**Table S1 The most significant dysregulated genes identified from transcriptional profiling.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Gene | Description | Gene ID | Regulation | Fold change | p-value |
| NEB | nebulin | 4703 | Up | 14.8994992 | 0.017850442 |
| TNC | tenascin C | 3371 | Up | 5.486877235 | 0.037742412 |
| NRIP1 | nuclear receptor interacting protein 1 | 8204 | Up | 3.298052886 | 0.041012046 |
| DLG1 | discs large MAGUK scaffold protein 1 | 1739 | Up | 3.242861896 | 0.038952227 |
| PTPN22 | protein tyrosine phosphatase non-receptor type 22 | 26191 | Up | 3.186197827 | 0.016261397 |
| BCL11B | BAF chromatin remodeling complex subunit BCL11B | 64919 | Up | 2.927032368 | 0.046573473 |
| KPNA5 | karyopherin subunit alpha 5 | 3841 | Up | 2.68649233 | 0.035853578 |
| MAP3K5 | mitogen-activated protein kinase kinase kinase 5 | 4217 | Up | 2.557043061 | 0.009847991 |
| PSMB1 | proteasome 20S subunit beta 1 | 5689 | Up | 2.496209862 | 0.00628758 |
| SFMBT2 | Scm like with four mbt domains 2 | 57713 | Up | 2.381790179 | 0.02055289 |
| SGMS1 | sphingomyelin synthase 1 | 259230 | Down | 0.332532325 | 0.010487991 |
| TET2 | tet methylcytosine dioxygenase 2 | 54790 | Down | 0.348102841 | 0.014933145 |
| SMO | smoothened, frizzled class receptor | 6608 | Down | 0.364485425 | 0.002777887 |
| PARD3 | par-3 family cell polarity regulator | 56288 | Down | 0.3688966 | 0.009925126 |
| ATP5C1 | ATP synthase F1 subunit gamma | 509 | Down | 0.376254014 | 0.01481178 |
| PPP4R1 | protein phosphatase 4 regulatory subunit 1 | 9989 | Down | 0.383802166 | 0.011271983 |
| SOGA2 | microtubule crosslinking factor 1 | 23255 | Down | 0.384345899 | 0.008928251 |
| MYO10 | myosin X | 4651 | Down | 0.387742531 | 0.028967478 |
| YTHDF2 | YTH N6-methyladenosine RNA binding protein 2 | 51441 | Down | 0.409053684 | 0.015799326 |
| TRPS1 | transcriptional repressor GATA binding 1 | 7227 | Down | 0.413680784 | 0.006940538 |

**Table S2 The GO terms including BP, CC and MP from the dysregulated genes**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Function | Rank | GO.ID | Description | BgRatio | pvalue | p.adjust | geneID | Count |
| MF | 1 | GO:0003714 | transcription corepressor activity | 238/176c96 | 0.000230269 | 0.090495577 | NRIP1/SFMBT2/N4BP2L2/CTBP1/ZMYND11/CBFA2T2/ATF7IP/GON4L/RBBP8 | 9 |
| 2 | GO:0030507 | spectrin binding | 28/17696 | 0.001771619 | 0.206760041 | CAMSAP1/ANK3/MYO10 | 3 |
| 3 | GO:0140142 | nucleocytoplasmic carrier activity | 31/17696 | 0.002385228 | 0.206760041 | KPNA5/NUP42/TNPO3 | 3 |
