

Supplementary

The Coordinated Activities of nAChR and Wnt Signaling Regulate Intestinal Stem Cell Function in Mice

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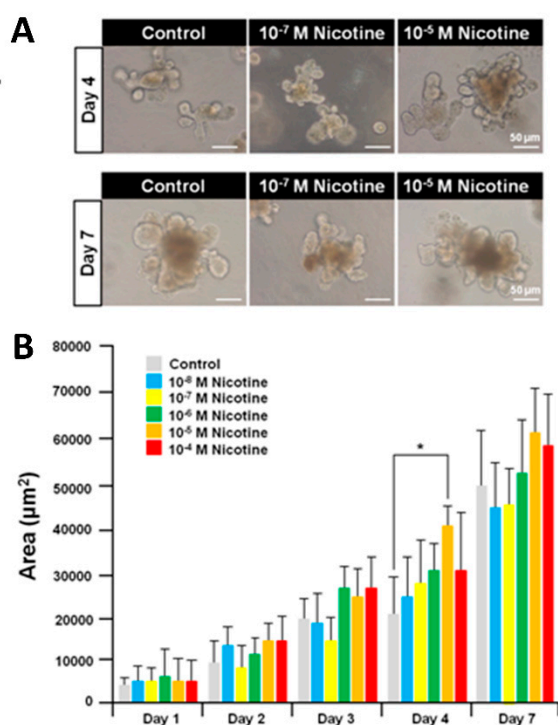


Figure S1. Effect of nicotine on organoid growth. (A) Micrographs of organoids after treatment with 10⁻⁷ M and 10⁻⁵ M nicotine for 4 days and 7 days of culture. (B) Effect of nicotine on the size of cultured organoids. Each sample represents an average of three independent experiments. Error bars represent the standard deviation of the mean. An asterisk indicates a statistically significant difference from untreated control organoids (Mann-Whitney test, *p<0.05).

Table S1. RNA-sequencing analysis of gene expression after 3 days and 7 days of nicotine treatment.

