**Supplementary Figure**

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**Supplementary Table 1. Differentially expressed genes between probands and siblings after controlling for age, sex, and family effects.** We fitted a linear model for each probeset to find significantly changed genes in probands after controlling for the other factors. A total of 189 probesets including 145 known genes were significant at nominal p-value (Diagnosis (Dx)) < 0.01, but not by the other factors such as age, sex, and familial effects. The false discovery rates for p-values (Dx) were estimated using Storey and Tibshirani’s method (see Methods).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ProbeID** | **Gene Symbol** | **Gene** | **Fold change** | **p-value (Dx)** | **p-value (Sex)** | **p-value (Age)** | **p-value (familyID)** | **False Discovery Rate (Dx)** |
| 7931899 | *IL15RA* | interleukin 15 receptor, alpha | -2.16 | 0.000017 | 0.310213 | 0.021721 | 0.023763 | 0.043 |
| 7894611 | *--* | -- | -2.57 | 0.000047 | 0.926191 | 0.904586 | 0.687649 | 0.099 |
| 7991602 | *PCSK6* | proprotein convertase subtilisin/kexin type 6 | -2.11 | 0.000088 | 0.506090 | 0.118864 | 0.056974 | 0.157 |
| 7894584 | *--* | -- | -2.65 | 0.000096 | 0.901791 | 0.907958 | 0.966256 | 0.162 |
| 8165705 | *ND6* | NADH-ubiquinone oxidoreductase chain 6 | -2.21 | 0.000116 | 0.646885 | 0.405567 | 0.158138 | 0.187 |
| 7895139 | *--* | -- | -2.40 | 0.000305 | 0.964142 | 0.948376 | 0.812158 | 0.382 |
| 8045848 | *UPP2* | uridine phosphorylase 2 | -2.10 | 0.000314 | 0.082130 | 0.304930 | 0.221452 | 0.382 |
| 7899898 | *HMGB4* | high-mobility group box 4 | -2.07 | 0.000341 | 0.903927 | 0.569997 | 0.127613 | 0.386 |
| 7893504 | *SLC39A9* | solute carrier family 39 (zinc transporter), member 9 | 2.11 | 0.000342 | 0.517077 | 0.635006 | 0.192391 | 0.386 |
| 7893306 | *--* | -- | -2.44 | 0.000360 | 0.851382 | 0.451857 | 0.934117 | 0.391 |
| 7973403 | *CMTM5* | CKLF-like MARVEL transmembrane domain containing 5 | -1.96 | 0.000379 | 0.012896 | 0.546004 | 0.093557 | 0.398 |
| 8159848 | *RNU2-2* | RNA, U2 small nuclear 1; RNA, U2 small nuclear 2 | 2.21 | 0.000450 | 0.717706 | 0.239975 | 0.532294 | 0.450 |
| 8177096 | *RBMY1F* | RNA binding motif protein, Y-linked, family 1, member F | 2.11 | 0.000473 | 0.391124 | 0.156195 | 0.320700 | 0.450 |
| 7894403 | *--* | -- | 2.08 | 0.000487 | 0.347256 | 0.268091 | 0.245462 | 0.450 |
| 7892925 | *--* | -- | -1.94 | 0.000535 | 0.134518 | 0.897353 | 0.063763 | 0.464 |
| 7928514 | *--* | -- | 2.14 | 0.000547 | 0.410595 | 0.072199 | 0.511049 | 0.464 |
| 7899905 | *HMGB4* | high-mobility group box 4 | -1.97 | 0.000548 | 0.213792 | 0.532377 | 0.088382 | 0.464 |
| 7895706 | *--* | -- | 1.77 | 0.000710 | 0.754710 | 0.144999 | 0.010172 | 0.585 |
| 8032608 | *C19ORF28* | chromosome 19 open reading frame 28 | -2.01 | 0.001056 | 0.454643 | 0.134340 | 0.301907 | 0.748 |
| 7896148 | *SLC25A3* | solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3 | 1.92 | 0.001171 | 0.354122 | 0.351546 | 0.134763 | 0.793 |
| 7893331 | *--* | -- | 2.12 | 0.001227 | 0.306148 | 0.362846 | 0.662427 | 0.800 |
| 7894843 | *--* | -- | 1.77 | 0.001236 | 0.308097 | 0.935680 | 0.018699 | 0.800 |
