# Supplementary Materials for

## Optineurin cooperates with NRF2 to regulate tooth root morphogenesis by controlling mitochondrial dynamics and apoptosis

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**This file includes:**

**Table S1.** Primers used in this study

| Gene | Forward | Reverse |
|---|---|---|
| **mus musculus (PCR)-*Optn* (1)** | CTTTGTTTCAGGGGAGGGGT | TCCAGATAGCAGCAAGGAGCTT |
| **mus musculus (PCR)-*Optn* (2)** | TTATTTATTTGCTGACATACCCATCC | CATCCTAATCTCTGCCCATCTACTCT |
| **mus musculus-*Gapdh*** | ACCACAGTCCATGCCATCAC | TCCACCACCCTGTTGCTGTA |
| **mus musculus-*Dmp1*** | CTGAAGAGAGGACGGGTGATT | CGTGTGGTCACTATTTGCCTG |
| **mus musculus-*Dspp*** | ATTCCGGTTCCCCAGTTAGTA | GCCTTCCTCTATCACCTTC |
| **mus musculus-Runx2** | AGAGTCAGATTACAGATCCCAGG | TGGCTCTTCTTACTGAGAGAGG |
| **mus musculus-Bmp4** | TTGATACCTGAGACCGGGAAG | GGCGACTCAGAGCACAAG |
| **mus musculus-*Drp1*** | CAGGAATTGTTACGGTTCCCTAA | CCTGAATTAACTTGTCCCGTGA |
| **mus musculus-*Opa1*** | TGGAAAATGGTTCGAGAGTCAG | CATTCCGTCTCTAGGTTAAAGCG |
| **mus musculus-*Mfn1*** | ATGGCAGAAACGGTATCTCCA | GCCCTCAGTAACAAACTCCAGT |
| **mus musculus-*Fis1*** | AGAGCACGCAATTTGAATATGCC | TGTGCCCCACGCCCTGATTC |
| **mus musculus-*Mfn2*** | AGAACTGGACCCGGTTACCA | CACTTCGCTGATACCCCTGA |
| **homo sapiens-*GAPDH*** | GAAGGTGAAGGTCGGAGTC | GAGATGGTGATGGGATTTO |
| **homo sapiens-*FIS1*** | TGGTGCGGAGCAAGTACAAT | TGCCCACGAGTCCATCTTTC |
| **homo sapiens-*BMP4*** | CTCCAAGAATGGAGGAGCTGTAGGAA | CCTATGAGAGAGCAGGCAAGA |
| **homo sapiens-*DMP1*** | GGAAGAGGTGGTGAGTGAG | TTGAGTGGGAGAGTGTG |
| **homo sapiens-*DSPP*** | CCATTCCAGTTCCTCAAA | GCCTTCCTCTATCACCTTC |
| **homo sapiens-*RUNX2*** | AGTTCCCAAGCATTTCATC | GGCAGGTAGGTGTGGTAGT |
| **homo sapiens-*DRP1*** | CTGCCTCAAATCGTCGTAGTG | GAGGTCTCCGGGTGACAATTC |
| **homo sapiens-*OPA1*** | TGTGAGGTCTGCCAGTCTTTA | TGTCCTTAATTGGGGTCGTTG |
| **homo sapiens-*MFN1*** | GTTGCCGGGTGATAGTTGGA | TGCCACCTTCATGTGTCTCC |
| **homo sapiens-*MFN2*** | CTCTCGATGCAACTCTATCGTC | TCCTGTACGTGTCTTCAAGGAA |

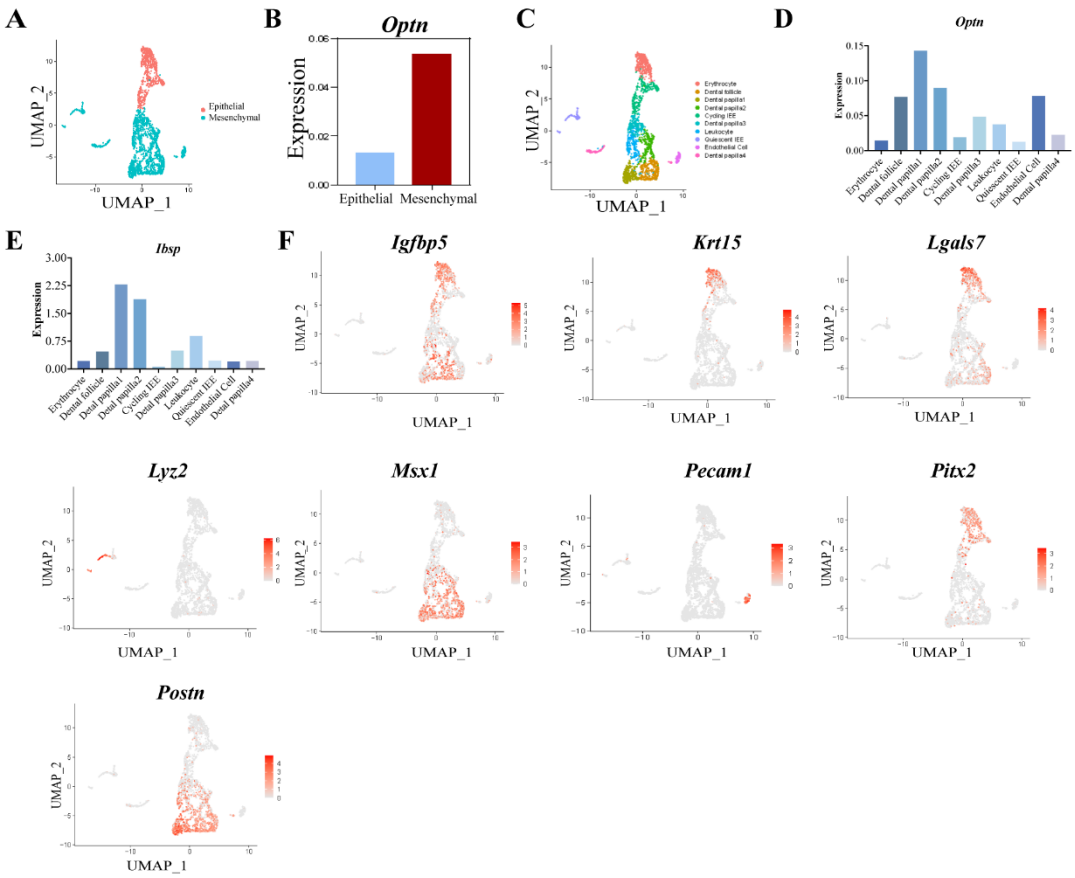


**Figure S1.** Characterization of gene expression of in mice bell stage tooth germ. (A) Distribution of epithelium and mesenchymal linage cells of mice bell stage tooth germ scRNA-seq analysis on UMAP plot. (B) Average expression of *Optn* between mesenchyme cells and epithelial cells. (C) UMAP of cells divided into different clusters. (D) Average gene expression of *Optn* and *Ibsp* (E) in different clusters. (F) Featureplots indicating marker genes in different clusters, *Igfbp5* for Quiescent IEE, *Krt15* for erythrocyte, *Lgals7* for dental follicle, *Lyz2* for leukocyte, *Msx1* for mesenchymal lineages, *Pecam1* for endothelial cell, *Pitx2* for epithelium linages and cycling IEE, and *Postn* for dental papilla.

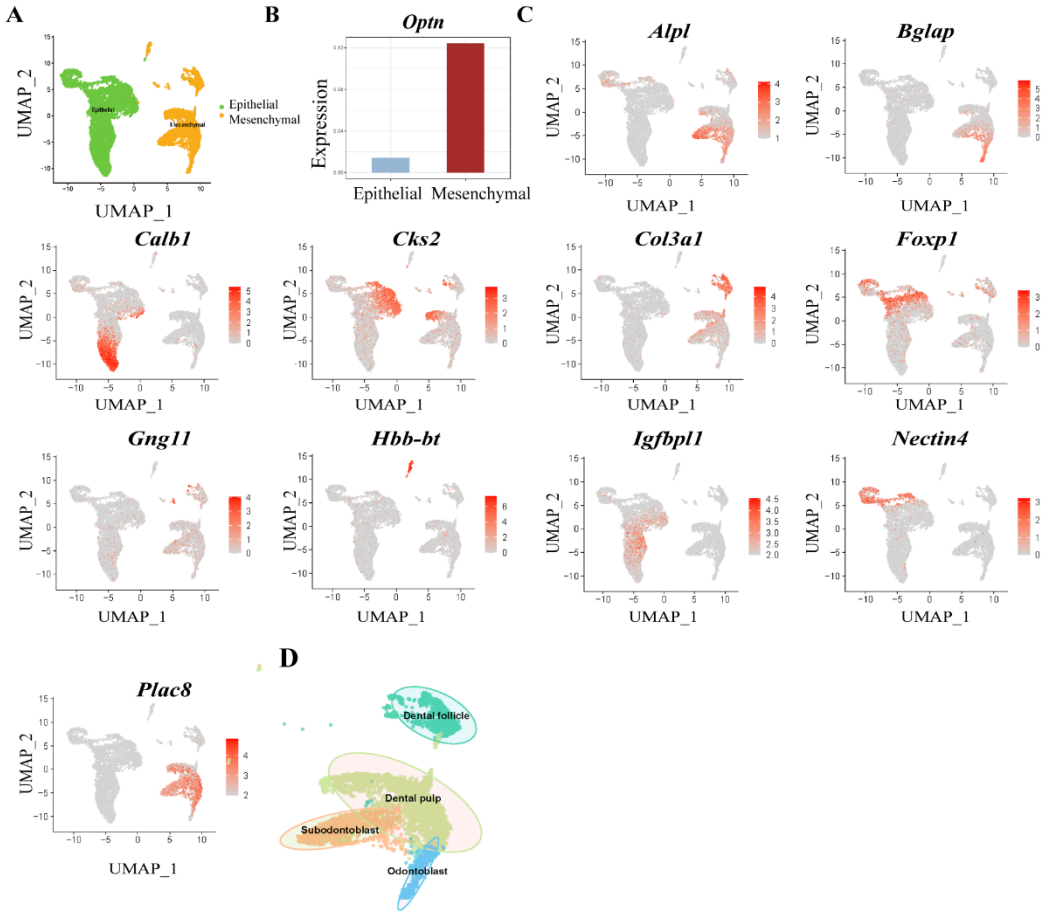


**Figure S2.** Characterization of gene expression in developing tooth root at P1. (A) UMAP plot of scRNA-seq data sets from mouse P1 molars, showing the distribution from the epithelium and mesenchyme. (B) Average expression of *Optn* between mesenchyme cells and epithelial cells. (C) Featureplots are pseudocolored for the expression of marker genes among different clusters. We identified subodontoblast cluster with *Alpl*, odontoblast with *Bglap*, ameloblast with *Calb1*, cycling iee with *Cks2*, dental follicle with *Col3a1*, quiescent-iee with *Foxp1*, endothelial cell with *Gng11*, erythrocyte with *Hbb-bt*, preameloblast with *Igfbpl1*, non ameloblast with *Nectin4*, dental pulp with *Plac8*. (D) UMAP of mesenchyme cells, including dental pulp, odontoblasts, subodontoblasts, and dental follicles colored by cell types.

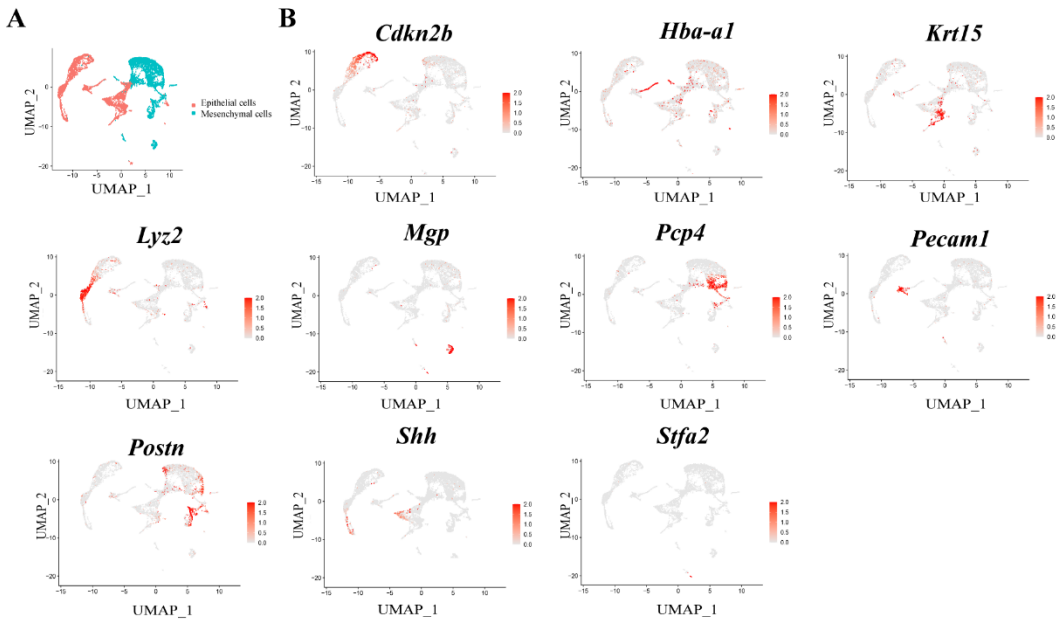


**Figure S3.** Characterization of gene expression in developing tooth root at P7. (A) UMAP plot of scRNA-seq data sets from mouse P7 molars, showing the distribution from the epithelium and mesenchyme. (B) Featureplots are pseudocolored for the expression of marker genes among different clusters. We identified *Cdkn2b* for IEE, *Hba-a1* for erythroid cells, *Krt15* for SI/SR, *Lyz2* for immune cells, *Mgp* for myoblasts, *Pcp4* for DPC, *Pecam1* for endothelial cells, *Postn* for odontoblasts, *Shh* for EK, and *Stfa2* for Neutrophil.