| Genbank ID | Gene Name | FPKM ¹ | | | | | | Fold change ² | | | | Pathway |
|--------------|-----------|-------------------|--------------------|--------------------|--------|--------------------|--------------------|--------------------------|--------------------|--------------------|--------------------|--------------------------------|
| | | 3 days | | | 7 days | | | 3 days | | 7 days | | |
| | | CTL | 10 ⁻⁷ M | 10 ⁻⁵ M | CTL | 10 ⁻⁷ M | 10 ⁻⁵ M | 10 ⁻⁷ M | 10 ⁻⁵ M | 10 ⁻⁷ M | 10 ⁻⁵ M | |
| NM_001164147 | Tcf3 | 21.36 | 27.80 | 26.99 | 3.04 | 27.13 | 90.34 | 1.30 | 1.26 | 8.91 | 29.67 | Stem |
| NM_011386 | Skil | 2.10 | 4.46 | 6.59 | 0.64 | 4.54 | 7.79 | 2.13 | 3.14 | 7.06 | 12.13 | Stem |
| NM_021878 | Jarid2 | 2.95 | 0.00 | 5.07 | 2.56 | 16.75 | 13.53 | 0.00 | 1.71 | 6.53 | 5.28 | Stem |
| NM_011548 | Tcf3 | 42.23 | 40.31 | 45.10 | 33.77 | 63.42 | 139.21 | 0.95 | 1.07 | 1.88 | 4.12 | Stem |
| NM_001039537 | Lif | 5.65 | 1.51 | 1.81 | 1.22 | 8.72 | 6.17 | 0.27 | 0.32 | 7.17 | 5.08 | Stem |
| NM_001164042 | Smad5 | 3.88 | 0.00 | 5.80 | 0.01 | 2.18 | 1.77 | 0.00 | 1.50 | 405.58 | 329.32 | Stem |
| NM_001081149 | Kat6a | 60.88 | 63.06 | 68.05 | 31.95 | 72.90 | 74.69 | 1.04 | 1.12 | 2.28 | 2.34 | Stem |
| NM_011263 | Rest | 23.40 | 25.66 | 24.51 | 14.76 | 36.25 | 35.08 | 1.10 | 1.05 | 2.46 | 2.38 | Stem |
| NM_007958 | Smarcacl1 | 35.76 | 45.53 | 38.51 | 21.00 | 38.01 | 48.28 | 1.27 | 1.08 | 1.81 | 2.30 | Stem |
| NM_001164153 | Tcf3 | 9.66 | 4.01 | 7.26 | 5.75 | 11.43 | 14.01 | 0.42 | 0.75 | 1.99 | 2.44 | Stem |
| NM_001205043 | Jarid2 | 16.25 | 15.39 | 22.60 | 14.27 | 22.90 | 32.82 | 0.95 | 1.39 | 1.60 | 2.30 | Stem |
| NM_175238 | Rif1 | 52.62 | 60.79 | 64.49 | 39.51 | 76.49 | 73.71 | 1.16 | 1.23 | 1.94 | 1.87 | Stem |
| NM_011535 | Tbx3 | 9.19 | 23.08 | 9.13 | 14.55 | 25.23 | 26.73 | 2.51 | 0.99 | 1.73 | 1.84 | Stem |
| NM_010560 | Il6st | 24.12 | 27.08 | 27.25 | 15.26 | 28.89 | 27.68 | 1.12 | 1.13 | 1.89 | 1.81 | Stem |
| NM_007496 | Zfxh3 | 8.76 | 8.75 | 8.78 | 6.47 | 11.87 | 11.59 | 1.00 | 1.00 | 1.83 | 1.79 | Stem |
| NM_001163641 | Setdb1 | 2.64 | 2.60 | 2.00 | 4.27 | 10.00 | 7.86 | 0.98 | 0.76 | 2.34 | 1.84 | Stem |
| NM_172716 | Pcgf3 | 88.05 | 87.14 | 97.56 | 57.17 | 89.48 | 96.34 | 0.99 | 1.11 | 1.57 | 1.68 | Stem |
| NM_007395 | Aevr1b | 141.2 | 139.4 | 146.1 | 112.2 | 183.0 | 183.6 | 0.99 | 1.03 | 1.63 | 1.64 | Stem |
| NM_001077495 | Pik3r1 | 113.9 | 122.5 | 124.7 | 82.1 | 156.6 | 149.2 | 1.08 | 1.09 | 1.91 | 1.82 | Stem, THS, Rap1, actin |
| NM_019827 | Gsk3b | 74.22 | 80.95 | 77.99 | 55.82 | 91.30 | 95.20 | 1.09 | 1.05 | 1.64 | 1.71 | Stem, THS, Hippo, Wnt |
| NM_007614 | Ctnnb1 | 952.8 | 864.2 | 747.4 | 511.6 | 824.8 | 963.8 | 0.91 | 0.78 | 1.61 | 1.88 | Stem, THSHippo, Wnt, Rap1 |
| NM_007561 | Bmpr2 | 23.86 | 24.02 | 25.36 | 18.57 | 29.62 | 31.49 | 1.01 | 1.06 | 1.60 | 1.70 | Stem, Hippo |
| NM_008055 | Fzd4 | 23.10 | 22.65 | 21.69 | 14.33 | 26.10 | 28.56 | 0.98 | 0.94 | 1.82 | 1.99 | Stem, Hippo, Wnt |
| NM_001162494 | Fzd6 | 14.48 | 14.75 | 15.65 | 10.40 | 20.86 | 19.53 | 1.02 | 1.08 | 2.01 | 1.88 | Stem, Hippo, Wnt |
| NM_022721 | Fzd5 | 99.59 | 104.59 | 88.47 | 36.53 | 67.40 | 65.63 | 1.05 | 0.89 | 1.84 | 1.80 | Stem, Hippo, Wnt |
| NM_007889 | Dvl3 | 74.16 | 79.85 | 75.89 | 45.13 | 78.74 | 78.07 | 1.08 | 1.02 | 1.74 | 1.73 | Stem, Hippo, Wnt |
| NM_001256224 | Wnt5a | 0.15 | 0.20 | 0.21 | 0.00 | 1.16 | 0.98 | 1.30 | 1.37 | 4624.5 | 3885.7 | Stem, Hippo, Wnt |
| NM_011719 | Wnt9b | 2.43 | 3.16 | 3.04 | 1.82 | 3.34 | 2.56 | 1.30 | 1.25 | 1.84 | 1.41 | Stem, Hippo, Wnt |
| NM_007462 | Apc | 65.36 | 69.78 | 66.21 | 35.33 | 68.58 | 70.15 | 1.07 | 1.01 | 1.94 | 1.99 | Stem, Hippo, Wnt |
| NM_010207 | Fgfr2 | 15.50 | 17.67 | 16.77 | 15.65 | 25.61 | 26.65 | 1.14 | 1.08 | 1.64 | 1.70 | Stem, MAPK, Endoc, Rap1, Actin |
| NM_001080118 | Med1 | 51.29 | 56.80 | 53.88 | 4.96 | 58.02 | 56.25 | 1.11 | 1.05 | 11.70 | 11.34 | THS |
| NM_012005 | Med14 | 13.53 | 12.72 | 11.40 | 3.89 | 16.82 | 17.62 | 0.94 | 0.84 | 4.33 | 4.53 | THS |
| NM_001205314 | Stat1 | 10.96 | 3.65 | 8.51 | 3.11 | 4.83 | 11.42 | 0.33 | 0.78 | 1.55 | 3.67 | THS |
| NM_001110350 | Sin3a | 8.08 | 8.96 | 12.06 | 6.11 | 16.69 | 19.70 | 1.11 | 1.49 | 2.73 | 3.22 | THS |
| NM_020005 | Kat2b | 20.88 | 14.04 | 13.74 | 6.25 | 15.35 | 15.95 | 0.67 | 0.66 | 2.45 | 2.55 | THS |
| NM_008678 | Ncoa2 | 39.88 | 40.39 | 41.79 | 23.07 | 43.82 | 52.20 | 1.01 | 1.05 | 1.90 | 2.26 | THS |
| NM_001252313 | Ncor1 | 124.8 | 132.4 | 132.4 | 77.40 | 143.1 | 152.4 | 1.06 | 1.06 | 1.85 | 1.97 | THS |
| NM_001080931 | Med13 | 58.06 | 59.16 | 60.77 | 30.90 | 57.87 | 60.93 | 1.02 | 1.05 | 1.87 | 1.97 | THS |
| NM_011062 | Pdpk1 | 76.03 | 87.35 | 85.04 | 41.64 | 77.22 | 80.73 | 1.15 | 1.12 | 1.85 | 1.94 | THS |
| NM_001286718 | Tsc2 | 10.21 | 28.26 | 24.48 | 8.81 | 17.51 | 16.87 | 2.77 | 2.40 | 1.99 | 1.92 | THS |
| NM_007503 | Fxyd2 | 0.00 | 0.26 | 0.00 | 0.00 | 0.52 | 0.78 | 264974 | 1.00 | 522973 | 781995 | THS |
| NM_008714 | Notch1 | 46.72 | 52.65 | 51.60 | 30.85 | 52.23 | 53.52 | 1.13 | 1.10 | 1.69 | 1.74 | THS |
| NM_001286713 | Tsc2 | 15.72 | 11.82 | 19.20 | 8.40 | 14.61 | 15.02 | 0.75 | 1.22 | 1.74 | 1.79 | THS |
| NM_172424 | Med13l | 36.02 | 32.56 | 35.60 | 25.49 | 47.51 | 43.44 | 0.90 | 0.99 | 1.86 | 1.70 | THS |
| NM_021521 | Med12 | 37.89 | 39.13 | 38.00 | 27.09 | 49.96 | 46.01 | 1.03 | 1.00 | 1.84 | 1.70 | THS |
| NM_011308 | Ncor1 | 51.04 | 56.99 | 52.30 | 30.92 | 54.40 | 52.07 | 1.12 | 1.02 | 1.76 | 1.68 | THS |
| NM_008716 | Notch3 | 0.91 | 1.35 | 1.08 | 3.14 | 5.47 | 5.81 | 1.49 | 1.20 | 1.74 | 1.85 | THS |
| NM_177229 | Ncor1 | 12.77 | 16.96 | 17.19 | 20.51 | 31.96 | 34.34 | 1.33 | 1.35 | 1.56 | 1.67 | THS |
| NM_011378 | Sin3a | 11.46 | 12.63 | 4.57 | 4.34 | 7.40 | 7.66 | 1.10 | 0.40 | 1.70 | 1.76 | THS |
| NM_001025432 | Crebbp | 37.65 | 37.26 | 36.89 | 17.36 | 38.44 | 37.54 | 0.99 | 0.98 | 2.21 | 2.16 | THS, Wnt |
| NM_177821 | Ep300 | 76.51 | 76.01 | 75.87 | 41.31 | 80.85 | 79.91 | 0.99 | 0.99 | 1.96 | 1.93 | THS, Wnt |
| NM_001145830 | Plcb1 | 0.00 | 0.07 | 2.02 | 0.00 | 1.97 | 3.52 | 359.67 | 10805.6 | 4295.0 | 7695.3 | THS, Wnt, Rap1 |
| NM_001005784 | Patj | 17.59 | 6.81 | 10.91 | 2.81 | 10.49 | 10.89 | 0.39 | 0.62 | 3.74 | 3.88 | Hippo |
| NM_026735 | Mob1b | 98.07 | 112.8 | 107.5 | 43.32 | 98.40 | 102.9 | 1.15 | 1.10 | 2.27 | 2.37 | Hippo |
| NM_007862 | Dlg1 | 36.66 | 43.47 | 43.25 | 37.47 | 65.31 | 73.37 | 1.19 | 1.18 | 1.74 | 1.96 | Hippo |
| NM_001252253 | Nf2 | 0.00 | 1.77 | 0.86 | 0.73 | 2.23 | 2.27 | 1770261 | 856702 | 3.07 | 3.11 | Hippo |
| NM_001109752 | Dlg4 | 0.04 | 0.68 | 0.30 | 1.07 | 2.44 | 2.80 | 16.37 | 7.20 | 2.28 | 2.62 | Hippo |
| NM_145571 | Mob1a | 261.5 | 272.1 | 273.8 | 179.4 | 295.0 | 330.2 | 1.04 | 1.05 | 1.64 | 1.84 | Hippo |
| NM_001166585 | Tead1 | 18.50 | 30.61 | 24.13 | 19.68 | 38.42 | 32.32 | 1.65 | 1.30 | 1.95 | 1.64 | Hippo |
| NM_010690 | Lats1 | 81.69 | 90.21 | 88.21 | 57.88 | 94.78 | 93.62 | 1.10 | 1.08 | 1.64 | 1.62 | Hippo |
| NM_134015 | Fbxw11 | 0.00 | 2.60 | 3.39 | 0.00 | 5.80 | 4.56 | 1819.1 | 2373.5 | 11826.2 | 9287.3 | Hippo, Wnt |
| NM_001271347 | Fbxw11 | 1.62 | 1.69 | 0.01 | 1.23 | 3.25 | 5.18 | 1.04 | 0.01 | 2.65 | 4.22 | Hippo, Wnt |
| NM_001271348 | Fbxw11 | 53.57 | 56.79 | 55.64 | 32.31 | 67.58 | 64.46 | 1.06 | 1.04 | 2.09 | 2.00 | Hippo, Wnt |
| NM_001142920 | Tcf7l2 | 19.60 | 24.13 | 24.20 | 13.06 | 24.64 | 23.58 | 1.23 | 1.23 | 1.89 | 1.81 | Hippo, Wnt |
| NM_009371 | Tgfbr2 | 68.42 | 45.51 | 62.30 | 30.71 | 101.4 | 96.22 | 0.67 | 0.91 | 3.30 | 3.13 | Hippo, MAPK, Endoc |
| NM_001122850 | Pard3 | 36.14 | 34.58 | 37.05 | 29.69 | 48.20 | 49.14 | 0.96 | 1.03 | 1.62 | 1.66 | Hippo, Endocytosis, Rap1 |
| NM_020601 | Tbl1x | 129.4 | 140.4 | 140.8 | 104.8 | 216.3 | 226.6 | 1.08 | 1.09 | 2.06 | 2.16 | Wnt |

