

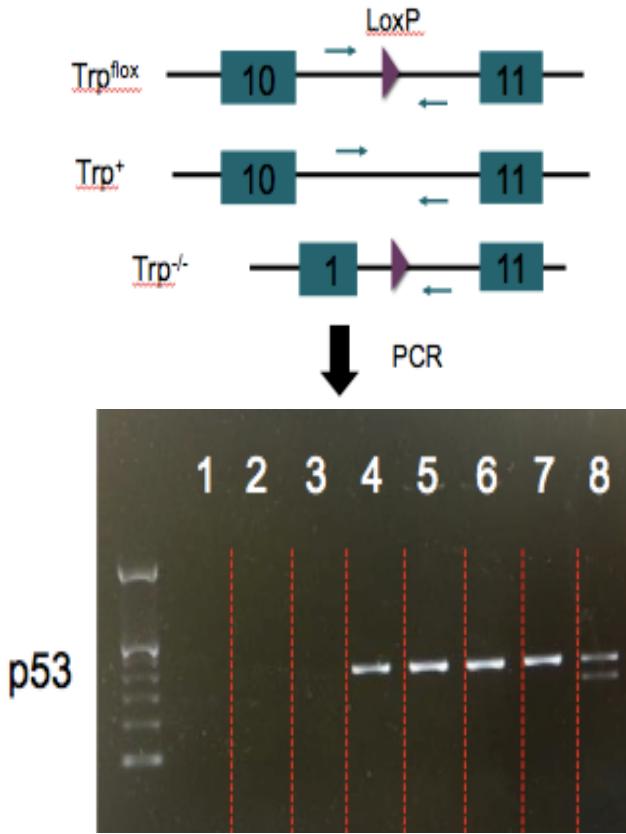
## **SUPPLEMENTARY INFORMATION**

### **Single-cell transcriptome analysis identifies distinct cell types and niche signaling in a primary gastric organoid model**

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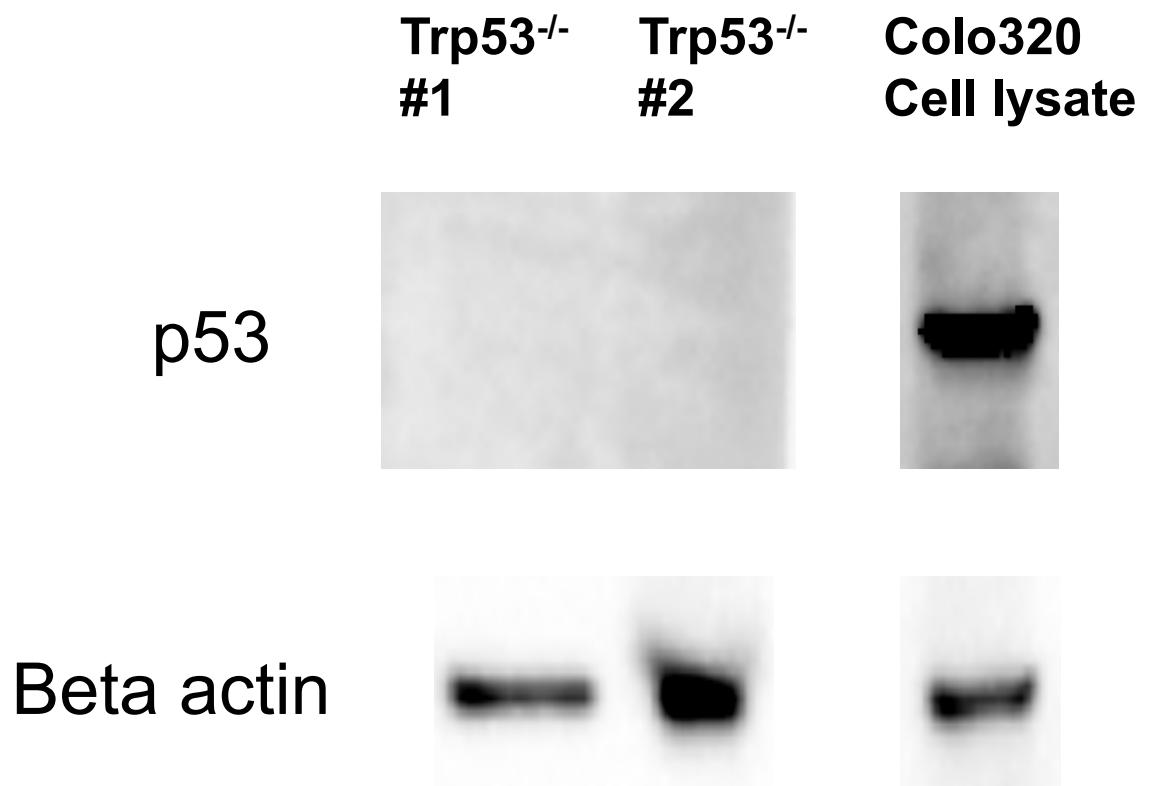
### **Organoids (after cre)**

1. *Trp53<sup>-/-</sup>*
2. *Trp53<sup>-/-</sup>*
3. *Trp53<sup>-/-</sup>*

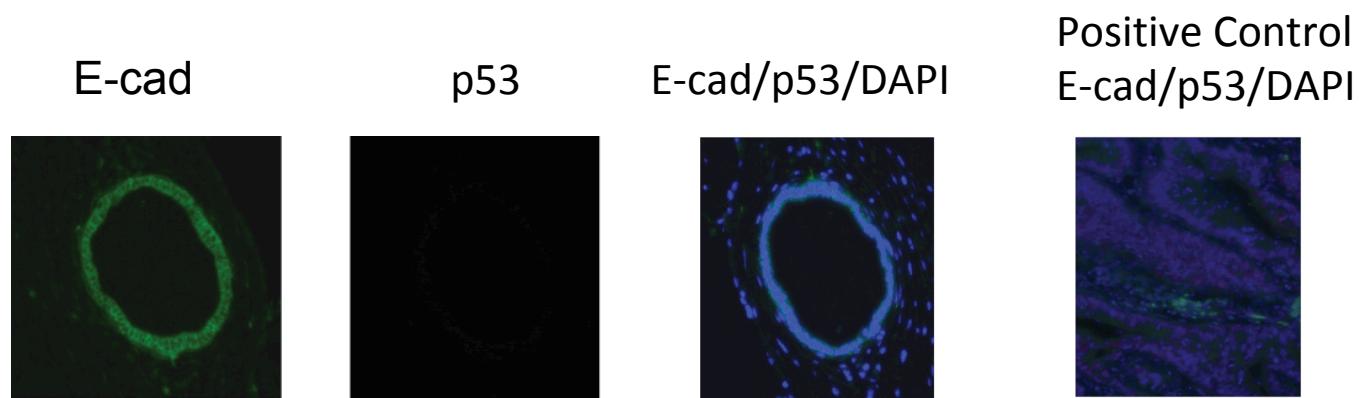
### **Mouse (before cre)**

4. *Trp53<sup>flox/flox</sup>*
5. *Trp53<sup>flox/flox</sup>*
6. *Trp53<sup>flox/flox</sup>*
7. *Trp53<sup>flox/flox</sup>*
8. *Trp53<sup>+/flox</sup>*