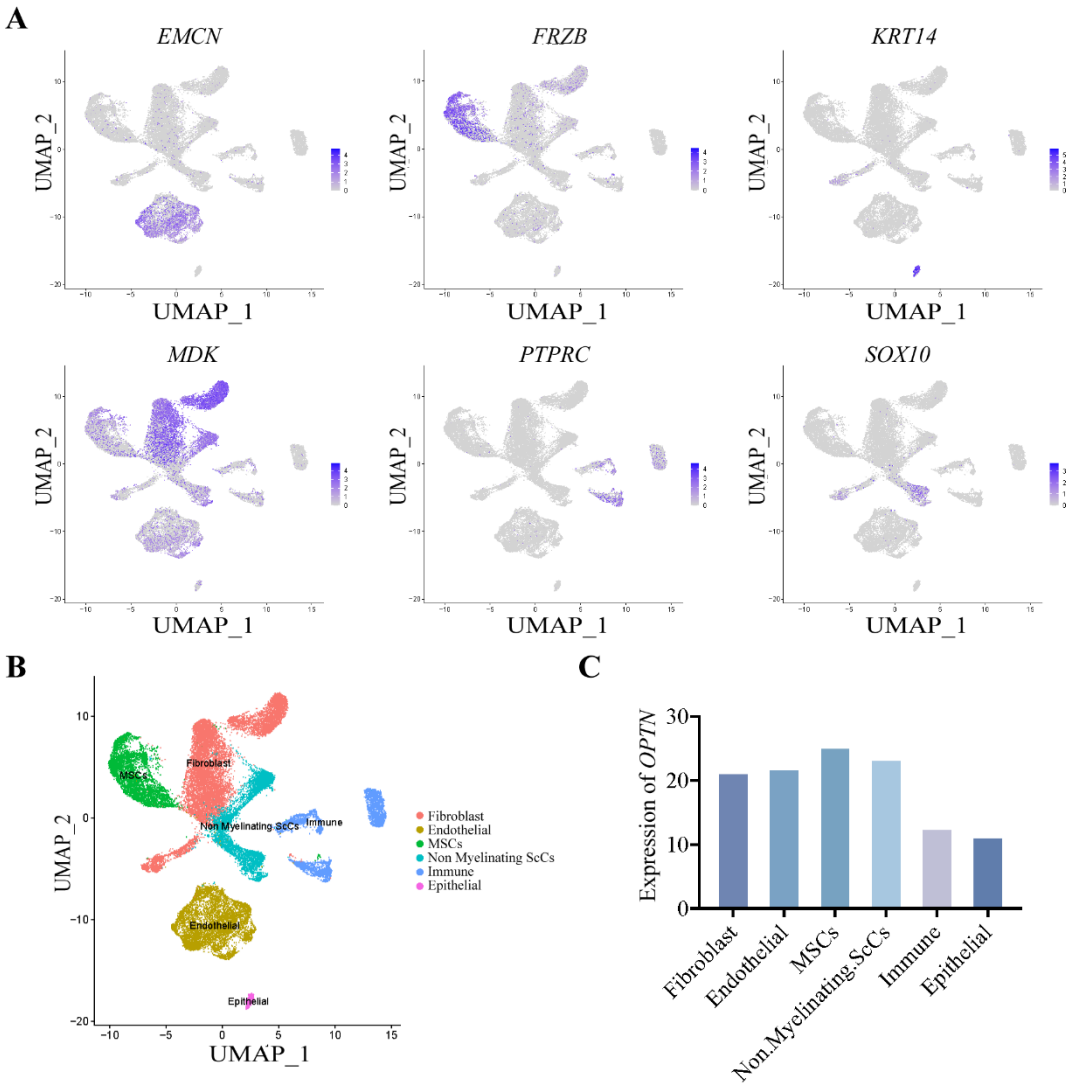


**Figure S4.** Characterization of gene expression of in human dental pulps. (A) Featureplots indicating marker genes average expression in different clusters, *EMCN* for endothelial cell, *FRZB* for MSCs, *KRT14* for epithlial cells, *MDK* for fibroblast, *PTPRC* for immune cell, *SOX10* for Non Myelinating ScCs. (B) UMAP of cells divided into six different clusters. (C) Average gene expression of *OPTN* in different clusters.

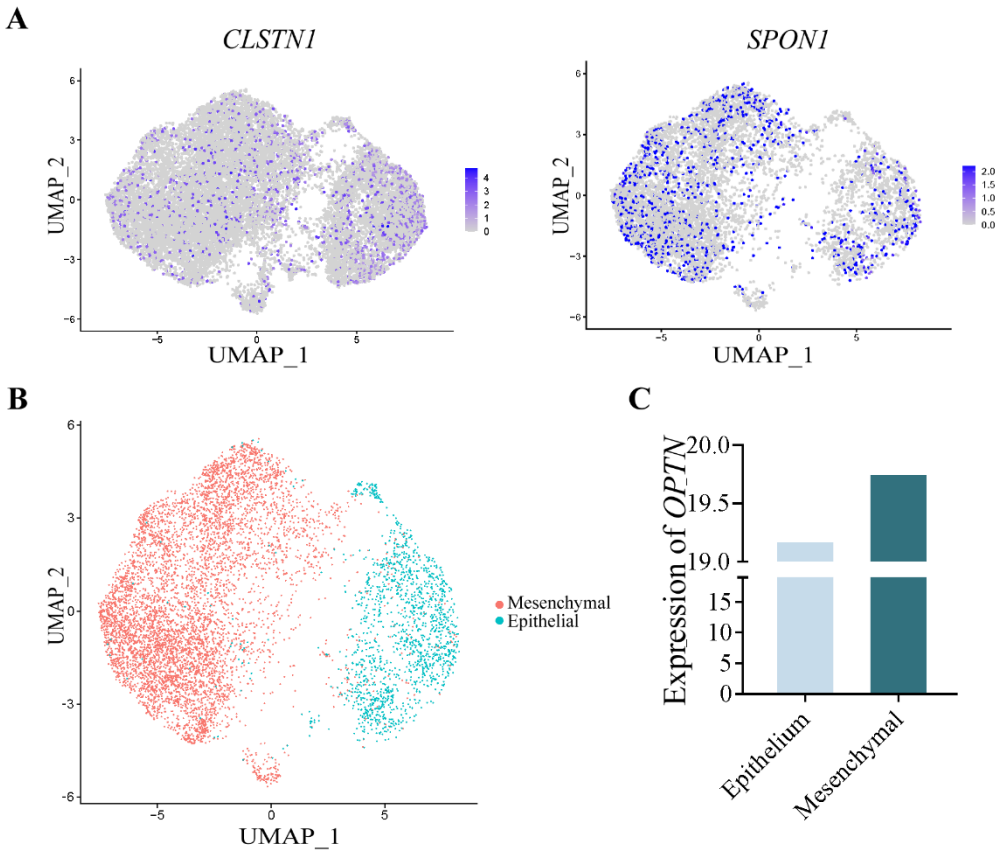


**Figure S5.** Characterization of gene expression of in human embryonic molars. (A) Featureplots indicating marker genes average expression in different clusters, *CLSTN1* for endothelial cells, *SPON1* for mesenchymal cells. (B) Distribution of epithelial cells and mesenchymal cells of human embryonic molars gern scRNA-seq analysis on UMAP plot. (C)Average expression of *OPTN* between mesenchyme cells and epithelial cells.

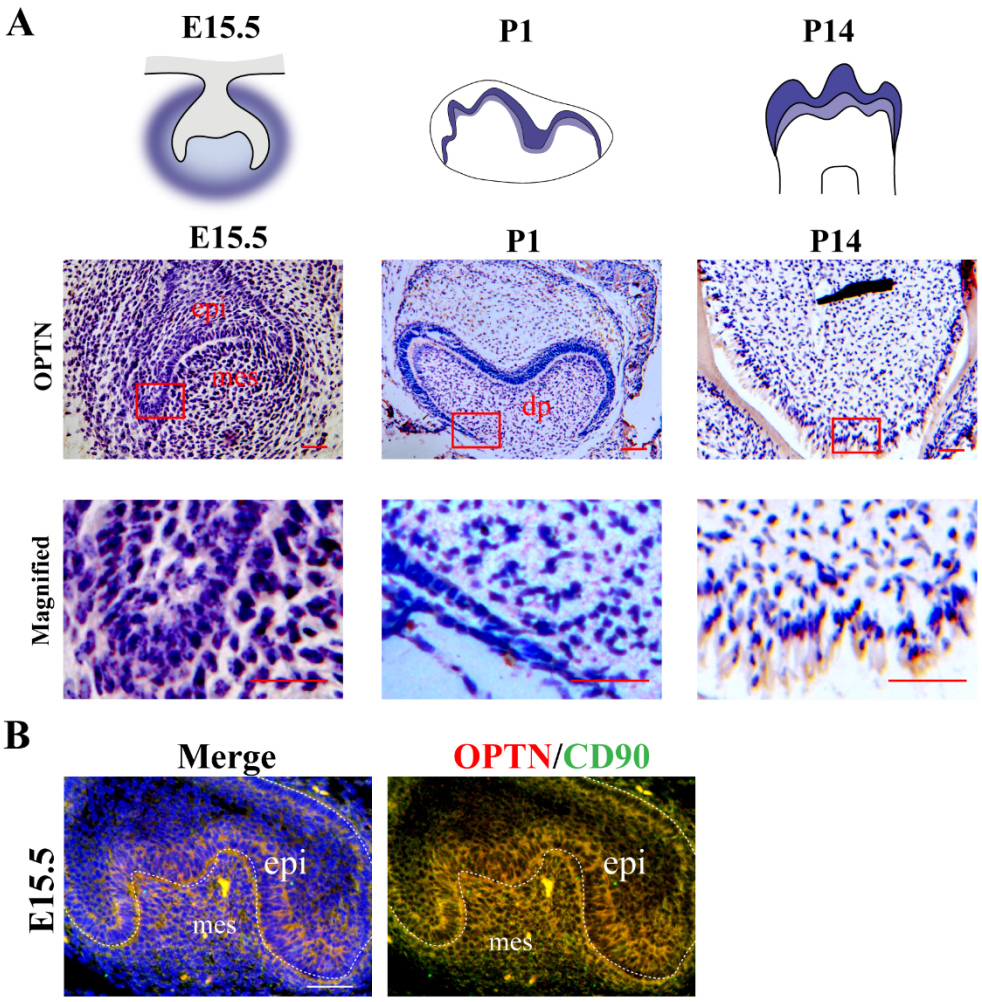


**Figure S6.** Original expression pattern of OPTN in developing tooth root. (A) Immunohistochemical staining of the OPTN in the developing tooth at E15.5, P1, and P14, respectively. epi: epithelium; mes: mesenchyme; dp: dental papilla. Scale bars: 80μm (up) and 40μm (below). (B) Representative images of immunofluorescent colocalization of OPTN and CD90, with or without DAPI staining in the developing tooth at E15.5. Scale bars: 40μm.