| | | | | | | | | | | | | |
|--------------|-----------|-------|-------|-------|--------|--------|--------|--------|--------|---------|----------|-------------------|
| NM_001004367 | Cxhc4 | 0.52 | 0.81 | 0.60 | 0.46 | 1.22 | 1.58 | 1.56 | 1.16 | 2.63 | 3.41 | Wnt |
| NM_008514 | Lrp6 | 70.38 | 74.94 | 78.31 | 47.65 | 80.35 | 82.44 | 1.06 | 1.11 | 1.69 | 1.73 | Wnt |
| NM_013502 | Ctbp1 | 40.62 | 41.05 | 44.38 | 25.53 | 42.38 | 42.60 | 1.01 | 1.09 | 1.66 | 1.67 | Wnt |
| NM_172688 | Map3k7 | 2.63 | 1.81 | 1.62 | 0.00 | 2.17 | 3.04 | 0.69 | 0.62 | 17479.4 | 24452.2 | Wnt, MAPK |
| NM_001164112 | Nfatc1 | 4.49 | 5.37 | 3.91 | 2.95 | 4.71 | 5.86 | 1.20 | 0.87 | 1.60 | 1.99 | Wnt, MAPK |
| NM_013931 | Mapk8ip3 | 1.66 | 13.56 | 9.65 | 0.00 | 6.35 | 11.29 | 8.18 | 5.82 | 5197650 | 9245016 | MAPK |
| NM_001163453 | Mapk8ip3 | 32.12 | 23.92 | 30.11 | 4.59 | 43.76 | 37.46 | 0.74 | 0.94 | 9.54 | 8.16 | MAPK |
| NM_008696 | Map4k4 | 6.43 | 4.14 | 7.18 | 0.00 | 1.97 | 5.78 | 0.64 | 1.12 | 446.54 | 1310.89 | MAPK |
| NM_001285488 | Mknk1 | 0.00 | 0.00 | 0.00 | 0.00 | 2.36 | 3.89 | 0.90 | 1.34 | 7221.68 | 11869.48 | MAPK |
| NM_001163643 | Map3k12 | 1.03 | 0.00 | 1.04 | 0.00 | 1.09 | 2.89 | 0.00 | 1.01 | 3543.67 | 9417.03 | MAPK |
| NM_009784 | Cacna2d1 | 1.36 | 2.25 | 1.86 | 0.01 | 2.21 | 2.61 | 1.65 | 1.36 | 350.92 | 414.06 | MAPK |
| NM_007923 | Elk4 | 36.98 | 38.84 | 41.78 | 12.93 | 43.41 | 40.98 | 1.05 | 1.13 | 3.36 | 3.17 | MAPK |
| NM_001038609 | Mapt | 2.22 | 0.00 | 2.23 | 1.00 | 3.33 | 3.69 | 0.00 | 1.00 | 3.33 | 3.68 | MAPK |
| NM_148945 | Rps6ka3 | 101.4 | 101.2 | 108.2 | 56.6 | 132.9 | 128.8 | 1.00 | 1.07 | 2.35 | 2.27 | MAPK |
| NM_172821 | Map3k13 | 20.32 | 21.87 | 23.39 | 8.59 | 19.08 | 19.42 | 1.08 | 1.15 | 2.22 | 2.26 | MAPK |
| NM_001161423 | Ikbkg | 0.72 | 1.08 | 0.00 | 0.00 | 0.23 | 1.07 | 1.50 | 0.00 | 690.35 | 3220.9 | MAPK |
| NM_001252060 | Cacna1a | 1.54 | 3.32 | 7.09 | 1.68 | 7.86 | 4.47 | 2.16 | 4.61 | 4.67 | 2.65 | MAPK |
| NM_001284371 | Atf2 | 2.68 | 3.62 | 2.82 | 1.53 | 2.85 | 3.76 | 1.35 | 1.05 | 1.86 | 2.45 | MAPK |
| NM_144825 | Taok1 | 41.52 | 45.14 | 46.44 | 26.07 | 48.80 | 48.77 | 1.09 | 1.12 | 1.87 | 1.87 | MAPK |
| NM_001252202 | Map4k4 | 20.13 | 23.46 | 29.01 | 24.23 | 44.84 | 45.25 | 1.16 | 1.44 | 1.85 | 1.87 | MAPK |
| NM_007746 | Map3k8 | 1.80 | 1.55 | 2.31 | 1.39 | 2.96 | 3.34 | 0.86 | 1.28 | 2.14 | 2.41 | MAPK |
| NM_013560 | Hspb1 | 1.04 | 0.28 | 0.28 | 0.00 | 0.27 | 0.77 | 0.27 | 0.27 | 267089 | 767023 | MAPK |
| NM_134080 | Flnb | 158.8 | 158.3 | 160.4 | 127.8 | 202.0 | 222.0 | 1.00 | 1.01 | 1.58 | 1.74 | MAPK |
| NM_010897 | Nfl | 23.12 | 24.34 | 23.48 | 17.16 | 29.67 | 30.39 | 1.05 | 1.02 | 1.73 | 1.77 | MAPK |
| NM_011946 | Map3k2 | 39.78 | 40.79 | 43.89 | 21.75 | 37.74 | 36.97 | 1.03 | 1.10 | 1.74 | 1.70 | MAPK |
| NM_001174049 | Cacna2d2 | 0.20 | 0.19 | 0.11 | 0.72 | 1.46 | 1.83 | 0.94 | 0.53 | 2.02 | 2.53 | MAPK |
| NM_001025093 | Atf2 | 23.47 | 24.38 | 22.69 | 12.38 | 32.70 | 20.71 | 1.04 | 0.97 | 2.64 | 1.67 | MAPK |
| NM_008301 | Hspa2 | 2.23 | 2.17 | 2.70 | 0.00 | 4.03 | 3.70 | 0.97 | 1.21 | 1853.2 | 1702.1 | MAPK, Endoc |
| NM_007764 | Crkl | 64.19 | 75.31 | 70.71 | 44.28 | 73.64 | 73.83 | 1.17 | 1.10 | 1.66 | 1.67 | MAPK, Rap1, Actin |
| NM_139294 | Braf | 17.69 | 20.93 | 20.70 | 16.86 | 27.69 | 28.10 | 1.18 | 1.17 | 1.64 | 1.67 | MAPK, Rap1, Actin |
| NM_001177558 | Gng12 | 31.82 | 18.23 | 30.57 | 8.08 | 23.46 | 24.62 | 0.57 | 0.96 | 2.90 | 3.05 | MAPK, Actin |
| NM_001162868 | Rab11fip3 | 9.01 | 0.03 | 15.19 | 0.01 | 4.50 | 12.85 | 0.00 | 1.69 | 440.48 | 1258.2 | Endocytosis |
| NM_007619 | Cbl | 42.11 | 44.01 | 45.33 | 9.18 | 44.98 | 50.96 | 1.05 | 1.08 | 4.90 | 5.55 | Endocytosis |
| NM_001134383 | Iqsec1 | 7.51 | 5.68 | 6.88 | 1.92 | 9.22 | 11.27 | 0.76 | 0.92 | 4.81 | 5.87 | Endocytosis |
| NM_001276462 | Asap1 | 0.00 | 4.21 | 0.40 | 1.08 | 3.38 | 5.32 | 1756.6 | 166.1 | 3.14 | 4.94 | Endocytosis |
| NM_001164056 | Pld1 | 12.30 | 10.84 | 6.85 | 8.05 | 13.95 | 19.38 | 0.88 | 0.56 | 1.73 | 2.41 | Endocytosis |
| NM_029438 | Smurf1 | 4.03 | 9.39 | 6.64 | 6.46 | 11.20 | 15.75 | 2.33 | 1.65 | 1.73 | 2.44 | Endocytosis |