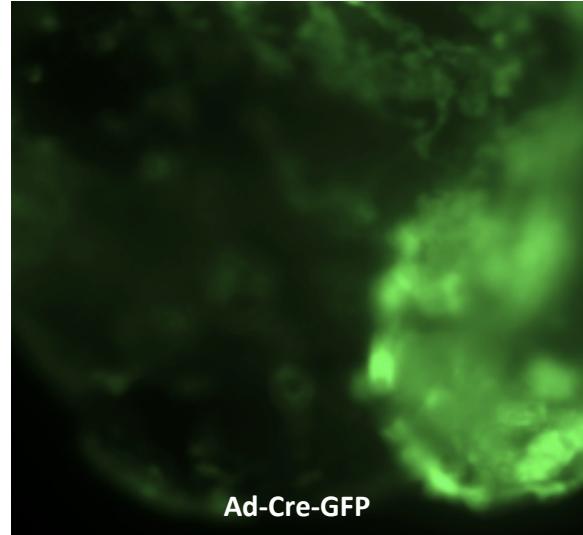
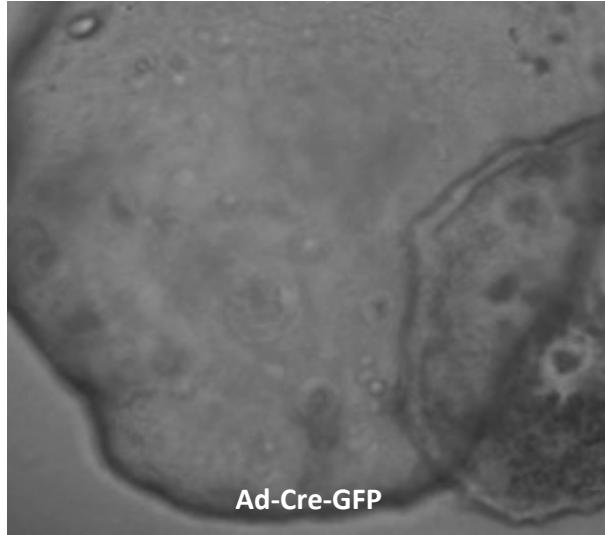
**Figure S1. Cre-mediated deletion of floxed *Trp53* is confirmed by genotyping.** The PCR scheme of genotyping is at the top and the PCR result is at the bottom. As expected, no products are generated from the *Trp53<sup>-/-</sup>* organoid samples (Well 1-3), one band is visible in the *Trp53<sup>flox/flox</sup>* mouse samples (Well 4-7), and two bands are visible from the *Trp53<sup>+/flox</sup>* mouse sample (Well 8). The PCR primers are blue arrows, and LoxP sites are purple arrowheads between exons. The PCR products run on 2% agarose gel.



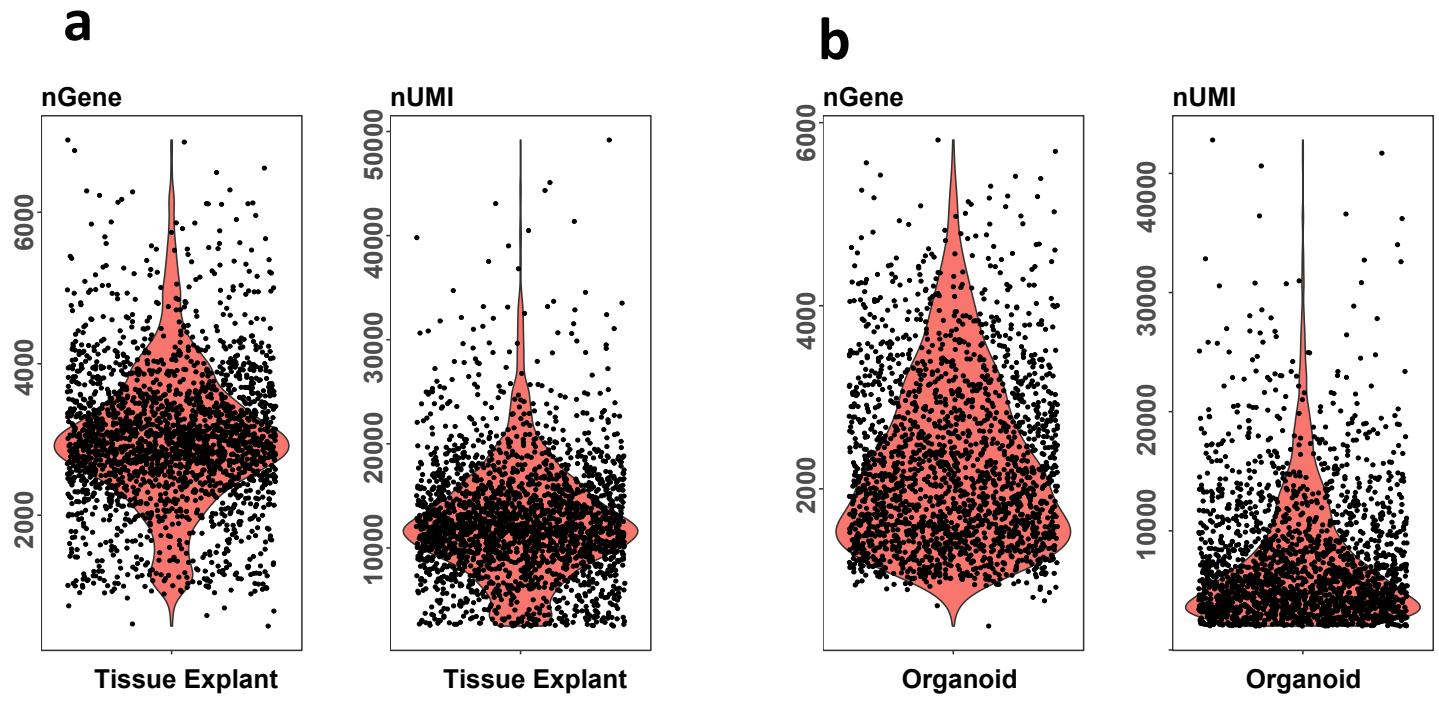
**Figure S2. Loss of p53 is confirmed by western blotting.** No p53 protein is detected in the *Trp53<sup>-/-</sup>* organoids cultured for two months (*Trp53<sup>-/-</sup>* #1) and three months (*Trp53<sup>-/-</sup>* #2). The whole cell lysate from Colo320 is used as the positive control for p53 protein. Beta actin is used as the loading control.