| 7896366 | *--* | -- | -1.86 | 0.001277 | 0.982021 | 0.324102 | 0.071766 | 0.800 |
| 8149849 | *GNRH1* | gonadotropin-releasing hormone 1 (luteinizing-releasing hormone) | 1.88 | 0.001354 | 0.395082 | 0.646159 | 0.090076 | 0.800 |
| 7894176 | *--* | -- | 2.12 | 0.001376 | 0.272693 | 0.838382 | 0.654494 | 0.800 |
| 8044258 | *LIMS1* | LIM and senescent cell antigen-like domains 1 | -2.08 | 0.001389 | 0.461613 | 0.783379 | 0.512213 | 0.800 |
| 7893130 | *--* | -- | -1.88 | 0.001476 | 0.329923 | 0.347666 | 0.118788 | 0.800 |
| 7948249 | *SLC43A1* | solute carrier family 43, member 1 | -1.74 | 0.001550 | 0.989137 | 0.091267 | 0.020714 | 0.814 |
| 7896160 | *--* | -- | -1.78 | 0.001647 | 0.469501 | 0.905713 | 0.033360 | 0.851 |
| 7945663 | *--* | -- | 1.85 | 0.001751 | 0.293636 | 0.216909 | 0.111235 | 0.858 |
| 8144719 | *RNY1* | RNA, Ro-associated Y1 | 1.91 | 0.001811 | 0.656562 | 0.087711 | 0.239176 | 0.858 |
| 8027884 | *--* | -- | -1.90 | 0.001824 | 0.881586 | 0.766073 | 0.159948 | 0.858 |
| 8083094 | *RASA2* | RAS p21 protein activator 2 | 2.02 | 0.001872 | 0.065566 | 0.673264 | 0.623044 | 0.858 |
| 7948332 | *LPXN* | leupaxin | 1.96 | 0.001957 | 0.431329 | 0.436166 | 0.338700 | 0.858 |
| 8148824 | *HSF1* | heat shock transcription factor 1 | -1.92 | 0.001971 | 0.885891 | 0.713935 | 0.214889 | 0.858 |
| 7906367 | *OR10R2* | olfactory receptor, family 10, subfamily R, member 2 | -2.02 | 0.001984 | 0.218971 | 0.796775 | 0.542014 | 0.858 |
| 7944876 | *NRGN* | neurogranin (protein kinase C substrate, RC3) | -1.97 | 0.002045 | 0.255562 | 0.224432 | 0.441197 | 0.858 |
| 7894412 | *C2orf24* | chromosome 2 open reading frame 24 | -1.89 | 0.002053 | 0.988482 | 0.215540 | 0.198401 | 0.858 |
| 7953547 | *ATN1* | atrophin 1 | -1.96 | 0.002084 | 0.758015 | 0.032831 | 0.501446 | 0.858 |
| 8152374 | *--* | -- | -2.03 | 0.002271 | 0.371704 | 0.922409 | 0.564354 | 0.874 |
| 8044333 | *LIMS3-LOC440895* | LIM and senescent cell antigen-like domains 3; LIMS3-LOC440895 read-through | -1.82 | 0.002478 | 0.999233 | 0.615582 | 0.098625 | 0.874 |
| 8054519 | *LIMS3* | LIM and senescent cell antigen-like domains 3 | -1.82 | 0.002478 | 0.999233 | 0.615582 | 0.098625 | 0.874 |
| 8168316 | *OGT* | O-linked N-acetylglucosamine (GlcNAc) transferase | 1.97 | 0.002531 | 0.015084 | 0.784649 | 0.736388 | 0.874 |
| 7893016 | *--* | -- | 1.78 | 0.002535 | 0.149975 | 0.121858 | 0.096587 | 0.874 |
| 8036883 | *HIPK4* | homeodomain interacting protein kinase 4 | -2.05 | 0.002552 | 0.944243 | 0.876421 | 0.663158 | 0.874 |
| 7894074 | *CANX* | calnexin | 1.77 | 0.002819 | 0.522432 | 0.261088 | 0.067348 | 0.874 |
| 8085393 | *TMEM40* | transmembrane protein 40 | -1.73 | 0.002821 | 0.468680 | 0.303916 | 0.037734 | 0.874 |
| 8109484 | *KIF4A* | kinesin family member 4B; kinesin family member 4A | -1.88 | 0.002923 | 0.124004 | 0.083245 | 0.384177 | 0.874 |
| 7898521 | *IGSF21* | immunoglobin superfamily, member 21 | -1.87 | 0.003007 | 0.900482 | 0.061582 | 0.323698 | 0.874 |
| 8023312 | *--* | -- | 1.71 | 0.003066 | 0.131669 | 0.028371 | 0.067139 | 0.874 |
| 7894734 | *LOC644063* | heterogeneous nuclear ribonucleoprotein K | 1.78 | 0.003107 | 0.138128 | 0.235433 | 0.119310 | 0.874 |
| 7894322 | *--* | -- | -1.73 | 0.003130 | 0.073066 | 0.015440 | 0.119054 | 0.874 |