| 4 | GO:0016791 | phosphatase activity | 270/17696 | 0.002443236 | 0.206760041 | DLG1/PTPN22/CTDP1/PIKFYVE/PPP3CC/UBASH3A/PTPN13/PPP4R1 | 8 |
| 5 | GO:0015631 | tubulin binding | 336/17696 | 0.002630535 | 0.206760041 | HTT/CCDC66/CLASP2/FCHO2/FYN/TBCEL/SBDS/CAMSAP1/MTCL1 | 9 |
| 6 | GO:0044325 | ion channel binding | 124/17696 | 0.004468033 | 0.214437218 | DLG1/SLC8A1/HTT/FYN/ANK3 | 5 |
| 7 | GO:0005547 | phosphatidylinositol-3,4,5-trisphosphate binding | 39/17696 | 0.004611174 | 0.214437218 | ARAP2/MYO10/PARD3 | 3 |
| 8 | GO:0005089 | Rho guanyl-nucleotide exchange factor activity | 79/17696 | 0.004885282 | 0.214437218 | ARHGEF4/ARHGEF12/ARHGEF28/DOCK1 | 4 |
| 9 | GO:0004721 | phosphoprotein phosphatase activity | 182/17696 | 0.005060833 | 0.214437218 | DLG1/PTPN22/CTDP1/PPP3CC/PTPN13/PPP4R1 | 6 |
| 10 | GO:0050681 | androgen receptor binding | 44/17696 | 0.006475735 | 0.214437218 | NRIP1/FOXP1/KDM1A | 3 |
| 11 | GO:0005088 | Ras guanyl-nucleotide exchange factor activity | 137/17696 | 0.006782278 | 0.214437218 | ARHGEF4/RAB3IP/ARHGEF12/ARHGEF28/DOCK1 | 5 |
| 12 | GO:0042393 | histone binding | 197/17696 | 0.007376641 | 0.214437218 | SFMBT2/DNAJC2/SMARCA5/SMARCC1/KDM1B/ZMYND11 | 6 |
| 13 | GO:0051015 | actin filament binding | 198/17696 | 0.007554265 | 0.214437218 | NEB/TNNC1/SLC6A4/UTRN/SYNE2/MYO10 | 6 |
| 14 | GO:0035254 | glutamate receptor binding | 47/17696 | 0.007780628 | 0.214437218 | DLG1/FYN/CANX | 3 |
| 15 | GO:0035258 | steroid hormone receptor binding | 92/17696 | 0.008335839 | 0.214437218 | NRIP1/FOXP1/CNOT1/KDM1A | 4 |
| 16 | GO:0034185 | apolipoprotein binding | 17/17696 | 0.00927591 | 0.214437218 | LRP6/CANX | 2 |
| 17 | GO:0042813 | Wnt-activated receptor activity | 17/17696 | 0.00927591 | 0.214437218 | LRP6/RYK | 2 |
| CC | 1 | GO:0031253 | cell projection membrane | 326/19717 | 0.000291899 | 0.058358164 | DLG1/CLASP2/ARHGEF4/UTRN/CD44/SLC11A2/SYNE2/DHRS3/MYO10/SMO | 10 |
| 2 | GO:0031527 | filopodium membrane | 18/19717 | 0.000370174 | 0.058358164 | UTRN/SYNE2/MYO10 | 3 |
| 3 | GO:0016234 | inclusion body | 82/19717 | 0.000500213 | 0.058358164 | SFMBT2/PICALM/HTT/ATXN1/SYNE2 | 5 |
| 4 | GO:0005938 | cell cortex | 308/19717 | 0.000828718 | 0.072512839 | SPINK5/MYO9B/CLASP2/ASPH/UTRN/CTBP1/EXOC6B/MYO10/PARD3 | 9 |
| 5 | GO:0000407 | phagophore assembly site | 32/19717 | 0.002073706 | 0.145159438 | ATG2B/ILRUN/PIK3C3 | 3 |
| 6 | GO:0030027 | lamellipodium | 193/19717 | 0.004538458 | 0.20997163 | KLHL2/RAB3IP/CD44/SYNE2/PTPN13/MYO10 | 6 |