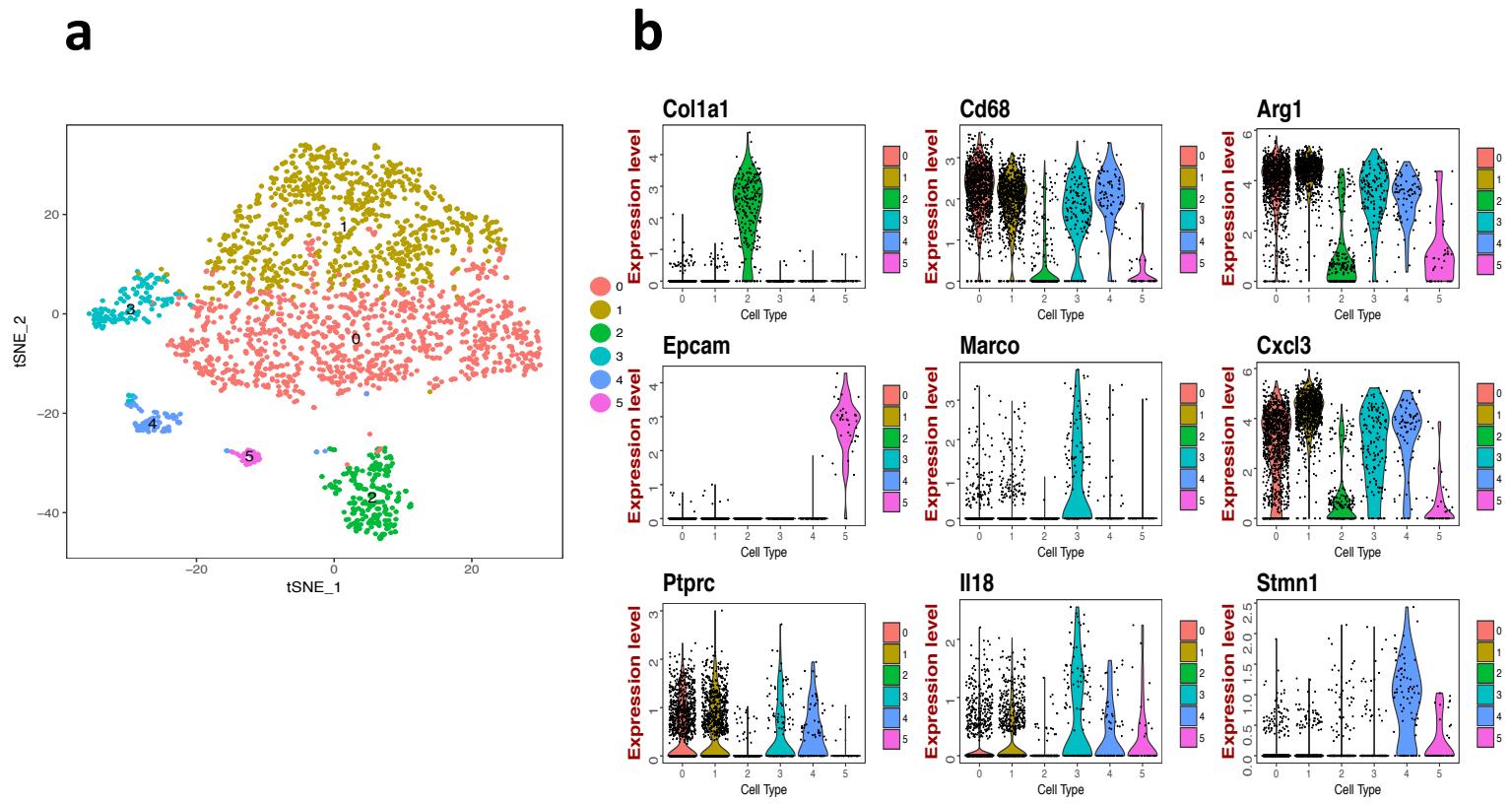
**Figure S3. Loss of p53 expression in the *Trp53*-/- organoids using immunofluorescence (IF).** E-cadherin (E-cad) is expressed in epithelial cells (green signal), and no expression of p53 was detected (red signal). Nuclei are counterstained with DAPI (blue signal). A colon tumor tissue section with p53 expression is used as a positive control.



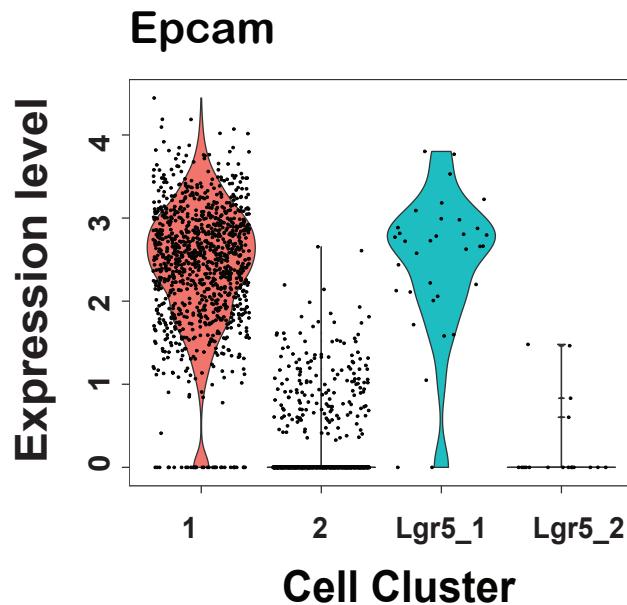
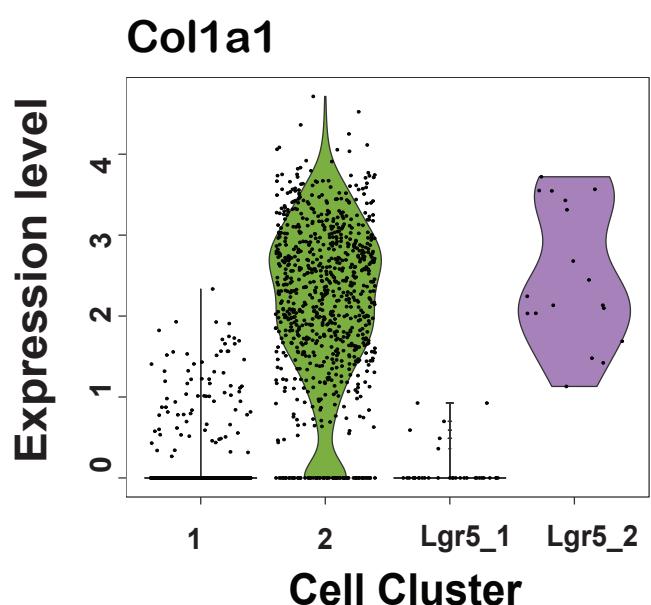
**Figure S4. Gastric tissue explants infected with Ad-Cre-GFP.** The cystic structures of tissue explants in collagen are examined under bright light (left panel) and fluorescent light (right panel) at day 3 post Ad-Cre-GFP infection.