| 8042464 | *RN7SL1* | RNA, 7SL, cytoplasmic 2; RNA, 7SL, cytoplasmic 1 | 1.80 | 0.003139 | 0.315516 | 0.063936 | 0.176264 | 0.874 |
| 7953303 | *PLEKHG6* | pleckstrin homology domain containing, family G (with RhoGef domain) member 6 | -1.84 | 0.003152 | 0.796198 | 0.949446 | 0.167219 | 0.874 |
| 7896365 | *--* | -- | 2.16 | 0.003243 | 0.340365 | 0.554572 | 0.983616 | 0.874 |
| 8159692 | *ARRDC1* | arrestin domain containing 1 | -1.84 | 0.003382 | 0.861574 | 0.720076 | 0.182063 | 0.874 |
| 8096032 | *PRDM8* | PR domain containing 8 | -1.75 | 0.003403 | 0.590203 | 0.712263 | 0.066680 | 0.874 |
| 7893075 | *--* | -- | -1.69 | 0.003429 | 0.140182 | 0.893747 | 0.030631 | 0.874 |
| 7923991 | *PLXNA2* | plexin A2 | -1.78 | 0.003611 | 0.357415 | 0.012812 | 0.245718 | 0.874 |
| 8126095 | *C6ORF129* | chromosome 6 open reading frame 129 | 1.82 | 0.003682 | 0.365827 | 0.798606 | 0.178498 | 0.874 |
| 8037816 | *STRN4* | striatin, calmodulin binding protein 4 | -1.78 | 0.003684 | 0.102512 | 0.058673 | 0.194484 | 0.874 |
| 8138581 | *TRA2A* | transformer 2 alpha homolog (Drosophila) | 1.97 | 0.003727 | 0.708980 | 0.638050 | 0.593111 | 0.874 |
| 8095680 | *IL8* | interleukin 8 | 1.71 | 0.003786 | 0.183504 | 0.084514 | 0.064603 | 0.874 |
| 8139796 | *LOC441233* | hypothetical LOC441233 | -1.86 | 0.003801 | 0.073120 | 0.372739 | 0.401724 | 0.874 |
| 8011875 | *DERL2* | Der1-like domain family, member 2 | 1.68 | 0.003922 | 0.394960 | 0.959332 | 0.030613 | 0.874 |
| 8169742 | *XIAP* | X-linked inhibitor of apoptosis | 1.76 | 0.003967 | 0.315226 | 0.833038 | 0.094168 | 0.874 |
| 8124534 | *HIST1H4D* | histone cluster 1, H4D | 1.64 | 0.003984 | 0.897865 | 0.040963 | 0.022608 | 0.874 |
| 7942204 | *CTTN* | cortactin | -1.93 | 0.004011 | 0.402337 | 0.919779 | 0.500286 | 0.874 |
| 7897277 | *C1ORF211* | chromosome 1 open reading frame 211 | 1.84 | 0.004015 | 0.495283 | 0.369522 | 0.245515 | 0.874 |
| 8180307 | *HMGA1* | hypothetical LOC100130009; high mobility group AT-hook 1 | -1.80 | 0.004034 | 0.506481 | 0.133013 | 0.185947 | 0.874 |
| 8108180 | *--* | -- | -1.85 | 0.004085 | 0.590750 | 0.695708 | 0.264036 | 0.874 |
| 8060745 | *SMOX* | spermine oxidase | -1.92 | 0.004158 | 0.799871 | 0.116285 | 0.585642 | 0.874 |
| 7966127 | *SELPLG* | selectin P ligand | 1.84 | 0.004300 | 0.038337 | 0.141225 | 0.480860 | 0.874 |
| 7893613 | *--* | -- | -1.77 | 0.004369 | 0.304721 | 0.701808 | 0.128897 | 0.874 |
| 7977214 | *MIR203* | microRNA 203 | -1.88 | 0.004408 | 0.199403 | 0.359812 | 0.467119 | 0.874 |
| 7972444 | *STK24* | serine/threonine kinase 24 (STE20 homolog, yeast) | -1.71 | 0.004414 | 0.562851 | 0.031003 | 0.096801 | 0.874 |
| 8102829 | *RNU6-2* | RNA, U6 small nuclear 2; RNA, U6 small nuclear 1 | 1.80 | 0.004441 | 0.887625 | 0.464531 | 0.179635 | 0.874 |
| 7984001 | *GCNT3* | glucosaminyl (N-acetyl) transferase 3, mucin type | -1.70 | 0.004493 | 0.936931 | 0.569299 | 0.044764 | 0.874 |
| 8136067 | *TSPAN33* | tetraspanin 33 | -1.88 | 0.004618 | 0.183926 | 0.656185 | 0.448593 | 0.874 |
| 7893233 | *--* | -- | 1.68 | 0.004654 | 0.618845 | 0.055835 | 0.054240 | 0.874 |
| 7975787 | *JDP2* | Jun dimerization protein 2 | -1.78 | 0.004675 | 0.762431 | 0.504347 | 0.141955 | 0.874 |