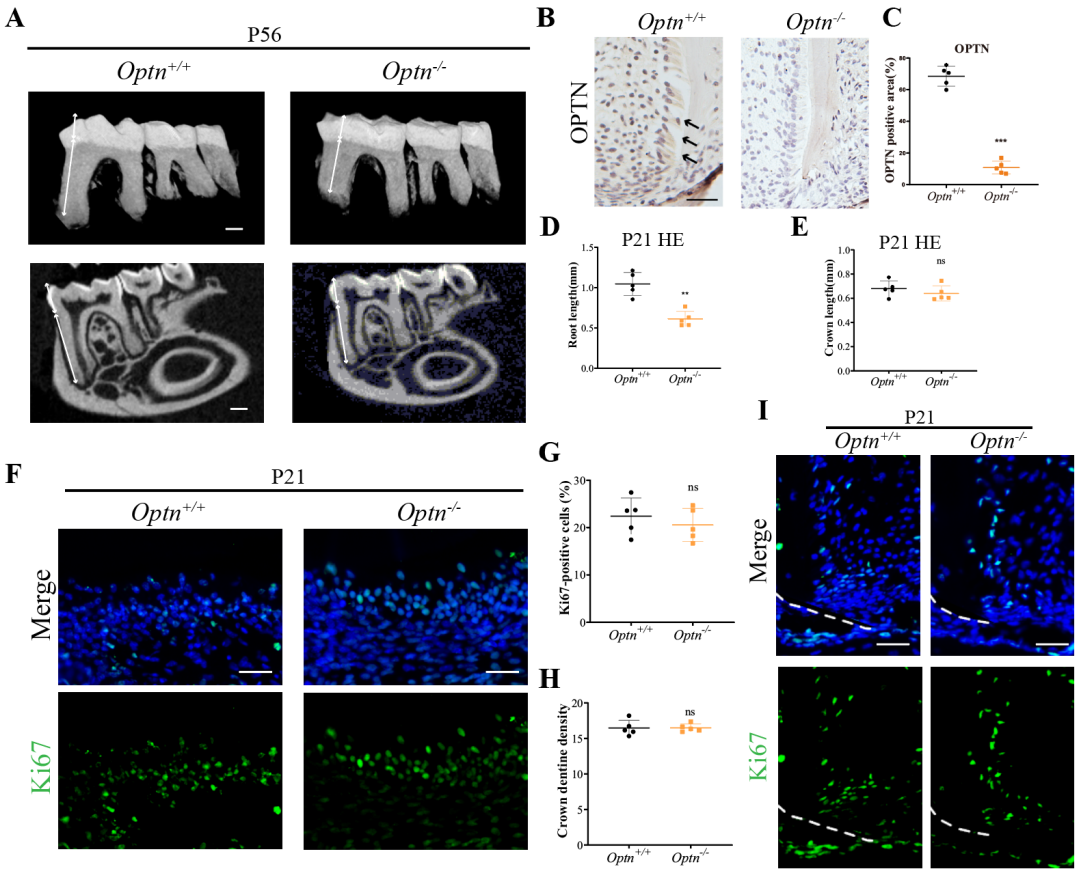


**Figure S7.** The loss of *Optn* resulted in root development defects. (A) Micro-CT of tooth development in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice at P56. Double-headed arrows indicate tooth crowns and tooth roots. Scale bars: 200μm. (B) Immunohistochemistry staining of apical regions showing the expression pattern of OPTN in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$mice siblings. Arrows indicate the OPTN-positive cells. Scale bars: 50 μm. (C) Quantification of OPTN-positive cells in the apical region is shown in (B). (D, E) Quantitative analysis of the root length and crown length in HE staining of tooth development in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice at P21. (F) Ki67-positive cells in the crown region in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice siblings at P21, Bar=40 μm. (G) Quantification of Ki67-positive cells in (F). (H) Quantification of dentine density in crown region in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice siblings at P21 from CT images. (I) The Ki67-positive

cells in the apical region in the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice siblings at P21. Dotted lines indicate the border between the dental epithelium and the dental mesenchyme. The results are presented above as the mean ± SD. SD, Standard Deviation. * $P < 0.05$, ** $P < 0.01$, ***$P < 0.001$, ns, no significance.

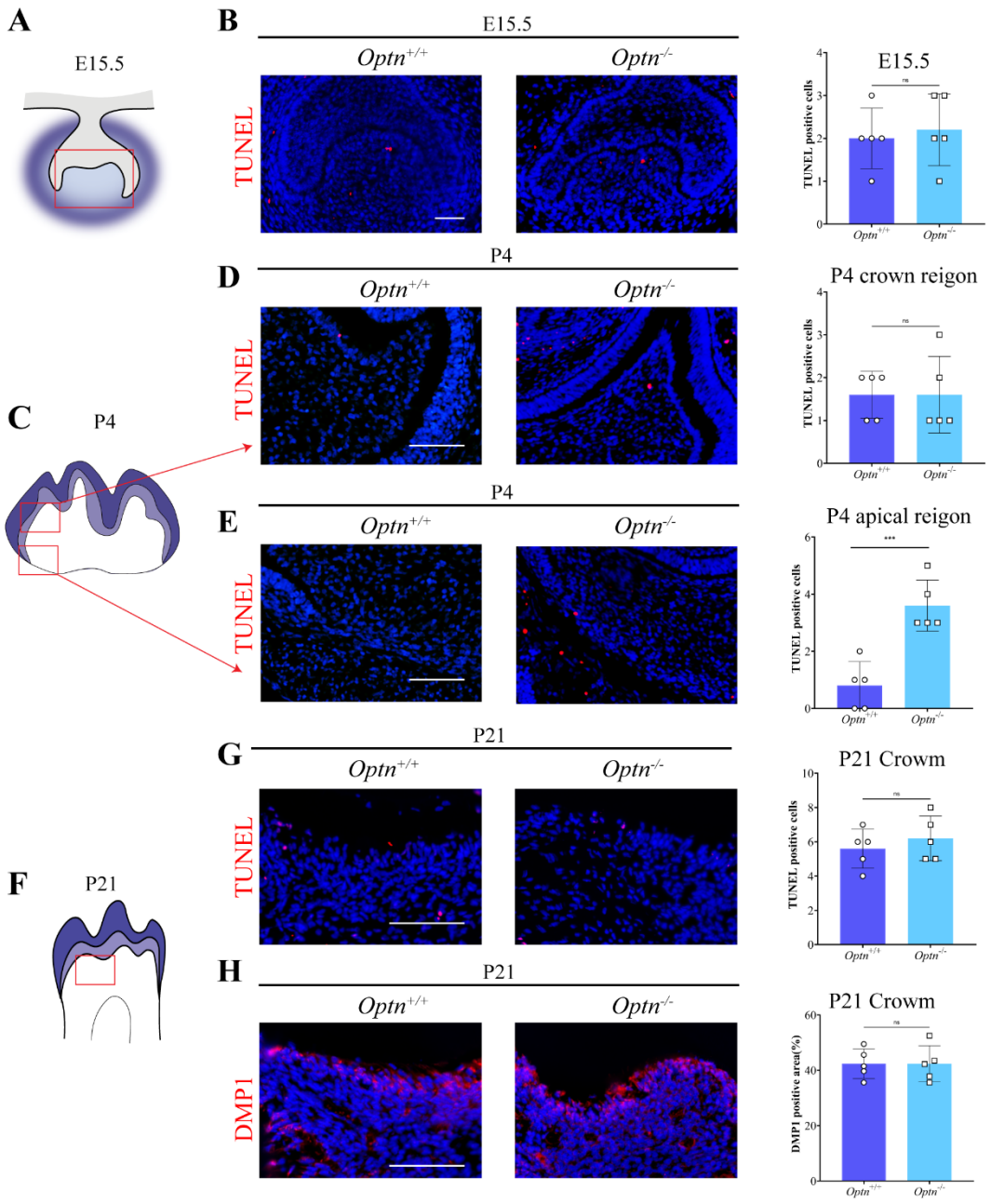


**Figure S8.** OPTN knockdown barely affects tooth crown development. (A) The schematic diagram of the developing tooth at E15.5. (B) Representative images of TUNEL staining with DAPI staining in the developing tooth were obtained from the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice at E15.5 with relative quantification analysis on the right. Scale bars: 80μm. (C) The schematic diagram of the developing tooth at P4 crown region and root region. (D) Representative images of TUNEL staining with DAPI

staining in the developing tooth obtained from the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice at P4 crown region and root region (E) with relative quantification analysis on the right. Scale bars: 80μm. (F) The schematic diagram of the developing tooth at P21. (G) Representative images of TUNEL staining with DAPI staining in the developing tooth were obtained from the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice at the P21 crown region with relative quantification analysis on the right. Scale bars: 30μm. (H) Representative images of immunofluorescent staining of DMP1 in the developing tooth obtained from the *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice with relative quantification analysis on the right. Scale bars: 30μm. The results are presented above as the mean ± SD. SD, Standard Deviation. * $P < 0.05$, ** $P < 0.01$, ***$P < 0.001$, ns, no significance.

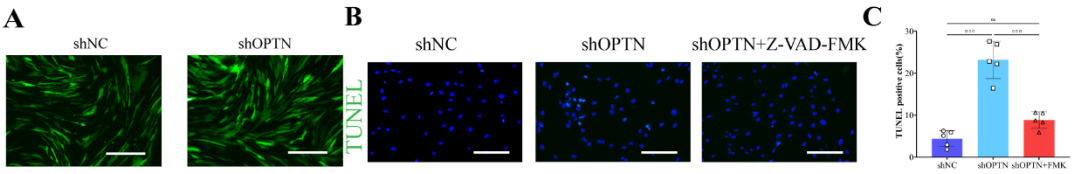


**Figure S9.** Z-VAD-FMK rescued the cell apoptosis induced by OPTN knockdown. (A) The fluorescence picture of SCAPs infected with shNC or shOPTN lentivirus. Scale bars: 30μm. (B) The appliance of FMK rescued the cell apoptosis in the shOPTN SCAPs. Scale bars: 30μm.(C) The quantification analysis of (B). The results are presented above as the mean ± SD. SD, Standard Deviation. * $P < 0.05$, ** $P < 0.01$, ***$P < 0.001$, ns, no significance.

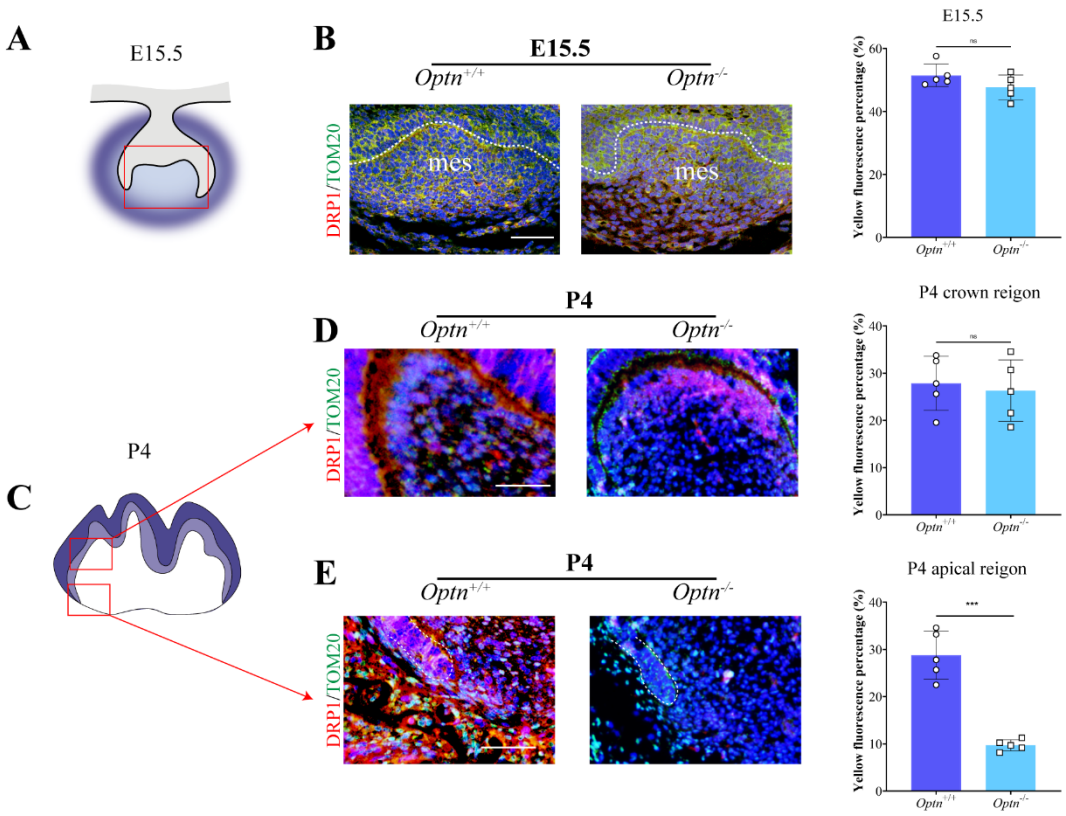


**Figure S10.** Mitochondria fission was less observed in tooth root region during tooth development. (A) The schematic diagram of the developing tooth at E15.5. (B) Representative images of immunofluorescent colocalization of DRP1 and TOM20, with DAPI staining in the developing tooth at E15.5, with relative quantification analysis on the right. (C) The schematic diagram of the crown region and the apical region of developing tooth at P4. (D) Representative images of immunofluorescent colocalization of DRP1 and TOM20, with DAPI staining in the crown reigon and the apical region (E) at P4 from obtained from *Optn*$^{+/+}$ and *Optn*$^{-/-}$ mice with relative quantification analysis on the right. Scale bars: 80μm. The results are presented above as the mean ± SD. SD, Standard Deviation. * $P < 0.05$, ** $P < 0.01$, ***$P < 0.001$, ns, no significance.