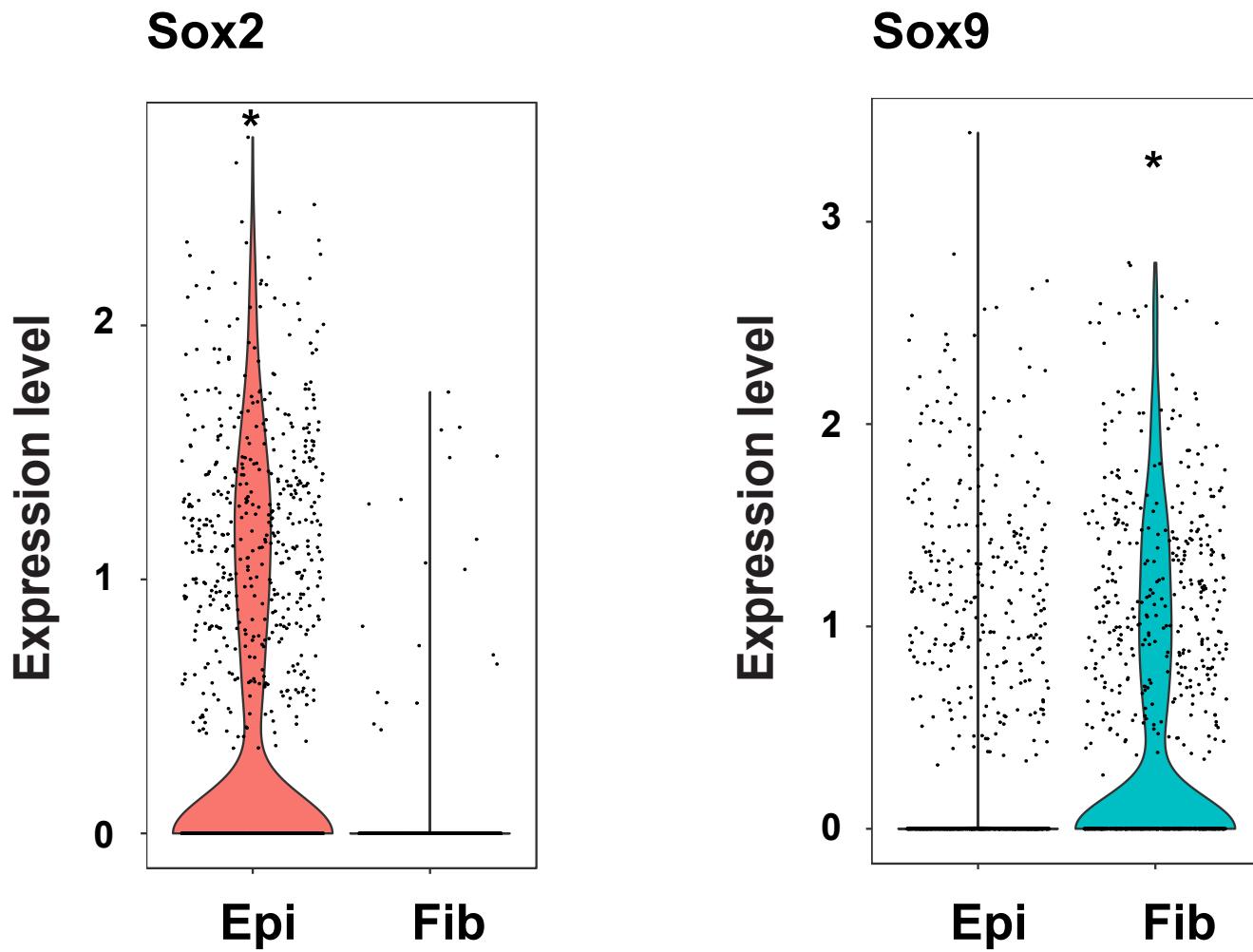
**Figure S5. The distribution of number of genes and UMI counts in tissue explants and organoids.** Violin plots display the distribution of number of genes (nGene) and number of unique mRNA transcript (nUMI) in single cells from tissue explant (a), Organoid (b). Each dot represents a single cell.



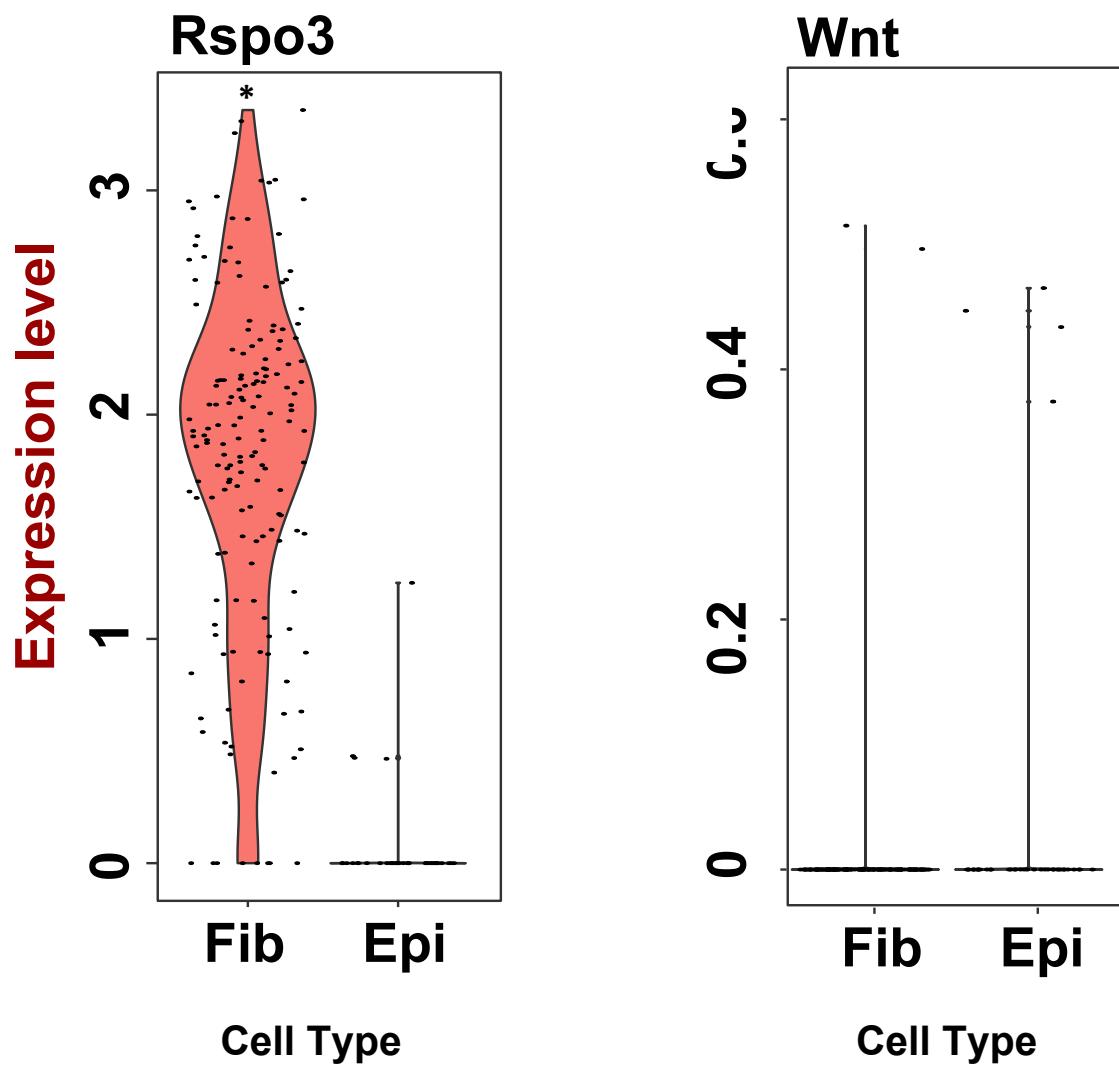
**Figure S6. An independent scRNA library confirmed cell types in ALI cultured tissue explants.** (a) A tSNE projection of 1961 cells from tissue explants. Cells are grouped into six clusters (0, 1, 2, 3, 4, 5) based on transcriptome profiles and are colored accordingly. The cell type assignment of each cluster is based on the gene expression analysis. (b) The expression of cell type specific genes in each cluster are displayed on violin plots. Specifically, fibroblast specific gene *Col1a1* in Cluster 2, epithelial specific gene *Epcam* in Cluster 5, and macrophage marker *Cd68* in Cluster 0, 1, 3, 4. Again, we observed three distinct subtypes of macrophage: Cluster 0 & 1 – *Arg1* (M2 like macrophage), Cluster 3 – Macro & *Il18* (M1 like macrophage), and Cluster 4 – *Stmn1* (proliferating macrophage). Every dot represents an individual cell in violin plots, and the gene expression level is the natural log of the normalized UMI counts.

**a****b**

**Figure S7.** The expression of epithelial and fibroblast lineage markers, *Col1a1* (a) and *Epcam* (b), in Lgr5+ cells. Cluster 1 – Epithelial, Cluster 2– Fibroblast. Lgr5\_1 is Lgr5+ cells in epithelial cell cluster and Lgr5\_2 is Lgr5+ cells in fibroblast cell cluster. The expression level of violin plot is the natural log of the normalized UMI counts.