| NM_001080813 | Rab11fip1 | 35.82 | 40.67 | 36.44 | 18.07 | 31.64 | 37.77 | 1.14 | 1.02 | 1.75 | 2.09 | Endocytosis |
| NM_001164678 | Pdcd6ip | 10.32 | 16.65 | 20.95 | 9.91 | 18.52 | 20.88 | 1.61 | 2.03 | 1.87 | 2.11 | Endocytosis |
| NM_010153 | Erbp3 | 219.6 | 223.5 | 233.1 | 106.7 | 208.8 | 214.5 | 1.02 | 1.06 | 1.96 | 2.01 | Endocytosis |
| NM_001114664 | Iqsec2 | 4.94 | 7.85 | 7.72 | 4.04 | 7.19 | 8.94 | 1.59 | 1.56 | 1.78 | 2.21 | Endocytosis |
| NM_001144988 | Spq20 | 17.52 | 12.64 | 14.73 | 4.51 | 12.59 | 9.73 | 0.72 | 0.84 | 2.79 | 2.16 | Endocytosis |
| NM_001285806 | Grk3 | 3.41 | 0.00 | 1.93 | 4.08 | 10.02 | 8.88 | 0.00 | 0.56 | 2.45 | 2.17 | Endocytosis |
| NM_001164367 | Rab11fip2 | 3.45 | 3.63 | 3.09 | 2.69 | 6.88 | 5.98 | 1.05 | 0.90 | 2.55 | 2.22 | Endocytosis |
| NM_027487 | Ccdc53 | 2.23 | 4.93 | 5.82 | 3.53 | 6.28 | 7.10 | 2.21 | 2.61 | 1.78 | 2.01 | Endocytosis |
| NM_030263 | Psd3 | 10.91 | 14.83 | 14.77 | 9.74 | 20.75 | 17.92 | 1.36 | 1.35 | 2.13 | 1.84 | Endocytosis |
| NM_173392 | Zfyve16 | 14.55 | 15.77 | 15.70 | 13.84 | 23.96 | 24.65 | 1.08 | 1.08 | 1.73 | 1.78 | Endocytosis |
| NM_001085495 | Arfgef2 | 81.76 | 87.55 | 87.71 | 43.69 | 72.39 | 75.94 | 1.07 | 1.07 | 1.66 | 1.74 | Endocytosis |
| NM_025519 | Chmp4c | 142.7 | 141.0 | 169.0 | 106.80 | 171.1 | 182.4 | 0.99 | 1.18 | 1.60 | 1.71 | Endocytosis |
| NM_175543 | Rab11fip4 | 2.83 | 2.38 | 3.41 | 3.65 | 6.81 | 6.83 | 0.84 | 1.21 | 1.87 | 1.87 | Endocytosis |
| NM_001122832 | Eps15l1 | 43.08 | 43.79 | 42.06 | 27.14 | 42.39 | 45.29 | 1.02 | 0.98 | 1.56 | 1.67 | Endocytosis |
| NM_001040111 | Arap1 | 30.20 | 26.74 | 28.65 | 16.39 | 25.83 | 27.38 | 0.89 | 0.95 | 1.58 | 1.67 | Endocytosis |
| NM_001033375 | A230046 | 47.18 | 50.63 | 52.02 | 34.17 | 53.32 | 56.10 | 1.07 | 1.10 | 1.56 | 1.64 | Endocytosis |
| NM_010515 | Igf2r | 83.47 | 89.92 | 88.18 | 63.01 | 102.43 | 102.81 | 1.08 | 1.06 | 1.63 | 1.63 | Endocytosis |
| NM_001122733 | Kit | 7.64 | 7.51 | 10.68 | 4.01 | 16.48 | 14.59 | 0.98 | 1.40 | 4.11 | 3.64 | Endoc, Rap1 |
| NM_001167745 | Wasl | 1.46 | 2.42 | 2.61 | 0.66 | 1.82 | 2.66 | 1.66 | 1.79 | 2.77 | 4.03 | Endoc, Actin |
| NM_001286785 | Magi1 | 2.66 | 0.00 | 4.29 | 0.00 | 5.87 | 4.04 | 0.00 | 1.61 | 22016.1 | 15153.3 | Rap1 |
| NM_001167983 | Sipal11 | 17.00 | 20.16 | 17.18 | 9.07 | 31.30 | 40.89 | 1.19 | 1.01 | 3.45 | 4.51 | Rap1 |
| NM_001162425 | Efnal | 1.11 | 1.13 | 2.20 | 0.00 | 1.18 | 2.25 | 1.02 | 1.99 | 11176.7 | 21339.5 | Rap1 |
| NM_178900 | Prkd2 | 2.16 | 2.68 | 5.14 | 0.53 | 3.69 | 3.55 | 1.24 | 2.37 | 6.97 | 6.70 | Rap1 |
| NM_001204165 | Rapgef4 | 0.00 | 0.00 | 0.00 | 0.00 | 2.59 | 1.64 | 91.70 | 403.31 | 2881.4 | 1824.2 | Rap1 |
| NM_001171004 | Prkd3 | 20.24 | 24.80 | 26.47 | 14.58 | 41.91 | 37.37 | 1.23 | 1.31 | 2.87 | 2.56 | Rap1 |
| NM_001145834 | Ralgds | 10.22 | 0.00 | 15.63 | 8.96 | 27.76 | 22.40 | 0.00 | 1.53 | 3.10 | 2.50 | Rap1 |
| NM_175930 | Rapgef5 | 15.41 | 14.72 | 15.09 | 9.90 | 21.57 | 24.16 | 0.95 | 0.98 | 2.18 | 2.44 | Rap1 |
| NM_009624 | Adcy9 | 15.19 | 13.48 | 14.21 | 7.09 | 12.95 | 16.23 | 0.89 | 0.94 | 1.83 | 2.29 | Rap1 |
| NM_172803 | Dock4 | 4.70 | 6.21 | 6.53 | 3.06 | 7.27 | 7.57 | 1.32 | 1.39 | 2.38 | 2.48 | Rap1 |
| NM_001085450 | Ctnnd1 | 23.76 | 41.94 | 29.08 | 27.28 | 43.09 | 55.86 | 1.77 | 1.22 | 1.58 | 2.05 | Rap1 |
| NM_001163269 | Lpar5 | 70.77 | 80.03 | 82.57 | 33.98 | 55.19 | 64.75 | 1.13 | 1.17 | 1.62 | 1.91 | Rap1 |
| NM_001286784 | Magi1 | 22.79 | 21.12 | 24.94 | 14.32 | 27.85 | 25.98 | 0.93 | 1.09 | 1.95 | 1.81 | Rap1 |
| NM_001159354 | Magi3 | 62.99 | 69.44 | 62.65 | 39.27 | 67.84 | 69.86 | 1.10 | 0.99 | 1.73 | 1.78 | Rap1 |
| NM_175258 | Rapgef6 | 39.78 | 43.44 | 42.49 | 26.70 | 45.14 | 45.61 | 1.09 | 1.07 | 1.69 | 1.71 | Rap1 |
| NM_009623 | Adcy8 | 9.17 | 11.75 | 9.43 | 5.17 | 7.95 | 9.07 | 1.28 | 1.03 | 1.54 | 1.76 | Rap1 |
| NM_001145886 | Tiam1 | 27.91 | 30.38 | 33.07 | 10.63 | 36.10 | 45.54 | 1.09 | 1.19 | 3.39 | 4.28 | Rap1, Actin |
| NM_001082960 | Itgam | 5.05 | 5.61 | 4.97 | 0.00 | 2.76 | 1.33 | 1.11 | 0.98 | 1350.3 | 650.99 | Rap1, Actin |
| NM_001130409 | Ptk2 | 12.68 | 11.15 | 10.93 | 4.89 | 13.38 | 17.31 | 0.88 | 0.86 | 2.74 | 3.54 | Actin |