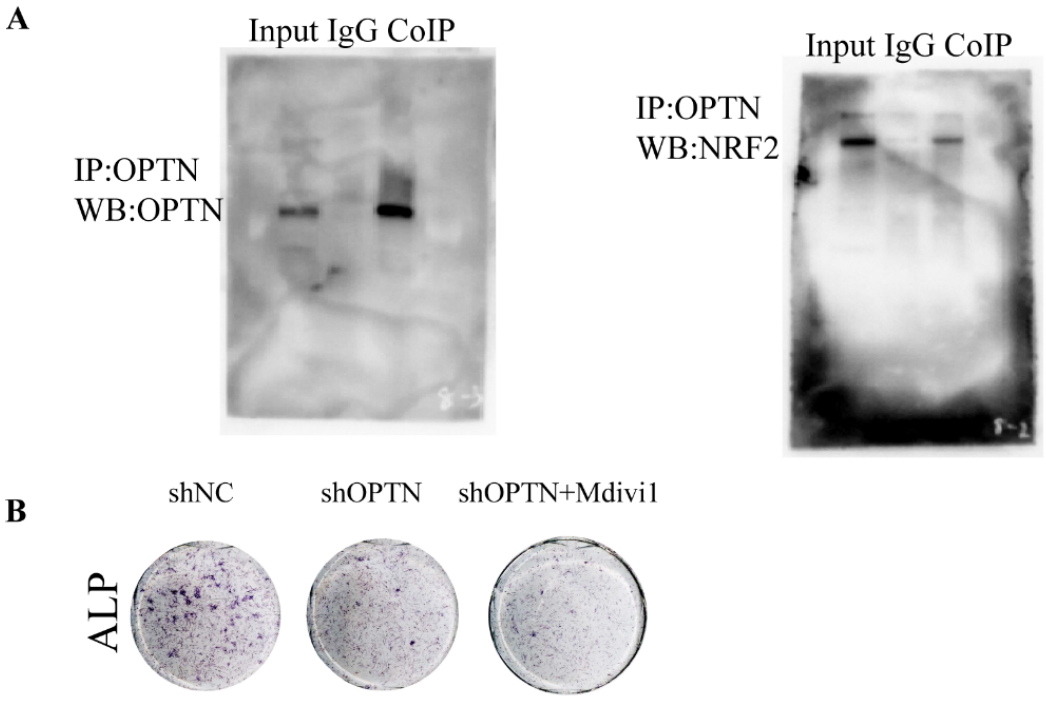


**Figure S11.** Decreasing phosphorylation of DRP1 worsens the decreased ALP activity in the shOPTN SCAPs. (A) The full loading band of CO-IP of OPTN with NRF2. (B) The appliance of Mdivi-1 decreased the ALP activity in the shOPTN SCAPs.

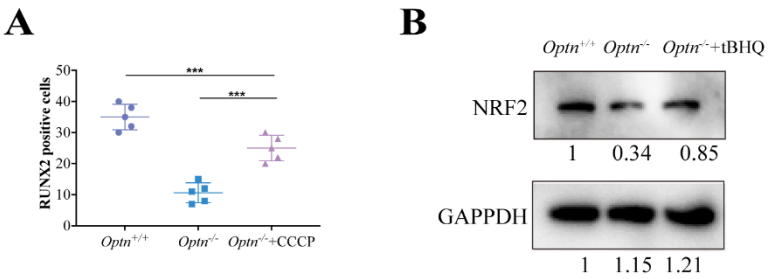


**Figure S12.** Subgingival injections rescued tooth root development. (A) The quantification of RUNX2-positive cells within the roots of the mandibular first molars, obtained from the *Optn*$^{+/+}$, *Optn*$^{-/-}$ and *Optn*$^{-/-}$ +CCCP group following subgingival injections. (B) The WB shows the succeseful appliance of tBHQ. The results are presented above as the mean ± SD. SD, Standard Deviation. * $P < 0.05$, ** $P < 0.01$, ***$P < 0.001$, ns, no significance.

**Table S2:** Lists of top 200 genes up/down-regulated in shOPTN SCAPs compared with shNC SCAPs (log2-fold changel> 0.584 and p-value < 0.05).