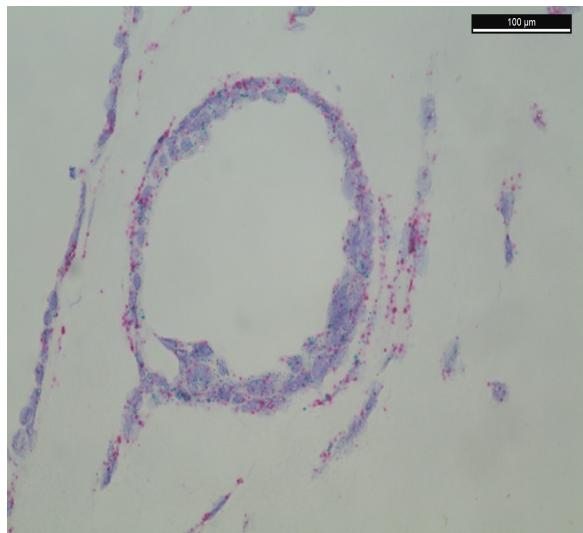


**Figure S8. The expression of lineage specific transcriptional factors, Sox2 and Sox9 in epithelial and fibroblast cell types.** The expression level on Y-axis is the natural log of the normalized UMI counts. \* Bonferroni adjusted  $p < 0.001$ . Epi - Epithelial, Fib – Fibroblast.

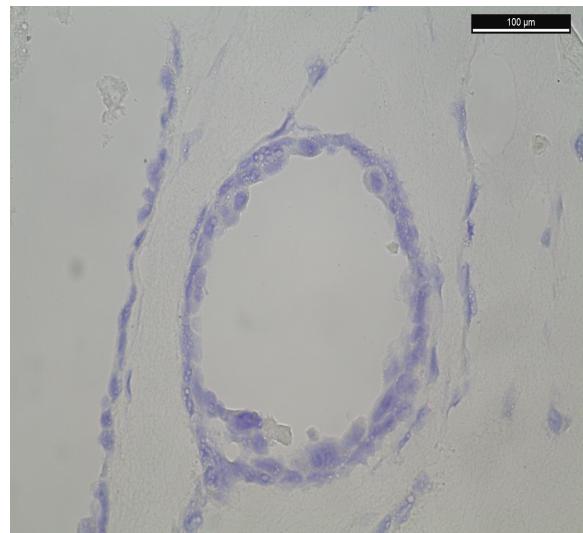


**Figure S9. Rspo3 and Wnt4 expression in tissue explants .** The expression level on Y-axis is the natural log of the normalized UMI counts. Epi – Epithelial, Fib – Fibroblast. \* Bonferroni adjusted  $p < 0.001$

**Ppib – green      Polr2a - red**



**E. coli DapB - green**



**Figure S10. Evaluation of RNA ISH by targeting housekeeping genes and an E.coli gene.** Two mouse housekeeping genes Ppib (green) and Polr2a (red) are detected simultaneously in all organoid cells. Negative control E.coli dapB mRNA is undetectable.

Table S1: Top 50 genes enriched in each cluster identified by differential analysis in tissue explants.

| Cluster | gene      | p value     | fold change * |
|---------|-----------|-------------|---------------|
| 1       | Sparc     | 0           | 3.55          |
| 1       | Dcn       | 0           | 3.45          |
| 1       | Bgn       | 0           | 3.28          |
| 1       | Col1a1    | 1.618916818 | 3.04          |
| 1       | Serpinh1  | 1.07E-307   | 2.90          |
| 1       | Col3a1    | 1.82E-303   | 3.06          |
| 1       | Grem1     | 1.81E-285   | 2.70          |
| 1       | Igfbp7    | 3.12E-285   | 3.02          |
| 1       | Col1a2    | 9.07E-284   | 2.65          |
| 1       | Timp1     | 1.78E-281   | 3.03          |
| 1       | Rcn3      | 5.17E-281   | 2.42          |
| 1       | Mgp       | 1.03E-272   | 3.12          |
| 1       | Efemp2    | 9.63E-272   | 1.57          |
| 1       | Igf1      | 7.76E-265   | 2.63          |
| 1       | Loxl1     | 3.43E-243   | 1.87          |
| 1       | Mfap4     | 6.61E-243   | 2.59          |
| 1       | Serpding1 | 2.28E-240   | 2.43          |
| 1       | Tmem176b  | 1.38E-239   | 2.55          |
| 1       | Serpina3n | 4.93E-239   | 2.21          |
| 1       | Tmem176a  | 2.40E-235   | 2.42          |
| 1       | Pcolce    | 5.50E-234   | 2.23          |
| 1       | Wbp5      | 1.17E-231   | 1.55          |
| 1       | Selm      | 7.49E-227   | 1.91          |
| 1       | Map1lc3a  | 5.46E-225   | 1.34          |
| 1       | Rspo3     | 1.08E-222   | 2.04          |
| 1       | Sfrp1     | 1.12E-220   | 2.32          |
| 1       | Serpinf1  | 3.07E-216   | 2.20          |
| 1       | Prnp      | 7.38E-216   | 1.66          |
| 1       | Col5a2    | 1.45E-213   | 1.78          |
| 1       | Olfml3    | 2.41E-209   | 1.67          |
| 1       | Itm2a     | 1.17E-208   | 2.15          |
| 1       | Mylk      | 2.00E-207   | 1.85          |
| 1       | Nedd4     | 4.28E-206   | 1.73          |
| 1       | Mfap2     | 7.69E-205   | 1.73          |
| 1       | Oat       | 3.38E-204   | 1.18          |
| 1       | Mxra8     | 5.82E-204   | 1.39          |
| 1       | Fbln2     | 1.92E-202   | 2.08          |
| 1       | Serpine2  | 3.61E-202   | 2.42          |
| 1       | Lox       | 6.65E-194   | 1.59          |
| 1       | Col4a2    | 7.25E-191   | 1.45          |
| 1       | Sod3      | 6.77E-189   | 1.80          |

Table S1: Top 50 genes enriched in each cluster identified by differential analysis in tissue explants.