| | | | | | | | | | | | | |
|--------------|----------|-------|-------|-------|-------|-------|--------|------|------|------|------|-------|
| NM_001081307 | Ppp1r12b | 8.37 | 8.95 | 8.29 | 2.09 | 7.17 | 7.45 | 1.07 | 0.99 | 3.44 | 3.57 | Actin |
| NM_008396 | Itga2 | 35.99 | 38.37 | 39.36 | 26.60 | 63.55 | 69.46 | 1.07 | 1.09 | 2.39 | 2.61 | Actin |
| NM_001005608 | Itgb4 | 0.69 | 6.09 | 3.09 | 1.84 | 4.62 | 4.79 | 8.86 | 4.49 | 2.52 | 2.61 | Actin |
| NM_001033228 | Itga1 | 16.08 | 17.78 | 17.15 | 16.27 | 30.11 | 31.77 | 1.11 | 1.07 | 1.85 | 1.95 | Actin |
| NM_172493 | Diaph2 | 11.13 | 11.55 | 10.16 | 9.96 | 19.11 | 19.42 | 1.04 | 0.91 | 1.92 | 1.95 | Actin |
| NM_027892 | Ppp1r12a | 75.89 | 82.69 | 78.50 | 54.66 | 96.74 | 102.46 | 1.09 | 1.03 | 1.77 | 1.87 | Actin |
| NM_027144 | Arhgef12 | 66.62 | 72.52 | 70.94 | 45.73 | 89.33 | 84.88 | 1.09 | 1.06 | 1.95 | 1.86 | Actin |
| NM_198127 | Abi2 | 0.60 | 1.08 | 0.98 | 0.19 | 1.41 | 1.16 | 1.80 | 1.63 | 7.28 | 5.99 | Actin |
| NM_153423 | Wasf2 | 130.8 | 145.1 | 135.4 | 85.11 | 150.2 | 152.1 | 1.11 | 1.03 | 1.76 | 1.79 | Actin |
| NM_001113517 | Arhgef7 | 1.88 | 3.07 | 1.42 | 1.34 | 3.43 | 3.16 | 1.63 | 0.76 | 2.55 | 2.35 | Actin |
| NM_177710 | Ssh2 | 29.89 | 33.83 | 33.78 | 19.91 | 32.84 | 33.83 | 1.13 | 1.13 | 1.65 | 1.70 | Actin |
| NM_015759 | Fgd3 | 0.97 | 0.78 | 1.47 | 1.35 | 2.34 | 2.85 | 0.80 | 1.52 | 1.74 | 2.12 | Actin |