| gene_id | gene_name | EntrezID | B_1 | B_2 | B_3 | A_1 | A_2 | A_3 | pval | qval | fc | log2(fc) | regulation | significant |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ENSG00000181195 | PENK | 5179 | 53.8020643 | 52.7164983 | 53.0173468 | 12.7855368 | 15.9729981 | 13.9237307 | 7.422E-110 | 2.405E-105 | 3.73775636 | 1.90217253 | up | yes |
| ENSG00000120738 | EGR1 | 1958 | 58.456051 | 86.069626 | 72.601799 | 23.51516 | 23.063789 | 22.768581 | 5.154E-53 | 8.3489E-49 | 3.13100519 | 1.6466259 | up | yes |
| ENSG00000171570 | RAB4B-EGLN2 | 100529264 | 0.092008047 | 0.062703616 | 0.073207422 | 3.5699286 | 1.57589272 | 3.61266729 | 4.5009E-52 | 4.8607E-48 | 0.02604226 | -5.2630015 | down | yes |
| ENSG00000170345 | FOS | 2353 | 4.66291121 | 4.80079631 | 4.41031053 | 1.10586957 | 1.09600366 | 0.97227101 | 1.5581E-47 | 1.262E-43 | 4.37094757 | 2.12794607 | up | yes |
| ENSG00000229124 | VIM-AS1 | 100507347 | 7.005203755 | 9.784609394 | 8.020905573 | 30.1017156 | 43.8061862 | 29.6765238 | 3.4748E-46 | 2.2515E-42 | 0.23952334 | -2.06176187 | down | yes |
| ENSG00000073756 | PTGS2 | 5743 | 3.409600732 | 2.752704689 | 3.346207645 | 0.72855415 | 0.47701661 | 0.60712694 | 5.7586E-45 | 3.1095E-41 | 5.24556889 | 2.39109924 | up | yes |
| ENSG00000259001 | ENSG00000259001 | | 169.369202 | 110.844093 | 149.285767 | 44.683563 | 34.346611 | 40.911938 | 1.0813E-44 | 5.0045E-41 | 3.58088627 | 1.8403167 | up | yes |
| ENSG00000120708 | TGFBI | 7045 | 29.979003735 | 31.339663 | 31.298060602 | 17.0920977 | 16.038095 | 16.4314139 | 1.4393E-44 | 5.8288E-41 | 1.86872668 | 0.90205558 | up | yes |
| ENSG00000110900 | TSPAN11 | 441631 | 19.373003038 | 15.974009822 | 17.122006084 | 8.44082579 | 8.31674545 | 8.31650158 | 1.8985E-38 | 6.8343E-35 | 2.09263548 | 1.06532103 | up | yes |
| ENSG00000181019 | NQO1 | 1728 | 79.088004155 | 80.848001888 | 77.542005302 | 43.8886172 | 47.6884264 | 44.3008789 | 1.4472E-34 | 4.6886E-31 | 1.74773893 | 0.8054897 | up | yes |
| ENSG00000123240 | OPTN | 10133 | 10.746000359 | 10.920006957 | 11.235000489 | 19.7180447 | 21.0886872 | 21.2520774 | 7.6902E-34 | 2.265E-30 | 0.53018329 | -0.91543689 | down | yes |
| ENSG00000095303 | PTGS1 | 5742 | 55.014003534 | 50.225000198 | 52.659000563 | 32.550000752 | 30.017006692 | 31.421008262 | 1.0936E-29 | 2.9525E-26 | 1.67995211 | 0.74842011 | up | yes |
| ENSG00000116741 | RGS2 | 5997,6012 | 50.734008596 | 35.697007018 | 42.457000481 | 19.467007306 | 14.933009686 | 16.502004188 | 5.4276E-29 | 1.3526E-25 | 2.53201603 | 1.34028654 | up | yes |
| ENSG00000072274 | TFRC | 7037 | 10.772008388 | 9.7648005855 | 10.017000256 | 5.98360004 | 6.05454185 | 6.18792398 | 1.3616E-27 | 3.151E-24 | 1.67642997 | 0.74539222 | up | yes |
| ENSG00000146250 | PRSS35 | 167681 | 38.859000044 | 26.371000082 | 30.885000368 | 14.047000457 | 11.220000821 | 12.699000424 | 1.6979E-27 | 3.6673E-24 | 2.53151718 | 1.34000228 | up | yes |
| ENSG00000011105 | TSPAN9 | 10867 | 49.951005604 | 50.163001737 | 48.993003847 | 32.357004262 | 28.166007494 | 29.380002966 | 2.1085E-27 | 4.2695E-24 | 1.65851726 | 0.72989403 | up | yes |
| ENSG00000186469 | GNG2 | 54331 | 16.789003247 | 14.972002278 | 15.495009028 | 8.71708308 | 8.7589753 | 9.14803737 | 2.8123E-27 | 5.3596E-24 | 1.77498818 | 0.82780942 | up | yes |
| ENSG00000123358 | NR4A1 | 3164 | 4.132504632 | 3.661904174 | 4.32104 | 1.57731852 | 1.62422551 | 1.85670649 | 1.9153E-26 | 3.4473E-23 | 2.39520126 | 1.26014689 | up | yes |
| ENSG00000137975 | CLCA2 | 9635 | 3.513008691 | 2.082706103 | 2.781007599 | 0.68584746 | 0.33311302 | 0.44725482 | 3.238E-25 | 5.5213E-22 | 5.71329732 | 2.51432361 | up | yes |
| ENSG00000141526 | SLC16A3 | 9123 | 14.045002792 | 12.587002996 | 13.492007474 | 8.09775661 | 8.06500086 | 7.72421481 | 3.698E-25 | 5.9904E-22 | 1.67979959 | 0.74828912 | up | yes |
| ENSG00000110092 | CCND1 | 595 | 65.159002798 | 64.948000804 | 64.248003786 | 97.197969 | 97.1990962 | 97.997005264 | 3.0497E-24 | 4.7049E-21 | 0.6647036 | -0.58921692 | down | yes |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ENSG00000168398 | BDKRB2 | 624 | 17.0553543 | 10.8435847 | 13.1325988 | 5.4613932 | 5.8727335 | 5.8996837 | 6.2244E-24 | 9.1662E-21 | 2.3807237 | 1.2514 9028 | up | yes |
| ENSG00000163531 | NFASC | 23114 | 1.2815 0794 | 1.3355 6491 | 1.3493 7254 | 2.3836 0135 | 3.0435 1145 | 2.6769 1117 | 1.2975 E-23 | 1.8277 E-20 | 0.4894 4147 | -1.0307 9175 | down | yes |
| ENSG00000129946 | SHC2 | 25759 | 0.4802 1705 | 0.4931 3737 | 0.4758 87 | 1.9702 3816 | 1.7378 078 | 1.7133 657 | 4.6521 E-23 | 6.28E-20 | 0.2673 1809 | -1.9033 7061 | down | yes |
| ENSG00000125730 | C3 | 718 | 5.9630 4009 | 3.4107 1523 | 4.6612 337 | 1.4159 9022 | 1.8670 8661 | 1.6218 2571 | 1.7164 E-22 | 2.2243 E-19 | 2.8614 2057 | 1.5167 3156 | up | yes |
| ENSG00000115594 | IL1R1 | 3554 | 232.08 593 | 191.00 4145 | 207.11 6068 | 133.58 9534 | 120.73 5197 | 125.33 2788 | 3.3396 E-22 | 4.1614 E-19 | 1.6599 3326 | 0.7311 2524 | up | yes |
| ENSG00000172379 | ARNT2 | 9915 | 3.8012 1636 | 4.6774 3464 | 3.7331 7245 | 8.0597 8031 | 9.0338 5192 | 7.5102 4744 | 2.7129 E-21 | 3.2553 E-18 | 0.4963 3731 | -1.0106 0719 | down | yes |
| ENSG00000096696 | DSP | 1832,1834 | 1.7083 3364 | 1.8664 8375 | 1.5686 5901 | 3.0846 5444 | 3.4463 3371 | 3.2065 4163 | 2.4589 E-20 | 2.8024 E-17 | 0.5282 1162 | -0.9208 1205 | down | yes |
| ENSG00000169429 | CXCL8 | 3576 | 2.4936 403 | 2.6151 1957 | 2.7167 3782 | 0.6159 4606 | 0.6828 0487 | 0.3650 7074 | 2.5085 E-20 | 2.8024 E-17 | 4.7033 2721 | 2.2336 817 | up | yes |
| ENSG00000126803 | HSPA2 | 3306 | 12.437 1049 | 10.513 1789 | 11.053 4891 | 6.2853 9562 | 6.6829 2672 | 6.3221 8612 | 2.8797 E-20 | 3.1099 E-17 | 1.7627 204 | 0.8178 0366 | up | yes |
| ENSG00000000971 | CFH | 3075 | 39.489 0485 | 31.676 9673 | 33.214 5898 | 20.240 1556 | 21.567 6324 | 21.176 2288 | 1.8616 E-19 | 1.9455 E-16 | 1.6572 5546 | 0.7287 96 | up | yes |
| ENSG00000175899 | A2M | 2,3494 | 1.5522 5237 | 1.0471 4804 | 0.9517 9046 | 0.2008 4692 | 0.2518 3402 | 0.3074 1116 | 3.9036 E-19 | 3.9522 E-16 | 4.6720 5334 | 2.2240 5674 | up | yes |
| ENSG00000089597 | GANAB | 23193 | 86.511 397 | 85.571 3285 | 81.442 9671 | 59.769 8977 | 59.019 6755 | 55.113 8998 | 4.7727 E-19 | 4.6856 E-16 | 1.4578 5296 | 0.5438 4521 | up | no |
| ENSG00000118515 | SGK1 | 6446 | 17.154 3312 | 17.906 2951 | 17.388 5444 | 10.764 5 | 6.9750 4865 | 8.5009 8987 | 5.755E -19 | 5.4838 E-16 | 1.9987 8408 | 0.9991 2263 | up | yes |
| ENSG00000171223 | JUNB | 3726,10535 | 39.052 315 | 40.912 731 | 37.934 898 | 23.164 331 | 14.783 875 | 16.185 043 | 8.9432 E-19 | 8.2784 E-16 | 2.1779 5802 | 1.1229 7615 | up | yes |
| ENSG00000064393 | HIPK2 | 28996 | 25.970 1034 | 24.283 1263 | 24.155 5199 | 14.685 7572 | 17.207 8569 | 15.757 4217 | 1.7425 E-18 | 1.5682 E-15 | 1.5615 3478 | 0.6429 647 | up | yes |
| ENSG00000119699 | TGFB3 | 7043 | 16.239 5057 | 15.371 3106 | 15.466 1274 | 10.225 3455 | 7.7728 4449 | 8.2756 4513 | 5.4099 E-18 | 4.7371 E-15 | 1.7917 8044 | 0.8413 9386 | up | yes |
| ENSG00000070214 | SLC44A1 | 23446 | 34.900 0117 | 31.158 5268 | 32.650 2169 | 23.065 9898 | 20.867 2748 | 21.785 2058 | 5.6047 E-18 | 4.7785 E-15 | 1.5019 9411 | 0.5868 7916 | up | yes |
| ENSG00000142949 | PTPRF | 5792 | 2.3530 7424 | 3.0153 7229 | 2.8337 3587 | 5.0509 0818 | 5.5786 7012 | 4.9059 4049 | 6.323E -18 | 5.2526 E-15 | 0.5279 6321 | -0.9214 9069 | down | yes |
| ENSG00000135842 | NIBAN1 | 116496 | 7.9097 5649 | 10.771 922 | 8.7731 6129 | 16.373 6915 | 16.931 1208 | 16.391 7849 | 9.2424 E-18 | 7.4859 E-15 | 0.5524 4909 | -0.8560 8658 | down | yes |
| ENSG00000140945 | CDH13 | 1012 | 8.2552 545 | 8.5878 9137 | 8.2293 3247 | 13.060 2158 | 12.211 2745 | 12.210 0733 | 1.9053 E-17 | 1.5055 E-14 | 0.6689 2829 | -0.5800 7653 | down | no |
| ENSG00000019991 | HGF | 3082,3569,6654 | 14.649 6419 | 10.877 5735 | 12.105 0428 | 6.9320 8923 | 6.1745 6448 | 7.3303 1283 | 2.0662 E-17 | 1.5938 E-14 | 1.8413 818 | 0.8807 8879 | up | yes |
| ENSG00000134853 | PDGFRA | 5156 | 184.14 0004 | 163.94 3783 | 164.03 8895 | 118.67 4219 | 110.92 9701 | 118.20 2557 | 3.0391 E-17 | 2.2898 E-14 | 1.4724 3573 | 0.5582 0466 | up | no |
| ENSG00000163453 | IGFBP7 | 3490 | 164.03 2831 | 153.53 1992 | 169.54 1804 | 113.15 3925 | 95.442 7521 | 88.904 7975 | 3.8197 E-17 | 2.8125 E-14 | 1.6373 2509 | 0.7113 4079 | up | yes |
| ENSG00000169744 | LDB2 | 9079 | 9.0522 6283 | 8.4014 0762 | 8.9235 0679 | 5.6683 0584 | 4.9601 256 | 4.9122 509 | 5.4412 E-17 | 3.9174 E-14 | 1.6972 9853 | 0.7632 4033 | up | yes |
| ENSG00000168385 | SEPTIN2 | 4735 | 69.768 611 | 68.405 8985 | 66.245 3869 | 49.931 5774 | 48.668 1669 | 48.349 5657 | 6.3775 E-17 | 4.4917 E-14 | 1.3910 9123 | 0.4762 1704 | up | no |
| ENSG00000152402 | GUCY1A2 | 2977 | 0.4931 3063 | 0.5535 8072 | 0.4957 2458 | 1.1132 0293 | 1.0070 8611 | 1.0842 9468 | 7.6632 E-17 | 5.2824 E-14 | 0.4813 2178 | -1.0549 | down | yes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | 264 | | |
| ENSG0000 0185567 | AHNAK2 | 113146 | 3.4515 9472 | 4.0685 3983 | 3.5272 5095 | 5.9509 3707 | 7.9383 7131 | 6.4116 7959 | 8.8383 E-17 | 5.9655 E-14 | 0.5441 797 | - 0.8778 4496 | down | yes |
| ENSG0000 0131389 | SLC6A6 | 6533 | 25.247 8199 | 23.639 0211 | 23.488 6813 | 16.327 1438 | 11.615 6526 | 12.882 2119 | 1.0118 E-16 | 6.6896 E-14 | 1.7728 2321 | 0.8260 4868 | up | yes |
| ENSG0000 0106948 | AKNA | 80709 | 2.4346 7068 | 2.4195 8981 | 2.4833 647 | 4.1548 579 | 3.8938 0953 | 4.0272 8644 | 1.5613 E-16 | 1.0117 E-13 | 0.6076 2282 | - 0.7187 5203 | down | yes |
| ENSG0000 0130203 | APOE | 348 | 22.382 7087 | 17.404 8313 | 18.947 6468 | 11.016 1557 | 10.932 2928 | 10.034 0329 | 2.2175 E-16 | 1.4086 E-13 | 1.8364 7998 | 0.8769 4317 | up | yes |
| ENSG0000 0163739 | CXCL1 | 2919 | 5.6729 3524 | 3.5486 5343 | 4.7589 2006 | 1.4002 9797 | 1.0870 0197 | 1.0416 1319 | 3.1393 E-16 | 1.9559 E-13 | 3.9617 0385 | 1.9861 2104 | up | yes |
| ENSG0000 0164188 | RANBP3 L | 202151 | 3.3025 9822 | 3.1716 8858 | 3.0984 5878 | 1.6193 7328 | 1.2356 1191 | 1.0339 8955 | 6.1075 E-16 | 3.7334 E-13 | 2.4615 0881 | 1.2995 429 | up | yes |
| ENSG0000 0122642 | FKBP9 | 11328 | 32.890 7999 | 31.586 5078 | 32.244 7075 | 45.369 656 | 53.860 2652 | 48.829 0302 | 1.2283 E-15 | 7.3691 E-13 | 0.6532 6692 | - 0.6142 5551 | down | yes |
| ENSG0000 0160963 | COL26A 1 | 136227 | 1.3329 1123 | 1.4809 1744 | 1.6565 3295 | 0.4304 1197 | 0.2951 7834 | 0.3323 0389 | 1.2625 E-15 | 7.4369 E-13 | 4.2257 171 | 2.0791 9619 | up | yes |
| ENSG0000 0008256 | CYTH3 | 9265 | 11.947 8432 | 15.423 1456 | 13.890 1823 | 22.154 4762 | 26.505 2562 | 23.229 4424 | 1.4298 E-15 | 8.2718 E-13 | 0.5739 5527 | - 0.8009 8978 | down | yes |
| ENSG0000 0139324 | TMTC3 | 160418 | 9.0226 8157 | 8.9280 5088 | 8.9386 3398 | 5.1682 5295 | 4.7766 6055 | 5.9688 7125 | 1.4625 E-15 | 8.3127 E-13 | 1.6896 9022 | 0.7567 5877 | up | yes |
| ENSG0000 0120659 | TNFSF11 | 8600 | 1.7932 4258 | 0.9227 7852 | 1.3890 7206 | 0.2355 1122 | 0.1667 0035 | 0.2324 1189 | 1.5427 E-15 | 8.6173 E-13 | 6.4685 493 | 2.6934 422 | up | yes |
| ENSG0000 0113369 | ARRDC3 | 57561 | 8.7237 3836 | 6.3604 141 | 7.1932 4924 | 3.8545 2273 | 3.2985 4113 | 4.0291 0518 | 2.8269 E-15 | 1.5523 E-12 | 1.9922 2545 | 0.9943 8092 | up | yes |
| ENSG0000 0101187 | SLCO4A 1 | 28231 | 5.1485 6016 | 6.0568 8052 | 5.2479 4956 | 2.4237 7938 | 1.1063 5816 | 2.0092 7596 | 4.4611 E-15 | 2.4088 E-12 | 2.9702 4048 | 1.5705 7974 | up | yes |
| ENSG0000 0108946 | PRKAR1 A | 5573 | 69.661 2235 | 52.746 7797 | 59.422 1229 | 39.922 9726 | 33.164 7838 | 36.948 2827 | 6.3782 E-15 | 3.3689 E-12 | 1.6524 5975 | 0.7246 1513 | up | yes |
| ENSG0000 0164171 | ITGA2 | 3673 | 15.998 5787 | 18.621 587 | 16.162 1186 | 10.413 8808 | 6.4945 1 | 9.0190 7048 | 6.4471 E-15 | 3.3689 E-12 | 1.9586 2926 | 0.9698 4434 | up | yes |
| ENSG0000 0128849 | CGNL1 | 84952 | 3.5975 1417 | 3.1035 8988 | 3.1884 8462 | 1.9873 0011 | 1.7448 024 | 1.5744 9584 | 7.4946 E-15 | 3.8541 E-12 | 1.8636 3995 | 0.8981 2316 | up | yes |