| 8095694 | *PF4V1* | platelet factor 4 variant 1 | -1.72 | 0.004701 | 0.944256 | 0.830264 | 0.063211 | 0.874 |
| 8050363 | *RNU6-2* | RNA, U6 small nuclear 2; RNA, U6 small nuclear 1 | 1.80 | 0.004765 | 0.664256 | 0.065291 | 0.269253 | 0.874 |
| 8024219 | *ATP5D* | ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit | -1.60 | 0.004799 | 0.211874 | 0.046147 | 0.014511 | 0.874 |
| 7925161 | *IRF2BP2* | interferon regulatory factor 2 binding protein 2 | -1.76 | 0.004871 | 0.693888 | 0.505409 | 0.118951 | 0.874 |
| 8180308 | *HMGA1* | hypothetical LOC100130009; high mobility group AT-hook 1 | -1.76 | 0.004901 | 0.459094 | 0.131281 | 0.171285 | 0.874 |
| 8100966 | *PF4* | platelet factor 4 | -1.63 | 0.004957 | 0.196211 | 0.200209 | 0.023171 | 0.874 |
| 8091658 | *CCNL1* | cyclin L1 | 1.73 | 0.004989 | 0.771181 | 0.267753 | 0.097781 | 0.874 |
| 7991516 | *ADAMTS17* | ADAM metallopeptidase with thrombospondin type 1 motif, 17 | -1.91 | 0.005010 | 0.565441 | 0.266722 | 0.567560 | 0.874 |
| 8156278 | *S1PR3* | sphingosine-1-phosphate receptor 3 | -1.60 | 0.005054 | 0.040705 | 0.067732 | 0.019908 | 0.874 |
| 8170420 | *MAMLD1* | mastermind-like domain containing 1 | -2.01 | 0.005090 | 0.458696 | 0.566617 | 0.867198 | 0.874 |
| 8031516 | *ZNF580* | zinc finger protein 580 | -1.90 | 0.005156 | 0.500564 | 0.458861 | 0.510528 | 0.874 |
| 7990555 | *NRG4* | neuregulin 4 | -1.91 | 0.005164 | 0.978492 | 0.918735 | 0.516143 | 0.874 |
| 8107066 | *LNPEP* | leucyl/cystinyl aminopeptidase | 1.61 | 0.005190 | 0.957564 | 0.361973 | 0.015170 | 0.874 |
| 7925561 | *NCRNA00201* | chromosome 1 open reading frame 199 | 1.83 | 0.005214 | 0.364560 | 0.089812 | 0.427309 | 0.874 |
| 7894011 | *ARF1* | ADP-ribosylation factor 1 | 1.59 | 0.005226 | 0.885718 | 0.188947 | 0.011176 | 0.874 |
| 7924403 | *MIR215* | microRNA 215 | 1.86 | 0.005324 | 0.098062 | 0.663946 | 0.479494 | 0.874 |
| 7896141 | *--* | -- | 1.87 | 0.005354 | 0.754649 | 0.543350 | 0.408381 | 0.874 |
| 7894386 | *FNTA* | farnesyltransferase, CAAX box, alpha | 1.63 | 0.005380 | 0.529085 | 0.397820 | 0.020805 | 0.874 |
| 7919761 | *--* | -- | 1.65 | 0.005384 | 0.112407 | 0.811500 | 0.036115 | 0.874 |
| 7977613 | *--* | -- | -1.77 | 0.005404 | 0.802101 | 0.010878 | 0.335936 | 0.874 |
| 7895220 | *--* | -- | -1.78 | 0.005445 | 0.248168 | 0.916049 | 0.196046 | 0.874 |
| 8043055 | *DNAH6* | dynein, axonemal, heavy chain 6 | -1.67 | 0.005458 | 0.458896 | 0.634118 | 0.041341 | 0.874 |
| 8160722 | *UBAP2* | ubiquitin associated protein 2 | -1.88 | 0.005494 | 0.914792 | 0.937268 | 0.432833 | 0.874 |
| 8003171 | *COTL1* | coactosin-like 1 (Dictyostelium) | -1.84 | 0.005582 | 0.638046 | 0.072113 | 0.455720 | 0.874 |
| 8039316 | *PPP1R12C* | protein phosphatase 1, regulatory (inhibitor) subunit 12C | -1.72 | 0.005618 | 0.733271 | 0.469524 | 0.098367 | 0.874 |
| 8135378 | *PRKAR2B* | protein kinase, cAMP-dependent, regulatory, type II, beta | -1.63 | 0.005718 | 0.428618 | 0.405051 | 0.025593 | 0.874 |
| 7968212 | *WASF3* | WAS protein family, member 3 | -1.87 | 0.005794 | 0.442679 | 0.534114 | 0.491443 | 0.874 |
| 7969675 | *--* | -- | 1.72 | 0.005832 | 0.437549 | 0.634139 | 0.097645 | 0.874 |
| 8053944 | *NEURL3* | neuralized homolog 3 (Drosophila) pseudogene | -1.89 | 0.005837 | 0.899006 | 0.933961 | 0.497071 | 0.874 |