| 7 | GO:0031252 | cell leading edge | 403/19717 | 0.005074705 | 0.20997163 | CLASP2/ARHGEF4/KLHL2/RAB3IP/SLK/CD44/SYNE2/PTPN13/MYO10 | 9 |
| 8 | GO:0099523 | presynaptic cytosol | 14/19717 | 0.005384096 | 0.20997163 | HTT/PPP3CC | 2 |
| 9 | GO:0030122 | AP-2 adaptor complex | 15/19717 | 0.006180101 | 0.20997163 | PICALM/FCHO2 | 2 |
| 10 | GO:0033268 | node of Ranvier | 15/19717 | 0.006180101 | 0.20997163 | DLG1/ANK3 | 2 |
| 11 | GO:0030128 | clathrin coat of endocytic vesicle | 16/19717 | 0.007026254 | 0.20997163 | PICALM/FCHO2 | 2 |
| 12 | GO:0014704 | intercalated disc | 50/19717 | 0.007382694 | 0.20997163 | DLG1/SLC8A1/ANK3 | 3 |
| 13 | GO:0045178 | basal part of cell | 51/19717 | 0.007798946 | 0.20997163 | CLASP2/SLC11A2/ANK3 | 3 |
| 14 | GO:0030175 | filopodium | 104/19717 | 0.009612528 | 0.213726104 | DEF6/UTRN/SYNE2/MYO10 | 4 |
| 15 | GO:0031965 | nuclear membrane | 296/19717 | 0.009665884 | 0.213726104 | DNAJC2/NUP42/MYOF/NUP205/SYNE2/PUM2/SMOX | 7 |
| 16 | GO:0016328 | lateral plasma membrane | 57/19717 | 0.010585183 | 0.213726104 | DLG1/ANK3/MTCL1 | 3 |
| 17 | GO:0030132 | clathrin coat of coated pit | 20/19717 | 0.010895721 | 0.213726104 | PICALM/FCHO2 | 2 |
| 18 | GO:0044232 | organelle membrane contact site | 21/19717 | 0.011980233 | 0.213726104 | ESYT2/CANX | 2 |
| 19 | GO:0031258 | lamellipodium membrane | 22/19717 | 0.013110008 | 0.213726104 | CD44/SYNE2 | 2 |
| 20 | GO:0045121 | membrane raft | 315/19717 | 0.013260046 | 0.213726104 | DLG1/SLC6A4/PIKFYVE/LRP6/FYN/MYOF/SMO | 7 |
| 21 | GO:0098857 | membrane microdomain | 316/19717 | 0.013472555 | 0.213726104 | DLG1/SLC6A4/PIKFYVE/LRP6/FYN/MYOF/SMO | 7 |
| 22 | GO:0045211 | postsynaptic membrane | 323/19717 | 0.015029198 | 0.213726104 | DLG1/PICALM/SLC8A1/SLC6A4/UTRN/CANX/ANK3 | 7 |
| 23 | GO:0099522 | region of cytosol | 24/19717 | 0.01550224 | 0.213726104 | HTT/PPP3CC | 2 |
| 24 | GO:0005925 | focal adhesion | 405/19717 | 0.016014875 | 0.213726104 | TNC/SLC6A4/USP33/CLASP2/HSPG2/PPFIA1/CD44/SYNE2 | 8 |
| 25 | GO:0098589 | membrane region | 328/19717 | 0.016216979 | 0.213726104 | DLG1/SLC6A4/PIKFYVE/LRP6/FYN/MYOF/SMO | 7 |
| 26 | GO:0098793 | presynapse | 491/19717 | 0.016997489 | 0.213726104 | PICALM/HTT/SLC6A4/PPP3CC/FCHO2/CANX/CTBP1/PPFIA1/WDR7 | 9 |
| 27 | GO:0044304 | main axon | 68/19717 | 0.017019363 | 0.213726104 | DLG1/ANK3/PARD3 | 3 |
| 28 | GO:0030055 | cell-substrate junction | 412/19717 | 0.017563649 | 0.213726104 | TNC/SLC6A4/USP33/CLASP2/HSPG2/PPFIA1/CD44/SYNE2 | 8 |
