1, SOX10, SATB2, EGR2, EFN1, CDK6, SLITRK1, BTG2, CCND2, NAB1, SIX1, EFNA5, SLITRK5, SOX1, ONECUT2, SOX5, CDH2, EPHB3, CDH4, TTC3, SEMA5A, HOXA2, C11ORF9, LHX1, BAI1, GBX2, POU3F2, NEFM, FOXA1, MAP1B, DOCK7, NTN1, CDKN1C, DLX2, EPHA4, DLX1, SEMA6C, ULK2, NTRK2, ID3	52	2.20E-11	2.30E-09
Generation of neurons (GO:0048699)	NRP2, FOXA2, SOX1, ONECUT2, SOX5, PAX3, JAG1, CDH2, EPHB3, PAX2, CDH4, TTC3, SEMA5A, WNT1, HOXA2, S1PR1, LHX1, BAI1, GBX2, LGI4, POU3F2, UNC5C, SEMA3A, NR2F2, NEFM, TWIST1, NR2F1, SATB2, EGR2, EFN1, MAP1B, FOXA1, DOCK7, NTN1, CDKN1C, SLITRK1, DLX2, EPHA4, DLX1, SEMA6C, BTG2, CCND2, ULK2, NTRK2, SIX1, EFNA5, ID3, SLITRK5	48	1.90E-10	1.80E-08
Neuron differentiation (GO:0030182)	NRP2, SOX1, FOXA2, ONECUT2, SOX5, PAX3, JAG1, EPHB3, PAX2, CDH4, SEMA5A, WNT1, HOXA2, S1PR1, LHX1, BAI1, GBX2, LGI4, POU3F2, UNC5C, SEMA3A, EGR2, EFN1, MAP1B, FOXA1, DOCK7, NTN1, CDKN1C, SLITRK1, DLX2, EPHA4, DLX1, SEMA6C, BTG2, ULK2, NTRK2, EFNA5, ID3, SLITRK5	39	5.10E-09	3.90E-07
Central nervous system development (GO:0007417)	SOX1, FOXA2, SOX5, ZEB2, PAX3, ZBTB16, ZEB1, EPHB3, TAGLN3, ZIC2, WNT1, HOXA2, CHD7, S1PR1, B3GNT5, C11ORF9, LHX1, GBX2, POU3F2, UNC5C, NR2F2, NR2F1, SOX10, EGR2, RFX4, MAP1B, EOMES, MECOM, PCDH18, DLX2, DLX1, HOXB2, MSX1, DRP2, ZIC5, EFNA5, LRP2, CHRD	38	7.40E-09	4.70E-07
Peripheral nervous system development (GO:0007422)	SOX10, EDNRB, GSTM3, EGR3, EGR2, BAI1, NAB1, ONECUT2, POU3F2, PMP22	10	7.40E-09	4.70E-07
Axonogenesis (GO:0007409)	NRP2, EGR2, EFN1, MAP1B, DOCK7, PAX2, EPHB3, CDH4, NTN1, SEMA5A, SLITRK1, EPHA4, HOXA2, SEMA6C, ULK2, BAI1, GBX2, EFNA5, SEMA3A, UNC5C, SLITRK5	21	8.90E-07	3.80E-05
Brain development (GO:0007420)	SOX1, FOXA2, ZEB2, ZIC2, WNT1, HOXA2, S1PR1, LHX1, GBX2, POU3F2, UNC5C, NR2F2, NR2F1, EGR2, RFX4, EOMES, MECOM, PCDH18, DLX2, DLX1, MSX1, HOXB2, ZIC5, EFNA5, LRP2, CHRD	26	2.40E-06	8.00E-05
Cell morphogenesis involved in neuron differentiation (GO:0048667)	NRP2, EGR2, EFN1, MAP1B, DOCK7, PAX2, EPHB3, CDH4, NTN1, SEMA5A, SLITRK1, EPHA4, HOXA2, SEMA6C, ULK2, BAI1, GBX2, EFNA5, SEMA3A, UNC5C, SLITRK5	21	5.60E-06	1.60E-04
Neuron projection morphogenesis (GO:0048812)	NRP2, EGR2, EFN1, MAP1B, DOCK7, PAX2, EPHB3, CDH4, NTN1, SEMA5A, SLITRK1, EPHA4, HOXA2, SEMA6C, ULK2, BAI1, GBX2, EFNA5, SEMA3A, UNC5C, SLITRK5	21	7.40E-06	2.00E-04
Axon guidance (GO:0007411)	NRP2, EGR2, EFN1, EPHB3, NTN1, CDH4, SEMA5A, EPHA4, HOXA2, SEMA6C, GBX2, EFNA5, SEMA3A, UNC5C	14	2.00E-05	4.70E-04
Neural tube development (GO:0021915)	RGMA, WNT1, FOXA2, ZIC5, GBX2, FZD3, ZEB2, PAX3, CHRD, ZIC2, TWIST1	11	3.50E-05	6.90E-04
Neuron development (GO:0048666)	NRP2, SOX1, ONECUT2, EPHB3, PAX2, CDH4, SEMA5A, HOXA2, BAI1, GBX2, LGI4, SEMA3A, UNC5C, EGR2, EFN1, MAP1B, DOCK7, NTN1, CDKN1C, SLITRK1, EPHA4, SEMA6C, ULK2, NTRK2, EFNA5, SLITRK5	26	3.80E-05	6.90E-04
Neural crest cell development (GO:0014032)	NRP2, EDNRA, EDNRB, EFN1, GBX2, ZEB2, PAX3, SOX9	8	4.80E-05	9.00E-04
Neural crest cell differentiation (GO:0014033)	NRP2, EDNRA, EDNRB, EFN1, GBX2, ZEB2, PAX3, SOX9	8	4.80E-05	9.00E-04
Regulation of neuron differentiation (GO:0045664)	FOXA2, FOXA1, MAP1B, SOX5, CDH2, NTN1, CDH4, TTC3, HOXA2, CCND2, SIX1, NTRK2, POU3F2, SEMA3A, NEFM	15	5.00E-05	9.30E-04
Neuron projection development (GO:0031175)	NRP2, EGR2, EFN1, MAP1B, DOCK7, PAX2, EPHB3, CDH4, NTN1, SEMA5A, SLITRK1, EPHA4, HOXA2, SEMA6C, ULK2, BAI1, GBX2, EFNA5, SEMA3A, UNC5C, SLITRK5	21	1.00E-04	1.90E-04
Forebrain development (GO:0030900)	RFX4, SOX1, ZEB2, MECOM, WNT1, DLX2, DLX1, MSX1, LHX1, ZIC5, POU3F2, LRP2, NR2F2, CHRD, NR2F1	15	2.10E-04	3.50E-03
Neural crest cell migration (GO:0001755)	NRP2, EDNRB, EFN1, GBX2, ZEB2, PAX3	6	5.30E-04	7.90E-03

Supporting Information Fig 3. Heat map of the normalized gene expression values in Twin-DS-iPSCs and Twin-N-iPSCs for the 96 downregulated genes involved in brain-related functions.

(A) Samples (columns) and genes (rows) are sorted according to hierarchical clustering based on normalized and z-transformed gene expression values. A negative z-score (in red) indicates low expression (below the mean) whereas a positive z-score (in green) shows high expression (above the mean). (B) The table lists the brain-related functions associated with these 96 downregulated genes.