¹The FPKM (Fragments Per Kilobase Mega read) values. CTL, Control.

²Fold change is defined as the ratio of the signal of non-treated organoids to that of treated organoids.

Table S2. RNA-sequencing analysis of gene expression after 7 days of mecamylamine treatment.

| Genbank ID | Gene Name | FPKM ¹ | | Fold change ² | | Pathway |
|--------------|-----------|-------------------|--------------------|--------------------------|--------------------|--------------------------------|
| | | CTL | 10 ⁻⁶ M | 10 ⁻⁶ M | 10 ⁻⁶ M | |
| NM_001164147 | Tcf3 | | 2.57 | 1.52 | 0.59 | Stem |
| NM_011386 | Skil | | 0.00 | 1.57 | 15909.89 | Stem |
| NM_021878 | Jarid2 | | 1.14 | 1.10 | 0.97 | Stem |
| NM_011548 | Tcf3 | | 5.30 | 6.24 | 1.18 | Stem |
| NM_001039537 | Lif | | 1.59 | 1.33 | 0.84 | Stem |
| NM_001164042 | Smad5 | | 0.00 | 0.00 | 0.53 | Stem |
| NM_001081149 | Kat6a | | 8.90 | 9.03 | 1.01 | Stem |
| NM_011263 | Rest | | 3.66 | 3.46 | 0.95 | Stem |
| NM_007958 | Smad4 | | 5.80 | 5.43 | 0.94 | Stem |
| NM_001164153 | Tcf3 | | 0.37 | 0.00 | 0.00 | Stem |
| NM_001205043 | Jarid2 | | 2.19 | 1.17 | 0.54 | Stem |
| NM_175238 | Rif1 | | 9.67 | 9.57 | 0.99 | Stem |
| NM_011535 | Tbx3 | | 1.89 | 0.07 | 0.04 | Stem |
| NM_010560 | Il6st | | 3.72 | 4.29 | 1.15 | Stem |
| NM_007496 | Zfhx3 | | 1.28 | 1.11 | 0.87 | Stem |
| NM_001163641 | Setdb1 | | 1.13 | 0.00 | 0.00 | Stem |
| NM_172716 | Pcgf3 | | 11.91 | 10.89 | 0.91 | Stem |
| NM_007395 | Acvr1b | | 21.70 | 19.61 | 0.90 | Stem |
| NM_001077495 | Pik3r1 | | 15.54 | 15.35 | 0.99 | Stem, THS, Rap1, actin |
| NM_019827 | Gsk3b | | 10.01 | 9.98 | 1.00 | Stem, THS, Hippo, Wnt |
| NM_007614 | Cttnb1 | | 81.21 | 68.20 | 0.84 | Stem, THSHippo, Wnt, Rap1 |
| NM_007561 | Bmpr2 | | 3.89 | 3.82 | 0.98 | Stem, Hippo |
| NM_008055 | Fzd4 | | 3.82 | 3.16 | 0.83 | Stem, Hippo, Wnt |
| NM_001162494 | Fzd6 | | 1.62 | 1.65 | 1.02 | Stem, Hippo, Wnt |
| NM_022721 | Fzd5 | | 7.96 | 7.76 | 0.97 | Stem, Hippo, Wnt |
| NM_007889 | Dvl3 | | 8.24 | 9.05 | 1.10 | Stem, Hippo, Wnt |
| NM_001256224 | Wnt5a | | 0.02 | 0.00 | 0.00 | Stem, Hippo, Wnt |
| NM_011719 | Wnt9b | | 0.05 | 0.18 | 0.29 | Stem, Hippo, Wnt |
| NM_007462 | Apc | | 8.54 | 8.23 | 0.96 | Stem, Hippo, Wnt |
| NM_010207 | Fgfr2 | | 1.92 | 2.39 | 1.25 | Stem, MAPK, Endoc, Rap1, Actin |
| NM_001080118 | Med1 | | 9.18 | 8.78 | 0.96 | THS |
| NM_012005 | Med14 | | 2.57 | 4.12 | 1.60 | THS |
| NM_001205314 | Stat1 | | 1.48 | 1.24 | 0.84 | THS |
| NM_001110350 | Sin3a | | 3.96 | 1.69 | 0.43 | THS |
| NM_020005 | Kat2b | | 1.10 | 0.41 | 0.37 | THS |
| NM_008678 | Ncoa2 | | 4.81 | 6.23 | 1.30 | THS |
| NM_001252313 | Ncor1 | | 18.51 | 18.04 | 0.97 | THS |
| NM_001080931 | Med13 | | 6.31 | 6.22 | 0.98 | THS |
| NM_011062 | Pdpk1 | | 9.16 | 7.76 | 0.85 | THS |
| NM_001286718 | Tsc2 | | 0.92 | 1.05 | 1.15 | THS |
| NM_007503 | Fxyd2 | | 0.00 | 0.00 | 1.00 | THS |
| NM_008714 | Notch1 | | 4.93 | 4.90 | 0.99 | THS |
| NM_001286713 | Tsc2 | | 0.00 | 1.76 | 1577.57 | THS |
| NM_172424 | Med13l | | 4.90 | 5.19 | 1.06 | THS |
| NM_021521 | Med12 | | 6.45 | 6.73 | 1.04 | THS |
| NM_011308 | Ncor1 | | 6.61 | 8.16 | 1.24 | THS |
| NM_008716 | Notch3 | | 0.51 | 0.36 | 0.71 | THS |
| NM_177229 | Ncor1 | | 3.83 | 2.86 | 0.75 | THS |