| 29 | GO:0016529 | sarcoplasmic reticulum | 71/19717 | 0.019078916 | 0.213726104 | ASPH/SYNE2/ANK3 | 3 |
| 30 | GO:0044291 | cell-cell contact zone | 71/19717 | 0.019078916 | 0.213726104 | DLG1/SLC8A1/ANK3 | 3 |
| 31 | GO:0048786 | presynaptic active zone | 71/19717 | 0.019078916 | 0.213726104 | CANX/CTBP1/PPFIA1 | 3 |
| 32 | GO:0030018 | Z disc | 132/19717 | 0.021319042 | 0.213726104 | NEB/SLC8A1/SYNE2/ANK3 | 4 |
| 33 | GO:0030125 | clathrin vesicle coat | 29/19717 | 0.02222148 | 0.213726104 | PICALM/FCHO2 | 2 |
| 34 | GO:0030131 | clathrin adaptor complex | 29/19717 | 0.02222148 | 0.213726104 | PICALM/FCHO2 | 2 |
| 35 | GO:0097060 | synaptic membrane | 432/19717 | 0.022580355 | 0.213726104 | DLG1/PICALM/SLC8A1/SLC6A4/UTRN/FCHO2/CANX/ANK3 | 8 |
| 36 | GO:0031594 | neuromuscular junction | 76/19717 | 0.022804954 | 0.213726104 | DLG1/UTRN/ANK3 | 3 |
| 37 | GO:0042383 | sarcolemma | 136/19717 | 0.02348242 | 0.213726104 | DLG1/SLC8A1/UTRN/ANK3 | 4 |
| 38 | GO:0017053 | transcription repressor complex | 77/19717 | 0.023594246 | 0.213726104 | N4BP2L2/CTBP1/RBBP8 | 3 |
| 39 | GO:0030017 | sarcomere | 204/19717 | 0.023815194 | 0.213726104 | NEB/TNNC1/SLC8A1/SYNE2/ANK3 | 5 |
| 40 | GO:0098858 | actin-based cell projection | 208/19717 | 0.02562256 | 0.217085477 | DEF6/UTRN/CD44/SYNE2/MYO10 | 5 |
| 41 | GO:0005901 | caveola | 80/19717 | 0.026050257 | 0.217085477 | LRP6/MYOF/SMO | 3 |
| 42 | GO:0016528 | sarcoplasm | 80/19717 | 0.026050257 | 0.217085477 | ASPH/SYNE2/ANK3 | 3 |
| 43 | GO:0031674 | I band | 143/19717 | 0.027579188 | 0.224481764 | NEB/SLC8A1/SYNE2/ANK3 | 4 |
| BP | 1 | GO:0043392 | negative regulation of DNA binding | 54/18670 | 7.44E-05 | 0.112187482 | ILRUN/IFI16/FBXW7/KDM1A/SMO | 5 |
| 2 | GO:0071679 | commissural neuron axon guidance | 12/18670 | 0.000108152 | 0.112187482 | NFIB/RYK/SMO | 3 |
| 3 | GO:1905475 | regulation of protein localization to membrane | 187/18670 | 0.00014306 | 0.112187482 | DLG1/PICALM/PPP3CC/FYN/PPFIA1/MAPK8/ANK3/MTCL1 | 8 |
| 4 | GO:0006914 | autophagy | 496/18670 | 0.000200621 | 0.112187482 | PTPN22/HTT/ATG2B/USP33/ILRUN/PLEKHM1/PIKFYVE/IFI16/STAM/FBXW7/PIK3C3/MAPK8/MTCL1 | 13 |
| 5 | GO:0061919 | process utilizing autophagic mechanism | 496/18670 | 0.000200621 | 0.112187482 | PTPN22/HTT/ATG2B/USP33/ILRUN/PLEKHM1/PIKFYVE/IFI16/STAM/FBXW7/PIK3C3/MAPK8/MTCL1 | 13 |
| 6 | GO:0031098 | stress-activated protein kinase signaling cascade | 315/18670 | 0.000249454 | 0.116245573 | DLG1/PTPN22/MAP3K5/ERCC6/RELL1/SLK/NEK4/ZMYND11/MAPK8/KLHDC10 | 10 |