| 8018860 | *EPR1* | effector cell peptidase receptor 1 (non-protein coding) | -1.82 | 0.005852 | 0.880778 | 0.724388 | 0.295631 | 0.874 |
| 8079021 | *CTNNB1* | catenin (cadherin-associated protein), beta 1, 88kDa | 1.66 | 0.005927 | 0.548921 | 0.026231 | 0.075038 | 0.874 |
| 7980296 | *TMED10* | transmembrane emp24-like trafficking protein 10 (yeast) | 1.78 | 0.005940 | 0.509902 | 0.252483 | 0.231667 | 0.874 |
| 8138718 | *HOXA2* | homeobox A2 | -1.71 | 0.005981 | 0.196966 | 0.541465 | 0.100178 | 0.874 |
| 8076161 | *DNAL4* | dynein, axonemal, light chain 4 | -1.86 | 0.006173 | 0.139509 | 0.090087 | 0.693532 | 0.874 |
| 8132465 | *HECW1* | HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1 | -1.67 | 0.006256 | 0.098894 | 0.536065 | 0.065978 | 0.874 |
| 8101086 | *NAAA* | N-acylethanolamine acid amidase | -1.70 | 0.006282 | 0.415189 | 0.416486 | 0.096163 | 0.874 |
| 7893184 | *RPL27* | ribosomal protein L27 | 1.66 | 0.006290 | 0.280238 | 0.035614 | 0.085601 | 0.874 |
| 7922823 | *EDEM3* | ER degradation enhancer, mannosidase alpha-like 3 | 1.60 | 0.006356 | 0.921473 | 0.215780 | 0.017416 | 0.874 |
| 7948902 | *SNORD29* | small nucleolar RNA, C/D box 29 | 1.72 | 0.006494 | 0.909559 | 0.194187 | 0.128677 | 0.874 |
| 7901854 | *RNU6-2* | RNA, U6 small nuclear 2; RNA, U6 small nuclear 1 | 1.66 | 0.006569 | 0.428935 | 0.250073 | 0.061580 | 0.874 |
| 7909503 | *SERTAD4* | SERTA domain containing 4 | -1.88 | 0.006689 | 0.995121 | 0.472140 | 0.549800 | 0.874 |
| 7937247 | *SYCE1* | synaptonemal complex central element protein 1 | -1.67 | 0.006697 | 0.840445 | 0.030884 | 0.094506 | 0.874 |
| 8123104 | *FNDC1* | fibronectin type III domain containing 1 | -1.76 | 0.006730 | 0.947318 | 0.208830 | 0.233920 | 0.874 |
| 8052123 | *RNU6-2* | RNA, U6 small nuclear 2; RNA, U6 small nuclear 1 | 1.76 | 0.006770 | 0.321129 | 0.955017 | 0.217119 | 0.874 |
| 8005245 | *RN7SL2* | RNA, 7SL, cytoplasmic 2; RNA, 7SL, cytoplasmic 1 | 1.70 | 0.006872 | 0.964914 | 0.027577 | 0.159941 | 0.874 |
| 7929282 | *HHEX* | hematopoietically expressed homeobox | -1.72 | 0.006920 | 0.193343 | 0.484300 | 0.148254 | 0.874 |
| 8036004 | *CEBPA* | CCAAT/enhancer binding protein (C/EBP), alpha | -1.69 | 0.006923 | 0.417129 | 0.822540 | 0.089640 | 0.874 |
| 7903401 | *--* | -- | -1.99 | 0.006932 | 0.723756 | 0.239509 | 0.927780 | 0.874 |
| 7895719 | *NONO* | non-POU domain containing, octamer-binding | 1.82 | 0.006938 | 0.327489 | 0.548785 | 0.388329 | 0.874 |
| 8047536 | *RN7SL1* | RNA, 7SL, cytoplasmic 2; RNA, 7SL, cytoplasmic 1 | 1.71 | 0.006950 | 0.080083 | 0.061614 | 0.230009 | 0.874 |
| 7983718 | *SCG3* | secretogranin III | -1.78 | 0.007002 | 0.150372 | 0.467031 | 0.313031 | 0.874 |
| 7973924 | *KIAA0391* | KIAA0391 | 1.73 | 0.007181 | 0.827101 | 0.865839 | 0.152448 | 0.874 |
| 8083409 | *AADACL2* | arylacetamide deacetylase-like 2 | -1.77 | 0.007204 | 0.422114 | 0.952875 | 0.239622 | 0.874 |
| 7919969 | *RN7SL1* | RNA, 7SL, cytoplasmic 2; RNA, 7SL, cytoplasmic 1 | 1.87 | 0.007209 | 0.574422 | 0.771792 | 0.543273 | 0.874 |
| 8053610 | *ANAPC1* | anaphase promoting complex subunit 1 | 1.76 | 0.007229 | 0.107132 | 0.479176 | 0.287284 | 0.874 |