| <b>Cluster</b> | <b>gene</b> | <b>p value</b> | <b>fold change *</b> |
|----------------|-------------|----------------|----------------------|
| 1              | Myl9        | 1.75E-188      | 2.27                 |
| 1              | Plod2       | 8.07E-185      | 1.56                 |
| 1              | Wisp1       | 4.32E-184      | 1.34                 |
| 1              | Aebp1       | 5.57E-184      | 1.57                 |
| 1              | Gpx8        | 1.56E-183      | 1.50                 |
| 1              | Meg3        | 8.65E-179      | 2.44                 |
| 1              | Cxcl12      | 5.49E-178      | 2.12                 |
| 1              | C1s1        | 8.31E-178      | 1.28                 |
| 1              | Tpm1        | 9.19E-178      | 1.61                 |
| 2              | Clu         | 5.93E-195      | 3.76                 |
| 2              | Gsto1       | 1.05E-139      | 2.15                 |
| 2              | Krt14       | 4.50E-126      | 3.37                 |
| 2              | Wfdc2       | 9.97E-123      | 3.18                 |
| 2              | Spint2      | 1.53E-119      | 2.66                 |
| 2              | Sfn         | 1.62E-117      | 2.85                 |
| 2              | Krt7        | 5.32E-112      | 3.16                 |
| 2              | Cldn4       | 1.85E-107      | 2.86                 |
| 2              | Ly6a        | 5.14E-107      | 3.18                 |
| 2              | Nupr1       | 3.39E-97       | 2.49                 |
| 2              | Ltf         | 1.20E-96       | 2.73                 |
| 2              | Epcam       | 5.21E-91       | 2.67                 |
| 2              | Krt18       | 4.79E-88       | 2.73                 |
| 2              | Perp        | 1.27E-86       | 2.13                 |
| 2              | Gsta4       | 5.65E-85       | 2.33                 |
| 2              | Krt19       | 9.27E-82       | 2.81                 |
| 2              | Fxyd3       | 2.24E-81       | 2.15                 |
| 2              | Krt8        | 8.70E-80       | 2.60                 |
| 2              | S100a14     | 4.71E-78       | 2.28                 |
| 2              | Cldn7       | 1.13E-76       | 1.92                 |
| 2              | Tmc4        | 1.08E-73       | 1.30                 |
| 2              | Gpx2        | 1.83E-72       | 1.75                 |
| 2              | Krt17       | 4.85E-69       | 2.77                 |
| 2              | F11r        | 7.77E-65       | 1.23                 |
| 2              | 2200002D01  | 4.65E-62       | 1.78                 |
| 2              | Krtcap3     | 4.76E-62       | 1.05                 |
| 2              | Cystm1      | 7.38E-62       | 1.39                 |
| 2              | Urah        | 5.14E-61       | 1.19                 |
| 2              | Anxa8       | 3.75E-60       | 1.78                 |
| 2              | S100a16     | 8.13E-60       | 1.99                 |
| 2              | Psca        | 1.15E-59       | 2.07                 |
| 2              | Pdlm1       | 2.50E-59       | 1.55                 |

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| Cluster | gene      | p value   | fold change * |
|---------|-----------|-----------|---------------|
| 2       | Serpinb5  | 3.11E-59  | 0.93          |
| 2       | Dsp       | 9.46E-58  | 0.94          |
| 2       | Tnfrsf12a | 2.29E-57  | 1.71          |
| 2       | Lamc2     | 4.85E-57  | 1.47          |
| 2       | Tacstd2   | 7.79E-57  | 1.70          |
| 2       | Spint1    | 1.36E-56  | 1.12          |
| 2       | Rab25     | 1.46E-55  | 1.08          |
| 2       | Lad1      | 1.74E-55  | 1.05          |
| 2       | Tpm1      | 4.05E-55  | 1.77          |
| 2       | Ly6d      | 8.98E-55  | 2.30          |
| 2       | Serinc2   | 1.34E-54  | 1.24          |
| 2       | Fermt1    | 1.77E-54  | 1.11          |
| 2       | Crb3      | 4.81E-54  | 1.10          |
| 2       | Jup       | 6.93E-54  | 1.01          |
| 2       | Klf5      | 7.51E-54  | 1.26          |
| 2       | Sox11     | 1.60E-52  | 0.87          |
| 2       | Sdc1      | 1.69E-52  | 1.78          |
| 2       | Smim22    | 4.00E-52  | 0.90          |
| 3       | Ear2      | 8.57E-116 | 1.73          |
| 3       | Ltc4s     | 6.54E-96  | 1.32          |
| 3       | Mpc2      | 1.52E-89  | 0.98          |
| 3       | Wfdc21    | 1.72E-89  | 2.14          |
| 3       | Il18      | 4.95E-66  | 0.71          |
| 3       | Abcg1     | 4.95E-66  | 0.75          |
| 3       | Ramp1     | 6.75E-66  | 1.03          |
| 3       | Etfb      | 1.34E-56  | 0.70          |
| 3       | Unc119    | 1.39E-56  | 0.63          |
| 3       | Sept9     | 2.51E-51  | 0.56          |
| 3       | Axl       | 3.03E-49  | 0.77          |
| 3       | Chil3     | 2.36E-48  | 1.50          |
| 3       | Ucp2      | 5.33E-48  | 0.84          |
| 3       | Klhd4     | 3.93E-46  | 0.71          |
| 3       | Marco     | 7.68E-46  | 1.67          |
| 3       | Gngt2     | 3.62E-38  | 0.74          |
| 3       | Abcc5     | 7.85E-38  | 0.51          |
| 3       | Ear1      | 6.88E-37  | 0.52          |
| 3       | Sort1     | 6.93E-37  | 0.52          |
| 3       | Pmvk      | 2.53E-36  | 0.48          |
| 3       | Serpinb1a | 9.63E-36  | 0.79          |
| 3       | Gm1673    | 9.83E-36  | 0.79          |
| 3       | Msrb1     | 1.47E-35  | 0.66          |

Table S1: Top 50 genes enriched in each cluster identified by differential analysis in tissue explants.

| Cluster | gene        | p value     | fold change * |
|---------|-------------|-------------|---------------|
| 3       | Dgat1       | 2.23E-32    | 0.54          |
| 3       | Ly75        | 1.33E-31    | 0.41          |
| 3       | Ndufc1      | 1.48E-31    | 0.52          |
| 3       | Adipor2     | 2.00E-31    | 0.46          |
| 3       | Syk         | 3.57E-31    | 0.48          |
| 3       | Prkcd       | 1.86E-30    | 0.54          |
| 3       | Fcor        | 4.19E-30    | 0.55          |
| 3       | N4bp1       | 4.45E-30    | 0.41          |
| 3       | S100a1      | 1.16E-29    | 0.75          |
| 3       | Siglece     | 2.02E-29    | 0.43          |
| 3       | 2700094K13I | 2.97E-29    | 0.57          |
| 3       | Acp5        | 3.45E-29    | 1.03          |
| 3       | Iqsec1      | 3.58E-29    | 0.44          |
| 3       | Mgll        | 4.69E-29    | 0.76          |
| 3       | Hebp1       | 5.07E-29    | 0.56          |
| 3       | Ccnd2       | 4.14E-27    | 0.67          |
| 3       | Sirpa       | 2.51E-26    | 0.56          |
| 3       | Cd200r2     | 2.25E-25    | 0.44          |
| 3       | Olr1        | 1.40E-23    | 0.50          |
| 3       | F10         | 2.85E-22    | 0.74          |
| 3       | Serpine1    | 7.95E-22    | 0.83          |
| 3       | Car4        | 2.39E-20    | 1.02          |
| 3       | Tgm2        | 7.85E-18    | 0.49          |
| 3       | Lpl         | 8.26E-18    | 0.51          |
| 3       | Plet1       | 1.04E-16    | 0.82          |
| 3       | Atp6v0d2    | 1.50E-16    | 0.58          |
| 3       | Csf2rb      | 4.79E-13    | 0.44          |
| 4       | Fxyd5       | 0           | 0.85          |
| 4       | Lgals3      | 0           | 0.77          |
| 4       | Tyrobp      | 0           | 0.73          |
| 4       | Fcer1g      | 0           | 0.73          |
| 4       | Ctss        | 1.136350985 | 0.93          |
| 4       | Lilrb4a     | 1.854228368 | 1.13          |
| 4       | Srgn        | 3.56E-280   | 1.24          |
| 4       | H2-D1       | 7.74E-271   | 0.96          |
| 4       | Arg1        | 7.25E-262   | 1.17          |
| 4       | Capg        | 1.11E-256   | 0.63          |
| 4       | Fcgr3       | 1.25E-256   | 1.22          |
| 4       | Fcgr2b      | 1.49E-218   | 1.36          |
| 4       | Trf         | 4.00E-213   | 1.08          |
| 4       | Clec4d      | 3.93E-212   | 1.04          |