| 7 | GO:0022612 | gland morphogenesis | 120/18670 | 0.000433896 | 0.135137256 | TNC/AREG/LRP6/FBXW7/FGFR1/NFIB | 6 |
| 8 | GO:0051100 | negative regulation of binding | 169/18670 | 0.000455176 | 0.135137256 | USP33/ILRUN/IFI16/FBXW7/MAPK8/KDM1A/SMO | 7 |
| 9 | GO:1905477 | positive regulation of protein localization to membrane | 122/18670 | 0.000473851 | 0.135137256 | DLG1/PPP3CC/FYN/MAPK8/ANK3/MTCL1 | 6 |
| 10 | GO:0051101 | regulation of DNA binding | 124/18670 | 0.000516617 | 0.135137256 | ILRUN/IFI16/FBXW7/MAPK8/KDM1A/SMO | 6 |
| 11 | GO:1900744 | regulation of p38MAPK cascade | 47/18670 | 0.000559657 | 0.135137256 | DLG1/PTPN22/MAP3K5/RELL1 | 4 |
| 12 | GO:0090316 | positive regulation of intracellular protein transport | 176/18670 | 0.000579988 | 0.135137256 | PPP3CC/FYN/FBXW7/MAPK8/ANK3/MTCL1/SMO | 7 |
| 13 | GO:0038066 | p38MAPK cascade | 53/18670 | 0.00088496 | 0.179492898 | DLG1/PTPN22/MAP3K5/RELL1 | 4 |
| 14 | GO:0021537 | telencephalon development | 249/18670 | 0.000965799 | 0.179492898 | BCL11B/SLC8A1/LRP6/SYNE2/NFIB/RYK/KDM1A/SMO | 8 |
| 15 | GO:0048488 | synaptic vesicle endocytosis | 56/18670 | 0.001089394 | 0.179492898 | PICALM/PPP3CC/FCHO2/CANX | 4 |
| 16 | GO:0140238 | presynaptic endocytosis | 56/18670 | 0.001089394 | 0.179492898 | PICALM/PPP3CC/FCHO2/CANX | 4 |
| 17 | GO:0030900 | forebrain development | 381/18670 | 0.001091337 | 0.179492898 | BCL11B/SLC8A1/LRP6/FYN/FGFR1/SYNE2/NFIB/RYK/KDM1A/SMO | 10 |
| 18 | GO:0002831 | regulation of response to biotic stimulus | 400/18670 | 0.001568268 | 0.218082862 | PTPN22/PSMB1/FOXP1/SPINK5/ILRUN/ERCC6/IFI16/FYN/PUM2/YTHDF2 | 10 |
| 19 | GO:0050855 | regulation of B cell receptor signaling pathway | 29/18670 | 0.001624128 | 0.218082862 | PTPN22/FOXP1/ELF2 | 3 |
| 20 | GO:0051642 | centrosome localization | 29/18670 | 0.001624128 | 0.218082862 | DLG1/SYNE2/PARD3 | 3 |
| 21 | GO:2001233 | regulation of apoptotic signaling pathway | 406/18670 | 0.001749944 | 0.218082862 | HTT/PPP3CC/FYN/FBXW7/FGFR1/ZMYND11/MAPK8/CD44/KDM1A/SGMS1 | 10 |
| 22 | GO:0061842 | microtubule organizing center localization | 30/18670 | 0.001793958 | 0.218082862 | DLG1/SYNE2/PARD3 | 3 |
| 23 | GO:0090314 | positive regulation of protein targeting to membrane | 30/18670 | 0.001793958 | 0.218082862 | FYN/ANK3/MTCL1 | 3 |

**Table S3 Genes perturbed in each individual specimen by PEEPs algorithm**

|  |  |
| --- | --- |
| Case number | Genes |