| 8011339 | *OR1E1* | olfactory receptor, family 1, subfamily E, member 1 | -1.68 | 0.007345 | 0.654344 | 0.317669 | 0.089237 | 0.874 |
| 8109750 | *RPLP0* |  | 1.60 | 0.007349 | 0.860728 | 0.010394 | 0.041106 | 0.874 |
| 8042335 | *VDAC2* | voltage-dependent anion channel 2 | 1.74 | 0.007414 | 0.550429 | 0.186761 | 0.204441 | 0.874 |
| 8009324 | *--* | -- | 1.72 | 0.007448 | 0.407322 | 0.968722 | 0.146713 | 0.874 |
| 8087283 | *QARS* | glutaminyl-tRNA synthetase | 1.71 | 0.007449 | 0.959270 | 0.252608 | 0.146035 | 0.874 |
| 7894957 | *--* | -- | 1.71 | 0.007468 | 0.669731 | 0.571691 | 0.134086 | 0.874 |
| 7896466 | *--* | -- | -1.74 | 0.007519 | 0.624508 | 0.832444 | 0.174945 | 0.874 |
| 7959535 | *OGFOD2* | 2-oxoglutarate and iron-dependent oxygenase domain containing 2 | 1.84 | 0.007743 | 0.841621 | 0.614566 | 0.473996 | 0.874 |
| 8031522 | *ZNF581* | zinc finger protein 581 | -1.77 | 0.007826 | 0.450494 | 0.131946 | 0.357699 | 0.874 |
| 8146403 | *SNTG1* | syntrophin, gamma 1 | 1.75 | 0.007868 | 0.643769 | 0.243353 | 0.259835 | 0.874 |
| 8023382 | *MBD2* | methyl-CpG binding domain protein 2 | -1.73 | 0.007918 | 0.673668 | 0.250421 | 0.205225 | 0.874 |
| 8115756 | *KCNMB1* | potassium large conductance calcium-activated channel, subfamily M, beta member 1 | -1.63 | 0.007977 | 0.433520 | 0.179885 | 0.051373 | 0.874 |
| 8168357 | *RPS26P11* | ribosomal protein S26 pseudogene 11 | 1.57 | 0.008049 | 0.606828 | 0.042025 | 0.020972 | 0.874 |
| 7894002 | *--* | -- | 1.83 | 0.008075 | 0.288519 | 0.414452 | 0.541232 | 0.874 |
| 8034783 | *LPHN1* | latrophilin 1 | -1.62 | 0.008120 | 0.096449 | 0.018333 | 0.097168 | 0.874 |
| 8156923 | *LPPR1* | plasticity related gene 3 | -1.63 | 0.008120 | 0.313220 | 0.360480 | 0.049997 | 0.874 |
| 8112274 | *ELOVL7* | ELOVL family member 7, elongation of long chain fatty acids (yeast) | -1.57 | 0.008155 | 0.513390 | 0.560966 | 0.015049 | 0.874 |
| 7944765 | *--* | -- | -1.75 | 0.008161 | 0.790568 | 0.416820 | 0.227977 | 0.874 |
| 7999173 | *FAM100A* | family with sequence similarity 100, member A | -1.76 | 0.008165 | 0.426567 | 0.365436 | 0.290332 | 0.874 |
| 8104321 | *ADAMTS16* | ADAM metallopeptidase with thrombospondin type 1 motif, 16 | -1.88 | 0.008176 | 0.430128 | 0.766188 | 0.665268 | 0.874 |
| 7896638 | *--* | -- | 1.72 | 0.008185 | 0.302204 | 0.907739 | 0.184377 | 0.874 |
| 8087624 | *HYAL2* | hyaluronoglucosaminidase 2 | -1.82 | 0.008229 | 0.278149 | 0.857053 | 0.467179 | 0.874 |
| 7917156 | *FUBP1* | far upstream element (FUSE) binding protein 1 | 1.76 | 0.008283 | 0.598128 | 0.287695 | 0.280900 | 0.874 |
| 7895281 | *--* | -- | 1.68 | 0.008466 | 0.409785 | 0.113387 | 0.132084 | 0.874 |
| 8165866 | *STS* | steroid sulfatase (microsomal), isozyme S | -1.69 | 0.008478 | 0.035512 | 0.133926 | 0.247649 | 0.874 |
| 8141140 | *DLX5* | distal-less homeobox 5 | -1.97 | 0.008581 | 0.337703 | 0.732624 | 0.945870 | 0.874 |
| 8103462 | *--* | -- | -1.71 | 0.008673 | 0.012739 | 0.557983 | 0.345047 | 0.874 |
| 8005749 | *--* | -- | -1.66 | 0.008699 | 0.830854 | 0.031257 | 0.123227 | 0.874 |
| 8042283 | *HSPC159* | galectin-related protein | -1.73 | 0.008723 | 0.186090 | 0.144095 | 0.288481 | 0.874 |
| 7967900 | *ZMYM2* | zinc finger, MYM-type 2 | 1.62 | 0.008877 | 0.283322 | 0.095613 | 0.066619 | 0.874 |