| ENSG0000 0233695 | GAS6-AS1 | 650669 | 0.8544 2318 | 1.0460 5513 | 0.7362 7395 | 2.0863 0021 | 1.8974 8807 | 2.1090 7148 | 9.7425 E-15 | 4.7219 E-12 | 0.4327 6103 | - 1.2083 575 | down | yes |
| ENSG0000 0176438 | SYNE3 | 161176 | 2.7343 8412 | 4.1525 3609 | 3.9029 1117 | 6.4078 7287 | 7.7346 5412 | 7.0128 3638 | 9.7651 E-15 | 4.7219 E-12 | 0.5100 2818 | - 0.9713 5115 | down | yes |
| ENSG0000 0101825 | MXRA5 | 25878 | 62.941 483 | 55.625 713 | 57.585 663 | 40.234 516 | 40.006 123 | 42.412 75 | 9.5502 E-15 | 4.7219 E-12 | 1.4361 842 | 0.5222 4079 | up | no |
| ENSG0000 0185885 | IFITM1 | 8519 | 118.54 5335 | 78.658 0122 | 98.660 9187 | 55.277 1688 | 55.995 3122 | 52.326 7197 | 9.4312 E-15 | 4.7219 E-12 | 1.8084 7012 | 0.8547 6976 | up | yes |
| ENSG0000 0197930 | ERO1A | 30001 | 8.6053 5222 | 8.7350 3523 | 8.3799 3018 | 6.0057 3097 | 5.1139 9761 | 5.2663 9416 | 1.274E -14 | 6.0697 E-12 | 1.5696 4024 | 0.6504 3393 | up | yes |
| ENSG0000 0102996 | MMP15 | 4324 | 1.7167 8687 | 2.4342 3342 | 2.5559 8398 | 5.0705 3575 | 5.3920 357 | 4.6805 5126 | 1.3022 E-14 | 6.1145 E-12 | 0.4429 0761 | - 1.1749 2231 | down | yes |
| ENSG0000 0176907 | TCIM | 56892 | 5.8802 54 | 4.1264 58 | 4.3187 06 | 1.6389 46 | 1.4054 3 | 1.8436 17 | 1.8734 E-14 | 8.6706 E-12 | 2.9307 3619 | 1.5512 6311 | up | yes |
| ENSG0000 0156011 | PSD3 | 23362 | 11.027 0807 | 9.6896 4189 | 9.5879 4335 | 6.6881 794 | 6.8952 188 | 6.8965 416 | 2.4288 E-14 | 1.1083 E-11 | 1.4797 2436 | 0.5653 2846 | up | no |
| ENSG0000 0151176 | PLBD2 | 196463 | 25.115 804 | 23.539 651 | 24.816 5665 | 34.000 3166 | 36.646 3412 | 35.105 8381 | 2.8567 E-14 | 1.2854 E-11 | 0.6947 5449 | - 0.5254 2484 | down | no |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ENSG00000143369 | ECM1 | 1893 | 36.5231441 | 37.9627312 | 37.0477991 | 50.9944134 | 54.2761479 | 53.6959442 | 3.7078E-14 | 1.6233E-11 | 0.7016 1745 | -0.5112 4346 | down | no |
| ENSG00000184205 | TSPYL2 | 64061 | 11.753638 | 10.4390151 | 10.4895847 | 7.0255667 | 7.1425 5307 | 6.7735 8658 | 3.6754E-14 | 1.6233E-11 | 1.5606 2918 | 0.6421 2778 | up | yes |
| ENSG00000150681 | RGS18 | 64407 | 2.6838 0608 | 0.5480 332 | 1.2420 709 | 0.1234 1355 | 0.1391 0681 | 0.1574 4823 | 4.353E-14 | 1.8804E-11 | 10.652 9637 | 3.4131 8295 | up | yes |
| ENSG00000125637 | PSD4 | 23550 | 2.5598 2484 | 2.1827 5941 | 2.3367 5527 | 1.3837 0568 | 1.4468 846 | 1.3082 35 | 4.8795E-14 | 2.0801E-11 | 1.7104 7074 | 0.7743 9342 | up | yes |
| ENSG00000160932 | LY6E | 4061 | 96.944 0322 | 87.242 1913 | 94.444 4841 | 61.575 3531 | 66.498 9929 | 65.476 0707 | 7.6425E-14 | 3.2156E-11 | 1.4395 7689 | 0.5256 4485 | up | no |
| ENSG00000152558 | TMEM123 | 114908,10360 | 25.232 4468 | 23.103 1472 | 23.191 3117 | 33.388 5903 | 34.139 1494 | 34.281 5705 | 2.1526E-13 | 8.9411E-11 | 0.7025 5761 | -0.5093 1156 | down | no |
| ENSG00000026025 | VIM | 7431 | 1601.3 7173 | 1779.8 4851 | 1703.6 6814 | 2279.8 3748 | 2428.5 0903 | 2418.7 8585 | 2.4238E-13 | 9.9401E-11 | 0.7134 5502 | -0.4871 0561 | down | no |
| ENSG00000163661 | PTX3 | 5806,5309 | 51.978 645 | 72.393 196 | 62.874 233 | 101.78 2486 | 117.83 6411 | 100.91 1873 | 2.6181E-13 | 1.0603E-10 | 0.5841 7504 | -0.7755 2739 | down | yes |
| ENSG00000170801 | HTRA3 | 94031,726 | 22.702 9046 | 17.065 1984 | 20.521 6239 | 12.397 3517 | 10.224 2735 | 12.001 0475 | 3.8103E-13 | 1.524E-10 | 1.7413 3659 | 0.8001 951 | up | yes |
| ENSG00000087303 | NID2 | 22795 | 13.179 0219 | 11.666 7733 | 11.936 9036 | 6.5801 4318 | 8.4431 4363 | 7.4753 6688 | 6.159E-13 | 2.4334E-10 | 1.6348 8444 | 0.7091 8866 | up | yes |
| ENSG00000114948 | ADAM23 | 8745 | 1.0381 5295 | 0.9090 8513 | 0.8711 0444 | 2.3018 4113 | 1.7815 5624 | 1.9971 6506 | 6.6302E-13 | 2.588E-10 | 0.4635 003 | -1.1093 5782 | down | yes |
| ENSG00000170214 | ADRA1B | 147 | 3.9861 3922 | 5.6500 1597 | 5.5669 1623 | 9.3105 9516 | 11.307 7283 | 9.8108 101 | 7.3837E-13 | 2.8435E-10 | 0.4996 2222 | -1.0010 9044 | down | yes |
| ENSG00000170412 | GPRC5C | 55890 | 0.8565 2049 | 0.5754 8797 | 0.8238 2589 | 0.2356 3061 | 0.1990 5775 | 0.2424 7175 | 7.4603E-13 | 2.8435E-10 | 3.3313 1611 | 1.7360 9226 | up | yes |
| ENSG00000099194 | SCD | 6319 | 77.871 01 | 71.245 323 | 73.366 707 | 101.44 5175 | 99.703 56 | 103.97 6334 | 7.5866E-13 | 2.858E-10 | 0.7291 5359 | -0.4557 0535 | down | no |
| ENSG00000104321 | TRPA1 | 8989 | 20.143 3907 | 14.689 2501 | 17.234 4127 | 10.799 9671 | 9.2127 6309 | 10.789 0363 | 9.1712E-13 | 3.4153E-10 | 1.6903 9179 | 0.7573 5767 | up | yes |
| ENSG00000070756 | PABPC1 | 26986 | 63.593 7304 | 65.228 9876 | 62.745 7683 | 84.579 2122 | 88.870 8764 | 96.294 6107 | 1.053E-12 | 3.8767E-10 | 0.7101 8443 | -0.4937 3436 | down | no |
| ENSG00000259207 | ITGB3 | 3690 | 4.9305 4812 | 6.1361 5253 | 4.5095 2017 | 2.7136 6317 | 3.1336 4926 | 2.4495 9106 | 1.1895E-12 | 4.3302E-10 | 1.8773 535 | 0.9087 0033 | up | yes |
| ENSG00000085662 | AKR1B1 | 231 | 36.690 5993 | 29.452 1934 | 30.682 8791 | 21.951 149 | 17.252 8011 | 19.970 5287 | 1.3118E-12 | 4.722E-10 | 1.6362 7418 | 0.7104 1451 | up | yes |
| ENSG00000100234 | TIMP3 | 7078 | 137.53 3157 | 134.61 2244 | 133.44 9982 | 99.554 337 | 85.426 277 | 99.944 038 | 1.3945E-12 | 4.9649E-10 | 1.4235 1804 | 0.5094 6078 | up | no |
| ENSG00000152952 | PLOD2 | 5352 | 28.525 5126 | 27.026 6604 | 27.195 9719 | 20.509 4863 | 16.342 3339 | 18.681 3835 | 1.7811E-12 | 6.2723E-10 | 1.4900 6611 | 0.5753 7634 | up | no |
| ENSG00000065534 | MYLK | 4638 | 5.3245 0672 | 6.0937 5651 | 5.4669 1147 | 7.7105 393 | 9.4111 239 | 8.6134 8656 | 1.8807E-12 | 6.5517E-10 | 0.6561 1333 | -0.6079 8307 | down | yes |
| ENSG00000136960 | ENPP2 | 5168 | 16.157 0824 | 11.210 1856 | 12.318 3607 | 7.9437 1497 | 7.9087 5295 | 6.9285 3003 | 2.0055E-12 | 6.9121E-10 | 1.7420 4961 | 0.8007 8571 | up | yes |
| ENSG00000165806 | CASP7 | 840 | 9.6947 3109 | 8.8590 3485 | 9.1209 7394 | 5.7900 8302 | 6.0912 8788 | 5.3844 934 | 2.0797E-12 | 7.0925E-10 | 1.6028 5865 | 0.6806 472 | up | yes |
| ENSG00000221890 | NPTXR | 23467 | 1.6848 73 | 2.1979 85 | 1.8381 88 | 3.5342 38 | 3.5396 78 | 3.6582 47 | 2.1167E-12 | 7.1435E-10 | 0.5330 7483 | -0.9075 9002 | down | yes |
| ENSG0000 | TGM2 | 7052 | 3.9281 | 3.2000 | 3.3923 | 2.0426 | 2.0692 | 2.0844 | 3.3634 | 1.1234 | 1.6978 | 0.7637 | up | yes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0198959 | | | 5195 | 5144 | 5842 | 1011 | 4101 | 8655 | E-12 | E-09 | 6774 | 2408 | | |
| ENSG0000 0113583 | C5orf15 | 56951 | 39.420 5833 | 36.141 2186 | 34.031 0262 | 26.133 2608 | 24.161 6192 | 24.589 7149 | 4.3216 E-12 | 1.4287 E-09 | 1.4634 8963 | 0.5494 1252 | up | no |
| ENSG0000 0070193 | FGF10 | 2255 | 0.4899 9032 | 0.5279 0308 | 0.5982 2908 | 1.1497 9767 | 1.3430 4012 | 1.4360 788 | 4.366E -12 | 1.4288 E-09 | 0.4113 4049 | - 1.2815 95 | down | yes |
| ENSG0000 0166598 | HSP90B1 | 7184 | 35.238 4012 | 32.602 3525 | 31.975 8007 | 25.219 2166 | 23.820 7999 | 24.758 5044 | 4.662E -12 | 1.5104 E-09 | 1.3525 5495 | 0.4356 872 | up | no |
| ENSG0000 0134871 | COL4A2 | 1284 | 14.796 3591 | 16.347 8671 | 15.374 8861 | 11.667 4249 | 9.2015 699 | 10.310 037 | 5.4489 E-12 | 1.7479 E-09 | 1.4919 999 | 0.5772 4744 | up | no |
| ENSG0000 0150867 | PIP4K2A | 5305 | 7.3162 6085 | 8.5166 9753 | 7.8358 8238 | 12.376 7849 | 11.893 8523 | 11.608 9575 | 5.7516 E-12 | 1.8269 E-09 | 0.6596 7414 | - 0.6001 7454 | down | yes |
| ENSG0000 0128591 | FLNC | 2318 | 14.856 8399 | 19.746 5971 | 17.067 256 | 25.249 1375 | 29.600 1323 | 27.795 6053 | 5.9314 E-12 | 1.8487 E-09 | 0.6252 1352 | - 0.6775 7912 | down | yes |
| ENSG0000 0138829 | FBN2 | 2201 | 169.56 5745 | 220.19 3031 | 187.29 5154 | 283.76 8929 | 294.51 2493 | 287.95 3306 | 5.9345 E-12 | 1.8487 E-09 | 0.6661 6347 | - 0.5860 5186 | down | yes |
| ENSG0000 0125257 | ABCC4 | 10257 | 9.8473 4408 | 9.7950 6651 | 9.2770 0369 | 7.1575 2907 | 6.4914 6705 | 6.6540 5331 | 6.1736 E-12 | 1.8997 E-09 | 1.4243 8772 | 0.5103 419 | up | no |
| ENSG0000 0138944 | SHISAL1 | 85352 | 4.2275 9 | 2.8450 98 | 3.3625 13 | 1.9877 58 | 1.5301 82 | 1.5179 79 | 6.2155 E-12 | 1.8997 E-09 | 2.0721 5426 | 1.0511 3141 | up | yes |
| ENSG0000 0196526 | AFAP1 | 60312 | 10.440 2969 | 10.993 2793 | 10.450 3116 | 7.8181 784 | 7.5753 5316 | 7.6844 093 | 7.1947 E-12 | 2.1784 E-09 | 1.3815 742 | 0.4663 1305 | up | no |
| ENSG0000 0169851 | PCDH7 | 5099 | 0.8157 6593 | 0.9531 2597 | 0.9859 6995 | 0.4245 7786 | 0.3850 0665 | 0.4825 3292 | 8.1302 E-12 | 2.4389 E-09 | 2.1320 5223 | 1.0922 4278 | up | yes |
| ENSG0000 0121039 | RDH10 | 157506 | 8.0030 1692 | 5.0528 0893 | 6.8131 0069 | 3.2732 504 | 2.6313 187 | 3.6577 0727 | 8.3996 E-12 | 2.4966 E-09 | 2.0778 4483 | 1.0550 8792 | up | yes |
| ENSG0000 0179218 | CALR | 811 | 241.71 5029 | 215.33 7716 | 222.58 0807 | 168.13 7062 | 167.64 7746 | 168.75 8586 | 9.9645 E-12 | 2.9348 E-09 | 1.3470 2695 | 0.4297 7872 | up | no |
| ENSG0000 0102931 | ARL2BP | 23568 | 26.484 2936 | 25.274 8423 | 25.953 2581 | 16.363 4799 | 18.355 7379 | 17.359 5091 | 1.134E -11 | 3.2803 E-09 | 1.4922 0994 | 0.5774 5052 | up | no |
| ENSG0000 0140563 | MCTP2 | 55784 | 3.2965 9084 | 2.7236 1263 | 2.6038 7887 | 1.8254 8446 | 1.2711 3626 | 1.5700 4385 | 1.1272 E-11 | 3.2803 E-09 | 1.8480 1847 | 0.8859 7918 | up | yes |
| ENSG0000 0157613 | CREB3L 1 | 90993 | 19.822 2977 | 26.341 6207 | 23.657 5602 | 33.431 0543 | 40.687 2057 | 42.946 687 | 1.8051 E-11 | 5.1753 E-09 | 0.5964 3369 | - 0.7455 6634 | down | yes |
| ENSG0000 0125968 | ID1 | 3397 | 21.925 4612 | 13.481 7838 | 16.316 0417 | 7.9229 517 | 8.6524 4279 | 8.2437 6426 | 2.2895 E-11 | 6.5067 E-09 | 2.0840 0644 | 1.0593 5974 | up | yes |
| ENSG0000 0072041 | SLC6A15 | 55117 | 0.6018 9087 | 0.4313 9011 | 0.5987 8518 | 0.2698 1469 | 0.1397 3645 | 0.1538 7957 | 2.3509 E-11 | 6.623E -09 | 2.8966 5812 | 1.5343 8942 | up | yes |
| ENSG0000 0069869 | NEDD4 | 4734 | 14.082 8014 | 14.368 2095 | 13.414 4844 | 9.9901 3238 | 10.329 6006 | 10.337 16 | 2.6094 E-11 | 7.2878 E-09 | 1.3656 1443 | 0.4495 5021 | up | no |
| ENSG0000 0272636 | DOC2B | 8447 | 1.0892 6549 | 0.8737 38 | 0.9701 1845 | 0.4148 6145 | 0.3045 8877 | 0.3852 4648 | 2.7469 E-11 | 7.6063 E-09 | 2.6551 3779 | 1.4087 8673 | up | yes |
| ENSG0000 0174136 | RGMB | 285704 | 11.822 3691 | 13.464 5903 | 12.362 5013 | 17.590 6947 | 17.798 4354 | 18.193 7861 | 2.9016 E-11 | 7.9666 E-09 | 0.7026 3926 | - 0.5091 439 | down | no |
| ENSG0000 0058091 | CDK14 | 5218 | 5.9291 6962 | 5.0810 0455 | 5.0885 7776 | 2.8545 1632 | 3.4410 6357 | 3.4169 492 | 3.4003 E-11 | 9.2574 E-09 | 1.6575 2419 | 0.7290 2993 | up | yes |
| ENSG0000 0159322 | ADPGK | 83440 | 9.8119 3091 | 9.0100 0798 | 8.4905 3341 | 6.1571 0521 | 6.1211 2003 | 6.2593 361 | 3.542E -11 | 9.5628 E-09 | 1.4733 5843 | 0.5591 0844 | up | no |
| ENSG0000 0029364 | SLC39A9 | 55334 | 10.692 0612 | 10.134 781 | 9.8151 8702 | 7.1133 5378 | 6.3533 8358 | 7.3724 1934 | 3.608E -11 | 9.6604 E-09 | 1.4704 064 | 0.5562 1495 | up | no |
| ENSG0000 0168679 | SLC16A4 | 9122 | 4.3995 6617 | 2.8709 2746 | 3.7396 7161 | 1.2859 8704 | 1.5706 6192 | 1.7514 0297 | 3.919E -11 | 1.0407 E-08 | 2.3893 3185 | 1.2566 0724 | up | yes |
| ENSG0000 0159388 | BTG2 | 7832 | 1.4682 5505 | 1.8689 3937 | 1.7981 576 | 3.7948 2941 | 3.6425 1023 | 3.4519 7614 | 5.1677 E-11 | 1.3612 E-08 | 0.4715 9547 | - 1.0843 | down | yes |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | 7823 | | |
| ENSG0000 0112769 | LAMA4 | 3910 | 25.315 4347 | 22.777 7304 | 23.211 8643 | 16.048 6155 | 18.225 4741 | 17.005 7 | 6.2935 E-11 | 1.6312 E-08 | 1.3905 094 | 0.4756 135 | up | no |
| ENSG0000 0088826 | SMOX | 54498 | 14.245 058 | 8.9530 4944 | 11.970 6702 | 6.8790 4702 | 5.6138 5428 | 5.7424 203 | 6.2916 E-11 | 1.6312 E-08 | 1.9286 0748 | 0.9475 5955 | up | yes |
| ENSG0000 0156535 | CD109 | 135228 | 36.745 7128 | 41.954 2103 | 37.504 656 | 52.492 7402 | 52.695 7475 | 56.259 4251 | 6.9582 E-11 | 1.7892 E-08 | 0.7197 6514 | - 0.4744 0187 | down | no |
| ENSG0000 0092621 | PHGDH | 26227 | 15.273 2424 | 19.009 6396 | 16.921 8336 | 27.039 1737 | 24.500 4233 | 24.028 6019 | 7.7944 E-11 | 1.9884 E-08 | 0.6775 9608 | - 0.5615 0256 | down | no |