| R17004387LR01 | "TNC" "DLG1" "PTPN22" "BCL11B" "KPNA5" "MAP3K5" "PSMB1" "SFMBT2" "FOXP1" "PICALM" "CTDP1" "ABHD2" "UGP2" "ESYT2" "DNAJC2" "MYO9B" "ARAP2" "LZIC" "SLC8A1" "HTT" "KLHL8" "NUPL2" "ATG2B" "USP33"  "N4BP2L2" "BRWD1" "C6orf106" "PLEKHM1" "THSD1" "RBM33" "DEF6" "KLHL2" "KANSL1L" "PPP3CC" "RAB3IP" "FCHO2"  "SMARCA5" "IFI16" "SLK" "ARHGAP5" "TNPO3" "PPFIA1" "ZBTB44" "EXOC6B" "KLHDC10" "ATF7IP" "HPS5" "CLIP4"  "DCUN1D4" "TRPS1" "SMO" |
| R17004388LR01 | "NEB" "TNC" "NRIP1" "PTPN22" "KPNA5" "SFMBT2" "ZRANB1" "FOXP1" "ESYT2" "MYO9B" "ARAP2" "SLC8A1"  "HTT" "KLC1" "KLHL8" "NUPL2" "FGGY" "ATXN10" "STAU2" "ATG2B" "CLK1" "BRWD1" "CCDC9" "CCDC66"  "C6orf106" "ERCC6" "THSD1" "RBM33" "UTRN" "OGDH" "NDUFA10" "FAM73A" "SMARCC1" "RSL1D1" "HPS5" "RYK" "PTPN13" "TRPS1" "SMO" |
| R17004389LR01 | "NEB" "TNC" "NRIP1" "DLG1" "PTPN22" "BCL11B" "KPNA5" "MAP3K5" "PSMB1" "SFMBT2" "ZRANB1" "FOXP1" "PROSC" "PICALM" "CTDP1" "UGP2" "ESYT2" "AREG" "DNAJC2" "MYO9B" "ARAP2" "LZIC" "SLC8A1" "CCDC134" "HTT" "KLC1" "NUPL2" "FGGY" "ATG2B" "USP33" "N4BP2L2" "BRWD1" "SDF4" "ERCC6" "ARHGEF4" "RBM33" "DEF6" "UTRN" "RELL1" "SNRK" "STAM" "TNPO3" "ELF2" "RSL1D1" "EXOC6B" "SLC11A2" "DCUN1D4" "NDUFS1" "RYK" "SOGA2" "PPP4R1" "PARD3" |
| TI1707200244LR01 | "NEB" "TNC" "NRIP1" "DLG1" "PTPN22" "BCL11B" "KPNA5" "MAP3K5" "PSMB1" "SFMBT2" "FOXP1" "PROSC"  "PICALM" "CTDP1" "ABHD2" "UGP2" "ESYT2" "DNAJC2" "LZIC" "SLC8A1" "CCDC134" "KLC1" "KLHL8" "NUPL2"  "FGGY" "ATXN10" "STAU2" "ATG2B" "USP33" "CLK1" "N4BP2L2" "KIAA0146" "SDF4" "CLASP2" "C6orf106" "ERCC6"  "PIKFYVE" "THSD1" "RELL1" "PPP3CC" "FCHO2" "SMARCA5" "PCMTD1" "CANX" "ARHGAP5" "CTBP1" "PTGR1" "FNDC3B"  "PPFIA1" "PDS5A" "ATF7IP" "SLC11A2" "DCUN1D4" "PTPN13" "YTHDF2" "SOGA2" "ATP5C1" "SMO" |
| TI1707200245LR01 | "NEB" "NRIP1" "MAP3K5" "ZRANB1" "PROSC" "SPINK5" "ESYT2" "DNAJC2" "LZIC" "KLHL8" "ATXN10" "STAU2" "N4BP2L2" "KIAA0146" "C6orf106" "PLEKHM1" "PIKFYVE" "RBM33" "ASPH" "KLHL2" "KANSL1L" "FAM73A" "SMARCC1" "PPFIA1" "MAPK8" "ATF7IP" "ITM2B" "HPS5" "DCUN1D4" "NDUFS1" "PTPN13" "TRPS1" "SOGA2" |
| TI1707200246LR01 | "NEB" "DLG1" "BCL11B" "MAP3K5" "PSMB1" "ZRANB1" "PROSC" "PICALM" "SPINK5" "CTDP1" "ABHD2" "UGP2" "ESYT2" "DNAJC2" "ARAP2" "LZIC" "CCDC134" "HTT" "KLC1" "ATXN10" "ATG2B" "USP33" "CLK1" "N4BP2L2" "KIAA0146" "CCDC66" "C6orf106" "PLEKHM1" "ARHGEF4" "RBM33" "ASPH" "LRP6" "PPP3CC" "EPRS" "FCHO2" "SMARCC1" "PCMTD1" "LIFR" "RSL1D1" "PPFIA1" "KLHDC10" "ATF7IP" "SLC11A2" "HPS5" "NDUFS1" "RYK" "SOGA2" "SMO" |
| TI1707200247LR01 | "PIKFYVE" |
| TI1707200252LR01 | 0 |
| R17004390LR01 | 0 |
| R17004391LR01 | "SBDS" |
| R17004392LR01 | "KLC1" |
| R17004393LR01 | 0 |