| 7895901 | *SART3* | squamous cell carcinoma antigen recognized by T cells 3 | 1.57 | 0.008922 | 0.106049 | 0.178218 | 0.027510 | 0.874 |
| 8129761 | *RNY4P19* | RNA, Ro-associated Y4 pseudogene 19 | 1.83 | 0.009064 | 0.495595 | 0.221939 | 0.595544 | 0.874 |
| 7929689 | *LOC100270710* | hypothetical LOC100270710; MARVEL domain containing 1 | -1.64 | 0.009114 | 0.400516 | 0.241856 | 0.081545 | 0.874 |
| 7894259 | *--* | -- | 1.72 | 0.009149 | 0.231558 | 0.055131 | 0.317183 | 0.874 |
| 7962455 | *NELL2* | NEL-like 2 (chicken) | 1.61 | 0.009154 | 0.040831 | 0.134903 | 0.081431 | 0.874 |
| 7962537 | *SLC38A2* | solute carrier family 38, member 2 | 1.67 | 0.009159 | 0.407989 | 0.132065 | 0.137769 | 0.874 |
| 8082504 | *C3orf37* | chromosome 3 open reading frame 37 | 1.71 | 0.009320 | 0.741275 | 0.164320 | 0.213960 | 0.874 |
| 7956697 | *MON2* | MON2 homolog (S. cerevisiae) | 1.62 | 0.009414 | 0.176575 | 0.025174 | 0.097957 | 0.874 |
| 7999884 | *--* | -- | 1.63 | 0.009522 | 0.468401 | 0.602938 | 0.058121 | 0.874 |
| 7897953 | *SNORA59A* | small nucleolar RNA, H/ACA box 59A | 1.83 | 0.009540 | 0.212820 | 0.244957 | 0.697321 | 0.874 |
| 8005626 | *SNORA59A* | small nucleolar RNA, H/ACA box 59A | 1.83 | 0.009540 | 0.212820 | 0.244957 | 0.697321 | 0.874 |
| 8143749 | *ZNF467* | zinc finger protein 467 | -1.60 | 0.009616 | 0.173320 | 0.246774 | 0.046584 | 0.874 |
| 7969977 | *LOC390424* | similar to hCG1639781 | 1.62 | 0.009629 | 0.139996 | 0.713477 | 0.060986 | 0.874 |
| 8151279 | *RN7SL1* | RNA, 7SL, cytoplasmic 2; RNA, 7SL, cytoplasmic 1 | -1.97 | 0.009642 | 0.998728 | 0.196648 | 0.976121 | 0.874 |
| 8156261 | *--* | -- | -1.83 | 0.009694 | 0.472889 | 0.222970 | 0.658859 | 0.874 |
| 8049180 | *EIF4E2* | eukaryotic translation initiation factor 4E family member 2 | 1.67 | 0.009702 | 0.551121 | 0.023295 | 0.200947 | 0.874 |
| 8052526 | *XPO1* | exportin 1 (CRM1 homolog, yeast) | 1.67 | 0.009705 | 0.921145 | 0.355264 | 0.121688 | 0.874 |
| 8022488 | *ABHD3* | abhydrolase domain containing 3 | 1.62 | 0.009712 | 0.744240 | 0.107602 | 0.066980 | 0.874 |
| 7952103 | *DDX6* | DEAD (Asp-Glu-Ala-Asp) box polypeptide 6 | 1.65 | 0.009712 | 0.241475 | 0.134559 | 0.112016 | 0.874 |
| 8067033 | *KCNG1* | potassium voltage-gated channel, subfamily G, member 1 | -1.60 | 0.009791 | 0.043559 | 0.230872 | 0.061946 | 0.874 |
| 8095251 | *--* | -- | -1.72 | 0.009811 | 0.794249 | 0.013181 | 0.420307 | 0.874 |
| 8037123 | *POU2F2* | POU class 2 homeobox 2 | -1.63 | 0.009903 | 0.382549 | 0.283466 | 0.068684 | 0.874 |
| 7903878 | *RBM15* | RNA binding motif protein 15 | 1.86 | 0.009960 | 0.811248 | 0.708804 | 0.693443 | 0.874 |

**Supplementary Table 2. Significant KEGG pathways between control-like siblings and matched probands.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pathway** | | **Number of genes** | **Normalized enrichment score** | **Nominal p-value** | **False discovery rate** |
| *Up-regulated in probands* | |  |  |  |  |
|  | Spliceosome | 102 | 2.64 | <0.0001 | <0.0001 |
|  | Nucleotide Excision Repair | 38 | 2.52 | <0.0001 | <0.0001 |
|  | Aminoacyl tRNA Biosynthesis | 39 | 2.27 | <0.0001 | <0.0001 |
|  | Pyrimidine Metabolism | 87 | 2.19 | <0.0001 | 0.000329 |