| ENSG0000 0162645 | GBP2 | 2634 | 7.3045 6817 | 5.1997 5929 | 5.8701 5462 | 3.2162 4812 | 3.6754 6446 | 3.7332 0004 | 8.5035 E-11 | 2.1523 E-08 | 1.7293 7724 | 0.7902 5261 | up | yes |
| ENSG0000 0147119 | CHST7 | 56548 | 11.398 289 | 6.5095 96 | 9.8860 98 | 4.9450 13 | 3.2174 95 | 3.8965 2 | 1.1028 E-10 | 2.7696 E-08 | 2.3048 278 | 1.2046 5897 | up | yes |
| ENSG0000 0175455 | CCDC14 | 64770 | 6.8337 1032 | 6.4439 5197 | 6.4078 3029 | 8.8478 7522 | 10.337 1494 | 9.1536 7209 | 1.2515 E-10 | 3.119E -08 | 0.6946 506 | - 0.5256 406 | down | no |
| ENSG0000 0139289 | PHLDA1 | 22822 | 44.533 9567 | 31.753 3042 | 36.072 792 | 25.751 1925 | 21.760 04 | 23.588 676 | 1.3682 E-10 | 3.3837 E-08 | 1.5803 122 | 0.6602 096 | up | yes |
| ENSG0000 0166292 | TMEM10 0 | 55273 | 13.391 6478 | 6.9860 1248 | 10.822 6444 | 4.8396 5237 | 5.1435 0845 | 4.6808 8506 | 1.6711 E-10 | 4.0404 E-08 | 2.1276 7369 | 1.0892 7691 | up | yes |
| ENSG0000 0116711 | PLA2G4 A | 5321 | 4.9504 25 | 3.5588 77 | 4.3975 14 | 2.3970 97 | 1.6359 94 | 1.7448 24 | 1.6613 E-10 | 4.0404 E-08 | 2.2338 1895 | 1.1595 1226 | up | yes |
| ENSG0000 0196139 | AKR1C3 | 8644 | 4.9972 332 | 3.3632 4626 | 3.6489 1201 | 2.1770 7983 | 1.3360 5464 | 1.7141 1063 | 1.6471 E-10 | 4.0404 E-08 | 2.2974 6095 | 1.2000 4034 | up | yes |
| ENSG0000 0108846 | ABCC3 | 8714 | 1.6780 0623 | 1.7438 6375 | 1.6148 3321 | 1.0060 7482 | 0.9939 1296 | 0.9671 1042 | 1.7433 E-10 | 4.1836 E-08 | 1.6975 182 | 0.7634 2705 | up | yes |
| ENSG0000 0168016 | TRANK1 | 9881 | 5.4895 3951 | 4.5429 0053 | 4.6706 3197 | 7.1224 6985 | 7.2022 4953 | 7.1855 2062 | 1.9488 E-10 | 4.6423 E-08 | 0.6835 3826 | - 0.5489 06 | down | no |
| ENSG0000 0004399 | PLXND1 | 23129 | 27.887 2641 | 29.478 0338 | 29.528 9956 | 20.749 9862 | 22.745 1061 | 21.178 5381 | 2.2742 E-10 | 5.378E -08 | 1.3435 815 | 0.4260 8384 | up | no |
| ENSG0000 0099953 | MMP11 | 4320 | 2.9387 1943 | 2.8323 2607 | 2.7018 6662 | 4.5040 1465 | 4.4500 9408 | 4.4758 912 | 2.5311 E-10 | 5.9422 E-08 | 0.6308 9443 | - 0.6645 2949 | down | yes |
| ENSG0000 0118507 | AKAP7 | 9465 | 4.8122 9546 | 4.3543 1019 | 4.2484 229 | 2.7082 7456 | 1.7571 6831 | 2.4818 7731 | 2.9138 E-10 | 6.7915 E-08 | 1.9309 6449 | 0.9493 2163 | up | yes |
| ENSG0000 0126709 | IFI6 | 2537 | 71.667 5246 | 49.901 0414 | 59.224 1829 | 39.244 1271 | 35.967 9912 | 31.632 344 | 3.1041 E-10 | 7.1834 E-08 | 1.6921 1155 | 0.7588 2468 | up | yes |
| ENSG0000 0162745 | OLFML2 B | 25903 | 59.648 0572 | 60.554 2903 | 58.864 3773 | 42.658 2687 | 46.066 7439 | 45.714 6399 | 3.1626 E-10 | 7.2668 E-08 | 1.3319 4873 | 0.4135 3855 | up | no |
| ENSG0000 0253368 | TRNP1 | 388610,7207,7 217,7218 | 14.551 1785 | 16.688 2315 | 16.107 3304 | 22.241 1103 | 32.403 5381 | 26.625 0402 | 3.2926 E-10 | 7.5121 E-08 | 0.5825 8794 | - 0.7794 5226 | down | yes |
| ENSG0000 0166963 | MAP1A | 4130,23173 | 18.224 9639 | 17.686 585 | 17.719 947 | 22.670 3504 | 26.892 356 | 25.311 0003 | 3.4373 E-10 | 7.7875 E-08 | 0.7162 9278 | - 0.4813 7869 | down | no |
| ENSG0000 0269711 | ENSG00000269711 | | 0 | 0 | 0 | 0 | 14.071 763 | 0 | 4.0739 E-10 | 9.1657 E-08 | 2.1319 E-05 | - 15.517 4811 | down | yes |
| ENSG0000 0173546 | CSPG4 | 1464 | 9.8094 6 | 13.862 354 | 13.538 78 | 18.691 793 | 21.543 797 | 20.429 159 | 4.2486 E-10 | 9.4929 E-08 | 0.6133 8083 | - 0.7051 4502 | down | yes |
| ENSG0000 0156140 | ADAMT S3 | 9508 | 4.4175 0378 | 2.2723 1795 | 3.2739 5243 | 1.5262 9042 | 1.5327 096 | 1.5422 5703 | 4.4626 E-10 | 9.9027 E-08 | 2.1654 4611 | 1.1146 6427 | up | yes |
| ENSG0000 0065833 | ME1 | 4199,57717 | 24.334 219 | 26.182 657 | 24.322 132 | 18.675 474 | 17.462 675 | 18.192 055 | 4.7472 E-10 | 1.0463 E-07 | 1.3774 8439 | 0.4620 3597 | up | no |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ENSG00000159167 | STC1 | 6781 | 33.9830092 | 25.4328707 | 29.6421719 | 20.3051268 | 13.5270903 | 18.2022794 | 5.0191E-10 | 1.0987E-07 | 1.7115 1943 | 0.7752 7767 | up | yes |
| ENSG00000228594 | FNDC10 | 643988 | 1.219607 | 1.035271 | 1.000404 | 2.698091 | 2.870472 | 2.446078 | 5.6916E-10 | 1.2376E-07 | 0.4061 6691 | -1.2998 5537 | down | yes |
| ENSG00000132846 | ZBED3 | 84327 | 2.379488 17 | 2.355133464 | 2.317501261 | 3.474200773 | 4.241855102 | 3.807866273 | 5.9161E-10 | 1.2768E-07 | 0.6119 5622 | -0.7084 9965 | down | yes |
| ENSG00000120594 | PLXDC2 | 84898 | 21.425 5319 | 14.373 1115 | 17.017 015 | 11.251 0784 | 10.925 6281 | 11.245 8068 | 5.9508E-10 | 1.2768E-07 | 1.5802 4197 | 0.6601 4548 | up | yes |
| ENSG00000130766 | SESN2 | 83667 | 8.655149 | 12.387753 | 9.935103 | 17.155003 | 16.683147 | 16.967152 | 5.995E-10 | 1.2778E-07 | 0.6097 3961 | -0.7137 3483 | down | yes |
| ENSG00000075223 | SEMA3C | 10512 | 24.662 6818 | 23.237878 | 22.201794 | 17.943 2265 | 15.462 3249 | 17.101 0919 | 6.1223E-10 | 1.2964E-07 | 1.3879 8283 | 0.4729 8972 | up | no |
| ENSG00000134333 | LDHA | 3939 | 123.09 2729 | 117.18 0174 | 116.38 8548 | 95.344 7338 | 85.153 2438 | 91.505 8837 | 6.9998E-10 | 1.4726E-07 | 1.3112 3672 | 0.3909 2816 | up | no |
| ENSG00000145390 | USP53 | 54532 | 5.5118512 | 7.9803 1453 | 6.8131 9512 | 10.163 3637 | 11.325 6585 | 11.174 6883 | 7.2721E-10 | 1.52E-07 | 0.6216 4894 | -0.6858 2802 | down | yes |
| ENSG00000168000 | BSCL2 | 26580 | 4.3723 6018 | 3.5816 1649 | 4.0247 7084 | 2.0634 517 | 1.9694 9137 | 2.7328 3445 | 8.7539E-10 | 1.818E-07 | 1.7704 909 | 0.8241 4943 | up | yes |
| ENSG00000117298 | ECE1 | 1889 | 30.138 7685 | 28.245 0483 | 28.366 6109 | 20.578 7958 | 22.778 4824 | 21.536 112 | 8.8722E-10 | 1.8308E-07 | 1.3368 1454 | 0.4187 9933 | up | no |
| ENSG00000145362 | ANK2 | 287 | 0.4506 0943 | 0.4610 1415 | 0.4030 1074 | 0.6447 6589 | 0.7057 8187 | 0.6420 6122 | 9.1056E-10 | 1.8671E-07 | 0.6597 5529 | -0.5999 9708 | down | yes |
| ENSG00000151090 | THRB | 7068 | 3.2836 2704 | 3.0905 1451 | 3.0258 7272 | 2.2879 7508 | 1.8533 3875 | 1.8766 6075 | 9.2758E-10 | 1.8901E-07 | 1.5619 897 | 0.6433 8494 | up | yes |
| ENSG00000188641 | DPYD | 1806 | 8.9594 3086 | 8.3260 7461 | 7.6527 3228 | 4.7763 0782 | 5.6134 8414 | 5.9029 2171 | 9.545E-10 | 1.9327E-07 | 1.5306 3745 | 0.6141 3261 | up | yes |
| ENSG00000156804 | FBXO32 | 114907 | 27.045 4346 | 26.524 17 | 26.291 9618 | 20.481 32 | 19.391 093 | 20.915 2146 | 9.8468E-10 | 1.9815E-07 | 1.3137 7995 | 0.3937 2365 | up | no |
| ENSG00000187479 | C11orf96 | 387763 | 8.245682 | 5.592788 | 10.728172 | 3.643805 | 2.316556 | 3.174817 | 1.0515E-09 | 2.1029E-07 | 2.6892 3517 | 1.4271 9592 | up | yes |
| ENSG00000111897 | SERINC1 | 57515 | 70.732 155 | 72.258 003 | 71.174 576 | 55.162 766 | 55.504 044 | 55.523 129 | 1.0638E-09 | 2.1144E-07 | 1.2886 7448 | 0.3658 8789 | up | no |
| ENSG00000272779 | BMS1P20 | 96610 | 3.189718 | 4.046037 | 3.331377 | 1.309475 | 0.748244 | 1.1399 | 1.0741E-09 | 2.1218E-07 | 3.3046 8764 | 1.7245 1392 | up | yes |
| ENSG00000074695 | LMAN1 | 3998 | 43.547 8919 | 42.360 8861 | 42.855 296 | 34.051 7311 | 32.336 6419 | 33.510 0337 | 1.2299E-09 | 2.4149E-07 | 1.2889 5023 | 0.3661 9656 | up | no |
| ENSG00000105664 | COMP | 1311 | 2.1450 4617 | 1.9434 3213 | 2.6341 8888 | 0.8004 6655 | 0.8808 3343 | 1.0757 7156 | 1.3391E-09 | 2.6136E-07 | 2.4383 3614 | 1.2858 9702 | up | yes |
| ENSG00000162595 | DIRAS3 | 9077 | 7.0389 5557 | 3.4895 4925 | 4.7858 7943 | 2.0447 4833 | 1.4096 6746 | 2.3521 4212 | 1.3664E-09 | 2.6508E-07 | 2.6374 29 | 1.3991 3226 | up | yes |
| ENSG00000153071 | DAB2 | 1601 | 19.441 7644 | 24.239 06 | 20.432 3729 | 30.346 3124 | 31.039 6087 | 29.880 9188 | 1.4571E-09 | 2.81E-07 | 0.7024 8074 | -0.5094 6942 | down | no |
| ENSG00000213694 | S1PR3 | 1903 | 4.4061 8517 | 4.9555 3541 | 4.7573 8183 | 3.5709 6197 | 2.9307 5506 | 3.0644 8163 | 1.4832E-09 | 2.8433E-07 | 1.4759 3657 | 0.5616 3072 | up | no |
| ENSG00000141068 | KSR1 | 8844 | 2.1062 8338 | 1.2488 9638 | 1.5315 7091 | 0.9225 9093 | 0.7052 5608 | 0.7408 4358 | 1.5021E-09 | 2.8627E-07 | 2.0630 5994 | 1.0447 8573 | up | yes |
| ENSG00000104635 | SLC39A14 | 23516 | 26.874 0224 | 31.266 0297 | 27.264 1412 | 21.826 3904 | 18.300 179 | 20.127 8719 | 1.5972E-09 | 3.026E-07 | 1.4173 925 | 0.5032 3932 | up | no |
| ENSG00000144711 | IQSEC1 | 9922 | 3.2507 9354 | 3.3400 364 | 3.3450 2882 | 4.5982 0767 | 4.7060 9761 | 4.7441 0769 | 1.7239E-09 | 3.2472E-07 | 0.7072 5845 | -0.4996 9059 | down | no |
| ENSG00000135047 | CTSL | 1514 | 40.140 6062 | 32.101 8003 | 37.324 4062 | 27.635 8753 | 20.947 1069 | 23.869 5089 | 1.7819E-09 | 3.3371E-07 | 1.5122 5736 | 0.5967 0368 | up | yes |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ENSG00000117525 | F3 | 2152,1272 | 18.1797662 | 25.1761784 | 21.0017565 | 14.8842869 | 11.9717293 | 12.7098531 | 1.8168E-09 | 3.3827E-07 | 1.6265 | 0.7018 | up | yes |
| ENSG00000205413 | SAMD9 | 54809 | 7.2902 | 6.9805 | 6.1459 | 4.7189 | 4.7426 | 4.5991 | 2.0545 | 3.8035 | 1.4520 | 0.5380 | up | no |
| ENSG00000055163 | CYFIP2 | 26999 | 0.4281 | 0.3561 | 0.3687 | 1.0282 | 0.6588 | 0.9317 | 2.1734 | 3.9782 | 0.4402 | -1.1834 | down | yes |
| ENSG00000144802 | NFKBIZ | 64332 | 3.1496 | 3.3686 | 2.6797 | 1.4598 | 1.9961 | 1.3803 | 2.1678 | 3.9782 | 1.9018 | 0.9274 | up | yes |
| ENSG00000187193 | MT1X | 4501 | 7.4551 | 6.1254 | 7.3324 | 4.2393 | 2.9515 | 2.7476 | 2.3345 | 4.2491 | 2.1042 | 1.0733 | up | yes |
| ENSG00000168610 | STAT3 | 6774 | 20.184 | 16.797 | 17.942 | 13.130 | 13.008 | 13.724 | 2.36E-09 | 4.2715 | 1.3777 | 0.4623 | up | no |
| ENSG00000120129 | DUSP1 | 1843,11266 | 62.391 | 45.729 | 57.225 | 35.411 | 37.313 | 36.627 | 2.5312 | 4.5559 | 1.5120 | 0.5965 | up | yes |
| ENSG00000059377 | TBXAS1 | 6916 | 1.4497 | 1.6565 | 1.4853 | 0.7495 | 0.7039 | 0.8688 | 2.7815 | 4.9787 | 1.9770 | 0.9833 | up | yes |
| ENSG00000172667 | ZMAT3 | 64393 | 12.811 | 13.747 | 13.105 | 17.798 | 16.795 | 18.085 | 2.8751 | 5.118E-07 | 0.7529 | -0.4093 | down | no |
| ENSG00000115902 | SLC1A4 | 6509 | 4.5861 | 6.4647 | 5.2978 | 8.7455 | 8.7871 | 8.4408 | 2.9491 | 5.221E-07 | 0.6294 | -0.6678 | down | yes |
| ENSG00000115084 | SLC35F5 | 80255 | 5.3304 | 6.6199 | 5.4596 | 8.1002 | 8.4623 | 8.9343 | 3.1329 | 5.5164 | 0.6828 | -0.5504 | down | no |
| ENSG00000178988 | MRFAP1L1 | 114932 | 24.811 | 23.817 | 24.446 | 18.240 | 17.770 | 16.330 | 3.3537 | 5.8731 | 1.3961 | 0.4814 | up | no |
| ENSG00000139292 | LGR5 | 8549 | 0.5714 | 0.7553 | 0.6455 | 1.3212 | 1.5301 | 1.4444 | 3.7681 | 6.5634 | 0.4591 | -1.1230 | down | yes |
| ENSG00000145050 | MANF | 7873 | 12.193 | 10.454 | 10.665 | 7.1724 | 6.9624 | 7.2093 | 3.8231 | 6.6236 | 1.5607 | 0.6422 | up | yes |
| ENSG00000111801 | BTN3A3 | 10384 | 5.2274 | 4.1855 | 4.5923 | 2.8521 | 3.0378 | 2.9446 | 3.9136 | 6.7443 | 1.5852 | 0.6647 | up | yes |
| ENSG00000060982 | BCAT1 | 586 | 13.864 | 18.078 | 14.994 | 21.987 | 22.856 | 23.166 | 4.092E-09 | 7.0144 | 0.6901 | -0.5350 | down | no |
| ENSG00000105778 | AVL9 | 23080 | 2.7507 | 3.0081 | 2.8429 | 4.0121 | 4.1326 | 3.8617 | 4.4049 | 7.511E-07 | 0.7164 | -0.4810 | down | no |
| ENSG00000117862 | TXNDC12 | 51060 | 11.026 | 12.009 | 11.436 | 7.2266 | 8.3741 | 7.2750 | 4.4445 | 7.5388 | 1.5069 | 0.5916 | up | yes |
| ENSG00000183671 | CMKLR2 | 2825 | 10.078 | 11.349 | 10.264 | 17.837 | 14.591 | 15.452 | 4.6902 | 7.9142 | 0.6618 | -0.5953 | down | yes |
| ENSG00000101350 | KIF3B | 9371 | 13.733 | 13.990 | 12.648 | 19.912 | 17.388 | 18.164 | 5.0341 | 8.4505 | 0.7278 | -0.4581 | down | no |
| ENSG00000157240 | FZD1 | 8321 | 27.313 | 27.874 | 26.750 | 20.691 | 13.770 | 18.355 | 5.1205 | 8.5513 | 1.5513 | 0.6335 | up | yes |
| ENSG00000157191 | NECAP2 | 55707 | 8.5786 | 7.9445 | 8.5640 | 6.1914 | 5.4359 | 5.8845 | 6.0638 | 1.0075 | 1.4325 | 0.5186 | up | no |
| ENSG00000198682 | PAPSS2 | 9060 | 35.405 | 36.289 | 35.326 | 26.283 | 27.925 | 27.690 | 6.106E-09 | 1.0093 | 1.3067 | 0.3859 | up | no |
| ENSG00000176533 | GNG7 | 2788 | 0.5880 | 0.6210 | 0.6339 | 1.3817 | 1.2789 | 1.3428 | 6.2966 | 1.0355 | 0.4603 | -1.1191 | down | yes |
| ENSG0000 | IFITM3 | 10410 | 177.75 | 159.54 | 171.03 | 119.39 | 135.08 | 127.53 | 6.7315 | 1.1015 | 1.3306 | 0.4121 | up | no |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0142089 | | | 7153 | 2669 | 0607 | 422 | 2547 | 5385 | E-09 | E-06 | 656 | 4806 | |