| | | | | | |
|--------------|---------------|-------|-------|-----------|--------------------------|
| NM_011378 | Sin3a | 1.61 | 1.10 | 0.68 | THS |
| NM_001025432 | Crebbp | 3.83 | 3.80 | 0.99 | THS, Wnt |
| NM_177821 | Ep300 | 8.84 | 8.71 | 0.99 | THS, Wnt |
| NM_001145830 | Plcb1 | 0.32 | 0.02 | 0.07 | THS, Wnt, Rap1 |
| NM_001005784 | Patj | 0.76 | 0.81 | 1.06 | Hippo |
| NM_026735 | Mob1b | 11.70 | 9.75 | 0.83 | Hippo |
| NM_007862 | Dlg1 | 5.16 | 8.55 | 1.66 | Hippo |
| NM_001252253 | Nf2 | 0.00 | 0.40 | 397838.81 | Hippo |
| NM_001109752 | Dlg4 | 0.00 | 0.00 | 0.80 | Hippo |
| NM_145571 | Mob1a | 38.46 | 37.04 | 0.96 | Hippo |
| NM_001166585 | Tead1 | 4.36 | 4.91 | 1.13 | Hippo |
| NM_010690 | Lats1 | 11.01 | 10.81 | 0.98 | Hippo |
| NM_134015 | Fbxw11 | 0.71 | 0.00 | 0.00 | Hippo, Wnt |
| NM_001271347 | Fbxw11 | 0.63 | 0.00 | 0.00 | Hippo, Wnt |
| NM_001271348 | Fbxw11 | 8.64 | 7.20 | 0.83 | Hippo, Wnt |
| NM_001142920 | Tcf7l2 | 2.07 | 2.34 | 1.13 | Hippo, Wnt |
| NM_009371 | Tgfbr2 | 4.01 | 7.30 | 1.82 | Hippo, MAPK, Endoc |
| NM_001122850 | Pard3 | 5.91 | 4.94 | 0.84 | Hippo, Endocytosis, Rap1 |
| NM_020601 | Tb11x | 30.33 | 27.33 | 0.90 | Wnt |
| NM_001004367 | Cxxc4 | 0.05 | 0.15 | 3.04 | Wnt |
| NM_008514 | Lrp6 | 9.12 | 9.16 | 1.00 | Wnt |
| NM_013502 | Ctbp1 | 3.20 | 2.36 | 0.74 | Wnt |
| NM_172688 | Map3k7 | 0.58 | 0.53 | 0.91 | Wnt, MAPK |
| NM_001164112 | Nfatc1 | 0.48 | 0.00 | 0.00 | Wnt, MAPK |
| NM_013931 | Mapk8ip3 | 1.54 | 0.42 | 0.27 | MAPK |
| NM_001163453 | Mapk8ip3 | 4.57 | 2.47 | 0.54 | MAPK |
| NM_008696 | Map4k4 | 1.11 | 0.00 | 0.00 | MAPK |
| NM_001285488 | Mknk1 | 0.00 | 0.00 | 6.28 | MAPK |
| NM_001163643 | Map3k12 | 0.50 | 0.00 | 0.00 | MAPK |
| NM_009784 | Cacna2d1 | 0.21 | 0.39 | 1.84 | MAPK |
| NM_007923 | Elk4 | 6.27 | 6.61 | 1.05 | MAPK |
| NM_001038609 | Mapt | 0.00 | 0.00 | 1.16 | MAPK |
| NM_148945 | Rps6ka3 | 15.01 | 15.05 | 1.00 | MAPK |
| NM_172821 | Map3k13 | 2.66 | 2.98 | 1.12 | MAPK |
| NM_001161423 | Ikbkg | 0.43 | 0.00 | 0.00 | MAPK |
| NM_001252060 | Cacna1a | 1.09 | 0.99 | 0.91 | MAPK |
| NM_001284371 | Atf2 | 0.66 | 0.34 | 0.52 | MAPK |
| NM_144825 | Taok1 | 6.16 | 6.33 | 1.03 | MAPK |
| NM_001252202 | Map4k4 | 3.28 | 2.72 | 0.83 | MAPK |
| NM_007746 | Map3k8 | 0.75 | 1.02 | 1.37 | MAPK |
| NM_013560 | Hspb1 | 0.12 | 0.00 | 0.00 | MAPK |
| NM_134080 | Flnb | 30.98 | 27.32 | 0.88 | MAPK |
| NM_010897 | Nfi | 3.89 | 3.75 | 0.97 | MAPK |
| NM_011946 | Map3k2 | 4.29 | 4.15 | 0.97 | MAPK |
| NM_001174049 | Cacna2d2 | 0.36 | 0.17 | 0.48 | MAPK |
| NM_001025093 | Atf2 | 3.29 | 2.69 | 0.82 | MAPK |
| NM_008301 | Hspa2 | 0.65 | 0.37 | 0.57 | MAPK, Endoc |
| NM_007764 | Crkl | 8.08 | 7.49 | 0.93 | MAPK, Rap1, Actin |
| NM_139294 | Braf | 3.60 | 3.45 | 0.96 | MAPK, Rap1, Actin |
| NM_001177558 | Gng12 | 0.96 | 0.00 | 0.00 | MAPK, Actin |
| NM_001162868 | Rab11fip3 | 1.32 | 0.00 | 0.00 | Endocytosis |
| NM_007619 | Cbl | 7.00 | 7.29 | 1.04 | Endocytosis |
| NM_001134383 | Iqsec1 | 1.18 | 0.27 | 0.23 | Endocytosis |
| NM_001276462 | Asap1 | 0.71 | 0.00 | 0.00 | Endocytosis |
| NM_001164056 | Pld1 | 3.60 | 0.00 | 0.00 | Endocytosis |
| NM_029438 | Smurf1 | 0.94 | 1.43 | 1.51 | Endocytosis |
| NM_001080813 | Rab11fip1 | 6.24 | 5.41 | 0.87 | Endocytosis |
| NM_001164678 | Pdcd6ip | 1.29 | 1.95 | 1.51 | Endocytosis |
| NM_010153 | Erbp3 | 25.80 | 25.04 | 0.97 | Endocytosis |
| NM_001114664 | Iqsec2 | 0.79 | 0.93 | 1.18 | Endocytosis |
| NM_001144988 | Spg20 | 0.00 | 1.07 | 14798.36 | Endocytosis |
| NM_001285806 | Grk3 | 0.00 | 0.00 | 2.25 | Endocytosis |
| NM_001164367 | Rab11fip2 | 0.39 | 0.61 | 1.59 | Endocytosis |
| NM_027487 | Ccdc53 | 0.00 | 1.33 | 102631.60 | Endocytosis |
| NM_030263 | Psd3 | 2.60 | 2.45 | 0.94 | Endocytosis |
| NM_173392 | Zfyve16 | 3.00 | 2.85 | 0.95 | Endocytosis |
| NM_001085495 | Arfgef2 | 10.30 | 9.15 | 0.89 | Endocytosis |
| NM_025519 | Chmp4c | 22.60 | 23.80 | 1.05 | Endocytosis |
| NM_175543 | Rab11fip4 | 0.70 | 0.31 | 0.43 | Endocytosis |
| NM_001122832 | Eps15l1 | 6.59 | 5.20 | 0.79 | Endocytosis |
| NM_001040111 | Arap1 | 3.98 | 2.39 | 0.60 | Endocytosis |
| NM_001033375 | A230046K03Rik | 10.67 | 10.12 | 0.95 | Endocytosis |
| NM_010515 | Igf2r | 10.45 | 9.27 | 0.89 | Endocytosis |
| NM_001122733 | Kit | 2.58 | 1.13 | 0.44 | Endoc, Rap1 |
| NM_001167745 | Wasl | 0.51 | 0.33 | 0.65 | Endoc, Actin |
| NM_001286785 | Magi1 | 0.00 | 0.00 | 0.12 | Rap1 |
| NM_001167983 | Sipa1l1 | 4.58 | 3.27 | 0.71 | Rap1 |
| NM_001162425 | Efnal | 0.00 | 0.00 | 1.32 | Rap1 |
| NM_178900 | Prkd2 | 1.19 | 0.69 | 0.58 | Rap1 |
| NM_001204165 | Rapgef4 | 0.00 | 0.00 | 0.02 | Rap1 |