|  | DNA Replication | 34 | 2.18 | <0.0001 | 0.000534 |
|  | Valine Leucine And Isoleucine Degradation | 41 | 2.16 | <0.0001 | 0.000445 |
|  | Rna Degradation | 52 | 2.16 | <0.0001 | 0.000448 |
|  | Ubiquitin Mediated Proteolysis | 123 | 2.15 | <0.0001 | 0.000503 |
|  | Proteasome | 43 | 2.12 | <0.0001 | 0.000684 |
|  | RNA Polymerase | 23 | 2.10 | <0.0001 | 0.000801 |
|  | Glycosylphosphatidylinositol Gpi Anchor Biosynthesis | 23 | 2.04 | <0.0001 | 0.001451 |
|  | Mismatch Repair | 20 | 2.02 | <0.0001 | 0.001799 |
|  | Cytosolic DNA Sensing Pathway | 44 | 1.85 | 0.000788 | 0.010248 |
|  | Basal Transcription Factors | 30 | 1.84 | 0.002179 | 0.010635 |
|  | Protein Export | 21 | 1.83 | 0.008118 | 0.011447 |
|  | Amino Sugar And Nucleotide Sugar Metabolism | 43 | 1.83 | 0.000759 | 0.011106 |
|  | Cell Cycle | 106 | 1.82 | <0.0001 | 0.011727 |
|  | Citrate Cycle Tca Cycle | 29 | 1.81 | 0.003042 | 0.012011 |
|  | Graft Versus Host Disease | 27 | 1.79 | 0.001508 | 0.013287 |
|  | Ribosome | 78 | 1.74 | 0.000808 | 0.020008 |
|  | Base Excision Repair | 31 | 1.70 | 0.009455 | 0.027560 |
|  | Peroxisome | 70 | 1.67 | 0.001586 | 0.034194 |
|  | Oxidative Phosphorylation | 104 | 1.65 | <0.0001 | 0.035676 |
|  | Parkinsons Disease | 101 | 1.63 | 0.003249 | 0.040749 |
|  | Huntingtons Disease | 158 | 1.59 | <0.0001 | 0.050916 |
|  | Toll Like Receptor Signaling Pathway | 88 | 1.56 | 0.005747 | 0.060279 |
| *Down-regulated in probands* | |  |  |  |  |
|  | Olfactory Transduction | 349 | -3.06 | <0.0001 | <0.0001 |
|  | Neuroactive Ligand Receptor Interaction | 257 | -2.66 | <0.0001 | <0.0001 |
|  | Calcium Signaling Pathway | 171 | -2.00 | <0.0001 | 0.003799 |
|  | Maturity Onset Diabetes Of The Young | 24 | -1.94 | <0.0001 | 0.006747 |
|  | ECM Receptor Interaction | 78 | -1.90 | <0.0001 | 0.010011 |
|  | Drug Metabolism Cytochrome P450 | 53 | -1.89 | 0.000574 | 0.009447 |
|  | Axon Guidance | 125 | -1.77 | <0.0001 | 0.028772 |
|  | Metabolism Of Xenobiotics By Cytochrome P450 | 54 | -1.75 | 0.001174 | 0.030852 |
|  | Long Term Potentiation | 65 | -1.69 | 0.001183 | 0.049651 |
|  | Retinol Metabolism | 46 | -1.64 | 0.005360 | 0.067844 |
|  | Melanogenesis | 94 | -1.61 | 0.003917 | 0.080600 |
|  | Vascular Smooth Muscle Contraction | 109 | -1.54 | 0.009029 | 0.114424 |
|  | Cytokine-Cytokine Receptor Interaction | 239 | -1.43 | 0.006774 | 0.200967 |

**Supplementary Table 3. Significant KEGG pathways between proband-like siblings and matched probands.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pathway** | | **Number of genes** | **Normalized enrichment score** | **Nominal p-value** | **False discovery rate** |
| *Up-regulated in probands* | |  |  |  |  |
|  | Olfactory transduction | 349 | 2.04 | <0.0001 | 0.004056 |
|  | Ribosome | 78 | 2.00 | <0.0001 | 0.004502 |
|  | Drug Metabolism Cytochrome P450 | 53 | 1.72 | 0.003488 | 0.085713 |
|  | RIG-I-LIKE receptor signaling pathway | 63 | 1.61 | 0.009445 | 0.184783 |
| *Down-regulated in probands* | |  |  |  |  |
|  | Nucleotide excision repair | 38 | -1.87 | 0.000000 | 0.100820 |
|  | Lysosome | 119 | -1.85 | 0.000000 | 0.060783 |
|  | Chemokine signaling pathway | 170 | -1.60 | 0.000000 | 0.482411 |
|  | Endocytosis | 167 | -1.41 | 0.009582 | 0.504001 |