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|---------|---------|-----------|---------------|
| 4       | Ctsc    | 1.48E-207 | 0.93          |
| 4       | Cd53    | 9.60E-204 | 1.25          |
| 4       | Ccl3    | 2.33E-189 | 0.97          |
| 4       | Ctsa    | 7.79E-184 | 0.74          |
| 4       | Mmp12   | 4.33E-183 | 1.66          |
| 4       | Cd68    | 5.67E-183 | 0.91          |
| 4       | Lilr4b  | 1.48E-169 | 0.91          |
| 4       | Pf4     | 7.23E-166 | 1.46          |
| 4       | Lcp1    | 3.27E-163 | 0.75          |
| 4       | Pla2g7  | 7.88E-158 | 1.25          |
| 4       | Adam8   | 6.04E-155 | 1.10          |
| 4       | Mmp9    | 7.95E-154 | 1.41          |
| 4       | Grn     | 4.32E-151 | 0.60          |
| 4       | Hilpda  | 5.50E-147 | 0.86          |
| 4       | Bcl2a1b | 3.38E-137 | 0.80          |
| 4       | Sirpb1c | 3.55E-134 | 0.94          |
| 4       | Rac2    | 2.98E-133 | 0.67          |
| 4       | Ms4a6d  | 7.13E-131 | 0.97          |
| 4       | Ncf4    | 2.79E-129 | 0.79          |
| 4       | Card19  | 2.69E-128 | 0.83          |
| 4       | Itgam   | 4.27E-128 | 0.87          |
| 4       | Rgs1    | 1.22E-127 | 1.30          |
| 4       | Cd52    | 6.06E-126 | 0.73          |
| 4       | Emb     | 1.20E-125 | 0.93          |
| 4       | Mpeg1   | 9.86E-124 | 0.75          |
| 4       | Cfp     | 3.07E-123 | 0.92          |
| 4       | Ccl9    | 1.18E-120 | 0.75          |
| 4       | Trem2   | 1.24E-120 | 0.84          |
| 4       | Cxcl3   | 1.28E-117 | 1.22          |
| 4       | Msr1    | 7.50E-117 | 0.77          |
| 4       | Ccr1    | 1.42E-116 | 1.00          |
| 4       | Adgre1  | 1.39E-108 | 0.82          |
| 4       | Hmox1   | 6.06E-108 | 0.82          |
| 4       | Pid1    | 1.35E-107 | 1.01          |
| 4       | Mmp8    | 1.79E-107 | 1.44          |
| 4       | Itgb2   | 3.50E-107 | 0.71          |
| 5       | Tuba1b  | 2.15E-105 | 1.70          |
| 5       | Cdk1    | 1.53E-99  | 1.41          |
| 5       | Stmn1   | 5.02E-94  | 1.67          |
| 5       | Birc5   | 1.21E-81  | 1.59          |
| 5       | Top2a   | 7.80E-80  | 1.38          |

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| Cluster | gene        | p value  | fold change * |
|---------|-------------|----------|---------------|
| 5       | Cdca3       | 1.50E-77 | 1.35          |
| 5       | Tubb5       | 1.95E-75 | 1.46          |
| 5       | 2810417H13I | 1.01E-71 | 1.94          |
| 5       | Ube2c       | 6.37E-71 | 1.85          |
| 5       | Pmf1        | 6.03E-69 | 1.06          |
| 5       | Spc24       | 1.90E-67 | 1.13          |
| 5       | Cks1b       | 1.25E-66 | 1.28          |
| 5       | H2afv       | 2.00E-64 | 1.19          |
| 5       | Pttg1       | 1.18E-60 | 1.26          |
| 5       | Tk1         | 7.04E-59 | 1.08          |
| 5       | H2afz       | 2.87E-58 | 1.03          |
| 5       | Ccna2       | 4.17E-58 | 0.76          |
| 5       | Smc2        | 2.95E-57 | 1.12          |
| 5       | Cdca8       | 7.61E-57 | 1.03          |
| 5       | Ccnb1       | 3.56E-56 | 0.74          |
| 5       | Pbk         | 4.53E-56 | 0.75          |
| 5       | Mki67       | 9.38E-55 | 1.22          |
| 5       | Racgap1     | 3.57E-54 | 0.73          |
| 5       | Prc1        | 7.22E-53 | 0.67          |
| 5       | Hmgb2       | 1.60E-52 | 1.07          |
| 5       | Dut         | 3.65E-50 | 1.01          |
| 5       | Asf1b       | 1.02E-49 | 0.82          |
| 5       | Tyms        | 4.88E-49 | 1.05          |
| 5       | Rrm2        | 1.02E-48 | 0.89          |
| 5       | Cenpa       | 1.68E-48 | 1.14          |
| 5       | Smc4        | 2.47E-48 | 0.99          |
| 5       | Ccnb2       | 3.17E-48 | 0.93          |
| 5       | Spc25       | 3.33E-48 | 0.84          |
| 5       | Nusap1      | 5.33E-48 | 0.64          |
| 5       | Cenpf       | 1.54E-46 | 0.72          |
| 5       | Plk1        | 1.05E-44 | 0.45          |
| 5       | Hmmr        | 1.15E-44 | 0.56          |
| 5       | 2700094K13I | 2.28E-43 | 1.04          |
| 5       | Gmnn        | 8.46E-43 | 0.91          |
| 5       | Cenpm       | 3.04E-42 | 0.59          |
| 5       | Aurkb       | 3.45E-42 | 0.57          |
| 5       | Tacc3       | 1.55E-41 | 0.75          |
| 5       | Cenpe       | 2.80E-41 | 0.70          |
| 5       | Pcna        | 1.05E-39 | 0.86          |
| 5       | Hist1h1b    | 1.88E-39 | 0.54          |
| 5       | Tpx2        | 3.07E-39 | 0.69          |

Table S1: Top 50 genes enriched in each cluster identified by differential analysis in tissue explants.

| <b>Cluster</b> | <b>gene</b> | <b>p value</b> | <b>fold change *</b> |
|----------------|-------------|----------------|----------------------|
| 5              | Rad51       | 1.02E-38       | 0.51                 |
| 5              | Ranbp1      | 1.92E-38       | 0.90                 |
| 5              | Ube2t       | 1.94E-38       | 0.57                 |
| 5              | Rrm1        | 2.75E-36       | 0.73                 |

\* fold change for differentially expressed genes in each cluster is natural log transformed.