Note: A: The control group of SCAPs transfected with shNC Lentivirus, _1 represents the first duplicate, _2 represents the second duplicate, _3 represents the third duplicate; B: The experimental group of SCAPs transfected with shOPTN Lentivirus.

**Table S3.** The sequencing results of the F1 generation *Optn*$^{+/-}$ mice constructed using CRISPR/Cas9 technology.

| | |
|---|---|
| **DNA sequence** | 5'GNNNNNNNNNGNCNNNATNANTNNATGGCNATCGTTAACTTTGTAATCA<br>ATGAATGATAGGACCTCCCTCAGTCTCTTAGATTTCTAGTCATTAGCAGGAC<br>TTTATCTCTCAATTGGTTTTTATTTGGGAGAATTTGTTGTTTTGAGACACTGT<br>CTCATATAGTCCCACTTGGTAAACTAATTTTATTAGGGCTACTTATGGGGCAG<br>AATCAGTGAATGGTTACTTACAGAAGCAGAAATGACTCAGACAGATGCATC<br>ACCAAGGCCCACCCCTGCCGCAGACCCTCTGGTCCCCTGTGCCTGCGTAGG<br>AAAGAGTCTCTAGAGTAGATGGGCAGAGATTAGGATGTAGTGACAGTCAGA<br>CACACGAGAGTGGTGTTGGATCTGAATGTAATGTTCTGGTTGAGCTTCAGA<br>CTTATATTACAACGAATTATCAGAGGATACAAATCACAAAAAGACAAGATAC<br>ACTGAAATTCACCAGTTACAGCAGAAAGGAATTTGCAGGGACTAATTAAAT<br>GTTTACATTAGGGATAACAAGCCCTGCCTAGGATCAGCCTAAAAGCATCAG<br>GGGGTTGTTAACTCTTGATAGGCCTTAAGAGTAGTGTGTTATCAGGAGCTCT<br>AAATTCTTAGGTCTAGTAAAACTTATCCTGTCTGGAGAGTTCCCCCTTATCA<br>GGGTAGTATATCAACTTATACTTGACATGGAATGTAGCCTGTAGTAAAAGAT<br>TTCTATCTCAGTGAGACTTTTAGTCTCTATCTACAGACAGCTGAGTAAATGA<br>CAGATGTTTTATTGTTTTATGATACAGCTTAATTAATTACTGAATAGGTTAAG<br>CTCCTTGCTGCCTATCTGGAA 3' |