| | | | | | |
|--------------|----------|-------|-------|------|-------------|
| NM 001171004 | Prkd3 | 4.85 | 5.81 | 1.20 | Rap1 |
| NM 001145834 | Ralgds | 3.25 | 3.41 | 1.05 | Rap1 |
| NM 175930 | Rapgef5 | 3.54 | 3.39 | 0.96 | Rap1 |
| NM 009624 | Adcy9 | 1.87 | 1.22 | 0.65 | Rap1 |
| NM 172803 | Dock4 | 0.73 | 1.00 | 1.38 | Rap1 |
| NM 001085450 | Ctnnd1 | 4.76 | 3.79 | 0.80 | Rap1 |
| NM 001163269 | Lpar5 | 5.87 | 2.14 | 0.36 | Rap1 |
| NM 001286784 | Magi1 | 3.84 | 1.87 | 0.49 | Rap1 |
| NM 001159354 | Magi3 | 6.04 | 5.26 | 0.87 | Rap1 |
| NM 175258 | Rapgef6 | 4.91 | 5.11 | 1.04 | Rap1 |
| NM 009623 | Adcy8 | 0.23 | 0.33 | 1.40 | Rap1 |
| NM 001145886 | Tiam1 | 5.91 | 1.88 | 0.32 | Rap1, Actin |
| NM 001082960 | Itgam | 1.41 | 0.59 | 0.42 | Rap1, Actin |
| NM 001130409 | Ptk2 | 1.83 | 3.65 | 1.99 | Actin |
| NM 001081307 | Ppp1r12b | 0.82 | 1.07 | 1.30 | Actin |
| NM 008396 | Itga2 | 8.54 | 7.42 | 0.87 | Actin |
| NM 001005608 | Itgb4 | 0.14 | 0.55 | 3.96 | Actin |
| NM 001033228 | Itga1 | 2.26 | 3.02 | 1.34 | Actin |
| NM 172493 | Diaph2 | 2.22 | 2.62 | 1.18 | Actin |
| NM 027892 | Ppp1r12a | 18.43 | 19.40 | 1.05 | Actin |
| NM 027144 | Arhgef12 | 11.42 | 11.48 | 1.00 | Actin |
| NM 198127 | Abi2 | 0.42 | 0.32 | 0.77 | Actin |
| NM 153423 | Wasf2 | 20.78 | 19.01 | 0.92 | Actin |
| NM 001113517 | Arhgef7 | 0.21 | 0.22 | 1.05 | Actin |
| NM 177710 | Ssh2 | 3.59 | 3.91 | 1.09 | Actin |
| NM 015759 | Fgd3 | 0.50 | 0.27 | 0.54 | Actin |

[†]1The FPKM (Fragments Per Kilobase Mega read) values. CTL, Control.

^{*}2Fold change is defined as the ratio of the signal of non-treated organoids to that of treated organoids.

Table S3. Primers for RT-PCR.

| Gene | Forward primer | Reverse primer |
|--------------|-----------------------|-----------------------|
| $\alpha 1$ | TCCCTTCGATGAGCAGAACT | ATGATGGACGCAATGACAAA |
| $\alpha 2$ | TCCCTCACTGCTTTCCTGCT | ACACCCATGGAAGAGTCTGG |
| $\alpha 3$ | CCTTCCACCTCACTGGTCAT | CAGAGCAGACAGGGACAACA |
| $\alpha 4$ | CCGGAGACTTATCGAATCCA | TGGTCTGACACTGGAAGCTG |
| $\alpha 5$ | AAAAGTGGGTTTCGTCCTGTG | ATGAGCCGAATTCATGGAG |
| $\alpha 6$ | AACCTGCACTCCGGTTTATG | TCCAGGTATCACACCGTCA |
| $\alpha 7$ | CCCGGAGTGAAAATGTTTCGT | TGAGACAAGGAATGAGC |
| $\alpha 9$ | GATCGATGGGCTCATCACCT | AACGATATGAGGACGCAAGG |
| $\alpha 10$ | CGTTCCACTCATCGGAAAGT | GGCAATGGAAGCTACGTGAT |
| $\beta 1$ | GGAGAGGAGAGGCAGGAAGT | GGAGAAGGCGACAAGGACCA |
| $\beta 2$ | TTTGACCAGCAGAACTGCAC | GTACTTTCCCACCAGCGGTA |
| $\beta 3$ | CGATGGAATCCCAGAACTA | CAGGCAGGGGATTATCAAAA |
| $\beta 4$ | TTCCATCGTCACCACTGTGT | TCACTCTCCAAATGCTGTGC |
| <i>Lgr5</i> | GTCTCCTACATCGCCTCTGC | TTCCAAAGGCGTAGTCTGCT |
| <i>Sox9</i> | AGGAAGCTGGCAGACCAGTA | CCCTCTCGTTTACAGATCAAC |
| <i>Ngn3</i> | CCCAGAGACACAACAACCT | TCTGAGTCAGTGCCAGATG |
| <i>Hnf1</i> | GAGAGGTGGCTCAGCAATTC | GCCGCAGACACTGTGACTAA |
| <i>Klf4</i> | CAGCTTCAGCTATCCGATCC | CGCCTCTTGCTTAATCTTGG |
| <i>GAPDH</i> | AACTTTGGCATTGTGGAAGG | ACACATTGGGGGTAGGAACA |

Table S4. Primers for quantitative RT-PCR.

| Gene | Forward primer | Reverse primer |
|--------------|-----------------------|--------------------------|
| <i>Lgr5</i> | AGCATACCCGTTTCTGGATG | AGGACCGTTTCTCAACATCG |
| <i>Sox9</i> | ATAAGTTCCCCGTGTGCATC | TGACGTGTGGCTTGTTCTTG |
| <i>Ngn3</i> | AAGCAGAAGTGGGTGACTGC | TCTTCGCTGTTTGCTGAGTG |
| <i>Hnf1</i> | AAAACCCCAGCAAGGAAGAG | GGTTGGCAAACCAGTTGTAG |
| <i>Klf4</i> | AGCATACCCGTTTCTGGATG | CTGTGTGTTTGCGGTAGTGCC |
| <i>Wnt5a</i> | CAAATAGGCAGCCGAGAGAC | CTCTAGCGTCCACGAACTCC |
| $\alpha 2$ | ATCGTGCGCTTTGGACTATC | TTAGCCAGACATTGGTGGTC |
| $\beta 4$ | TGCTGGCACTCACATTCTTC | AGTGGTGACGATGGAAAAGG |
| <i>GAPDH</i> | TGACGTGCCGCCTGGAGAAA | AGTGTAGCCCAAGATGCCCTTCAG |