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value    | fold change * |
|---------|----------|------------|---------------|
| 1       | Sparc    | 0          | 2.823106377   |
| 1       | Col3a1   | 0          | 2.342912674   |
| 1       | Lgals1   | 0          | 2.337714967   |
| 1       | Bgn      | 0          | 2.310103026   |
| 1       | Igfbp7   | 0          | 2.276159903   |
| 1       | Col1a1   | 0          | 2.226378528   |
| 1       | Vim      | 0          | 2.095929529   |
| 1       | Serpinh1 | 0          | 2.079029089   |
| 1       | Serpinf1 | 0          | 1.966261368   |
| 1       | Rcn3     | 0          | 1.894706649   |
| 1       | Col1a2   | 0          | 1.882037613   |
| 1       | Aebp1    | 0          | 1.864543768   |
| 1       | B2m      | 0          | 1.856069855   |
| 1       | Selm     | 0          | 1.721362686   |
| 1       | Cst3     | 0          | 1.534867618   |
| 1       | Cald1    | 1.22972939 | 1.604614759   |
| 1       | Id3      | 2.76E-289  | 2.135119774   |
| 1       | Col5a2   | 1.55E-288  | 1.647767803   |
| 1       | Mxra8    | 1.07E-287  | 1.561020863   |
| 1       | Timp1    | 3.51E-283  | 2.023371424   |
| 1       | Pcolce   | 1.16E-266  | 1.592761513   |
| 1       | Cpxm1    | 2.16E-260  | 1.708798992   |
| 1       | Cd302    | 5.66E-256  | 1.252557056   |
| 1       | Mfap2    | 1.43E-254  | 1.324882514   |
| 1       | Fbln2    | 6.55E-247  | 1.523486824   |
| 1       | Dcn      | 1.58E-245  | 2.240119026   |
| 1       | Wbp5     | 1.49E-241  | 1.374587992   |
| 1       | Timp2    | 5.43E-237  | 1.235175164   |
| 1       | Tceal8   | 7.41E-234  | 1.326985066   |
| 1       | Efemp2   | 1.54E-232  | 1.314160723   |
| 1       | Ctsz     | 4.90E-231  | 1.19237118    |
| 1       | Ctla2a   | 2.24E-228  | 2.452867473   |
| 1       | Nsg1     | 2.95E-227  | 1.345003951   |
| 1       | Loxl1    | 7.51E-223  | 1.157656427   |
| 1       | Eva1b    | 1.59E-220  | 1.204036317   |
| 1       | Cxcl12   | 3.32E-220  | 1.79140212    |
| 1       | Igfbp4   | 1.44E-217  | 1.563361818   |
| 1       | Tmsb10   | 2.00E-216  | 1.17113605    |
| 1       | Sfrp1    | 1.65E-211  | 2.068755725   |
| 1       | Cdkn2a   | 1.16E-208  | 1.178921582   |
| 1       | Dynlrb1  | 1.13E-206  | 0.918181808   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene       | p value   | fold change * |
|---------|------------|-----------|---------------|
| 1       | Tagln      | 1.48E-206 | 1.773083318   |
| 1       | Myl9       | 3.56E-205 | 1.735182426   |
| 1       | Slc25a4    | 8.30E-203 | 0.781003512   |
| 1       | Cmtm3      | 3.44E-189 | 1.036968519   |
| 1       | Fstl1      | 1.34E-188 | 1.134151368   |
| 1       | Ccdc80     | 3.22E-188 | 1.487701293   |
| 1       | Emp3       | 3.87E-185 | 1.160380429   |
| 1       | Klf2       | 2.92E-184 | 1.720982709   |
| 1       | Tuba1a     | 9.83E-182 | 1.10258012    |
| 1       | Nradd      | 5.19E-177 | 0.829975834   |
| 1       | Mfap5      | 2.43E-173 | 1.570080775   |
| 1       | Fkbp7      | 6.41E-173 | 0.920517298   |
| 1       | Olfml3     | 8.50E-169 | 1.034695728   |
| 1       | Gpx7       | 3.07E-168 | 0.871665446   |
| 1       | Copz2      | 1.72E-165 | 0.950478243   |
| 1       | Grem1      | 1.72E-164 | 1.243865757   |
| 1       | Serpingle1 | 1.75E-164 | 1.453911548   |
| 1       | Lrp1       | 2.26E-164 | 1.058258171   |
| 1       | Gng11      | 3.51E-162 | 1.040215385   |
| 1       | Tubb6      | 3.83E-162 | 0.922207065   |
| 1       | Prrx1      | 3.71E-161 | 0.912486978   |
| 1       | Tpm1       | 1.37E-158 | 1.064227929   |
| 1       | Wisp1      | 5.58E-158 | 0.942127292   |
| 1       | Plat       | 1.21E-157 | 0.992409064   |
| 1       | Rcn1       | 2.26E-157 | 0.92348993    |
| 1       | Mfap4      | 1.22E-156 | 1.434147028   |
| 1       | Rhoc       | 2.56E-156 | 0.944064681   |
| 1       | Itm2a      | 4.50E-156 | 1.364623765   |
| 1       | Maged2     | 1.13E-155 | 0.937703177   |
| 1       | Pdlim2     | 4.13E-155 | 1.091061787   |
| 1       | Ctsl       | 7.94E-155 | 0.85476355    |
| 1       | Ctsk       | 2.27E-154 | 0.950439464   |
| 1       | Cryab      | 1.37E-153 | 1.195907564   |
| 1       | Tspan4     | 2.70E-151 | 0.991741107   |
| 1       | Rbp1       | 1.34E-149 | 1.557940113   |
| 1       | Csf1       | 1.62E-149 | 1.024696752   |
| 1       | Fbln1      | 3.87E-148 | 1.113955084   |
| 1       | Lhfp       | 6.87E-148 | 0.882464363   |
| 1       | Nnmt       | 7.65E-148 | 0.792178731   |
| 1       | Col12a1    | 9.96E-147 | 1.057037914   |
| 1       | Fcgtr      | 5.56E-146 | 0.878838571   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value   | fold change * |
|---------|----------|-----------|---------------|
| 1       | Rrbp1    | 5.63E-145 | 0.898576516   |
| 1       | Lox      | 4.21E-144 | 0.939329828   |
| 1       | Fhl2     | 4.05E-142 | 1.092939978   |
| 1       | Colec12  | 6.75E-142 | 0.715635669   |
| 1       | Plac8    | 1.37E-135 | 1.380802556   |
| 1       | Smmim3   | 6.18E-134 | 0.879690061   |
| 1       | Ccl2     | 2.14E-133 | 2.095040473   |
| 1       | Tpm2     | 5.98E-133 | 1.0556755     |
| 1       | Col6a1   | 7.88E-133 | 0.75087847    |
| 1       | Ctsb     | 7.34E-132 | 0.778124065   |
| 1       | Pdgfrb   | 7.70E-131 | 0.706540967   |
| 1       | Calu     | 1.49E-130 | 0.872245784   |
| 1       | Prkcdbp  | 1.72E-130 | 0.827357452   |
| 1       | Col5a1   | 4.08E-130 | 0.780999344   |
| 1       | Bst2     | 5.07E-130 | 1.070186434   |
| 1       | Acta2    | 1.54E-129 | 1.979004936   |
| 1       | Fkbp10   | 1.57E-129 | 0.683817728   |
| 1       | Ccl7     | 3.39E-129 | 1.818360978   |
| 1       | S100a1   | 1.48E-128 | 0.816236623   |
| 1       | Fkbp1a   | 3.28E-128 | 0.73114375    |
| 1       | Nbl1     | 4.25E-128 | 1.039864437   |
| 1       | Postn    | 2.00E-127 | 1.162605445   |
| 1       | H13      | 2.65E-127 | 0.830680073   |
| 1       | Rasl11a  | 1.04E-126 | 1.354354938   |
| 1       | Scarf2   | 1.07E-126 | 0.761975342   |
| 1       | Il11ra1  | 2.10E-126 | 0.797532994   |
| 1       | Timp3    | 4.24E-126 | 1.395347961   |
| 1       | Mxra7    | 7.17E-126 | 0.697404852   |
| 1       | Sdc2     | 1.02E-125 | 1.012867782   |
| 1       | Map1lc3a | 1.27E-125 | 0.765807669   |
| 1       | Lbh      | 6.83E-125 | 0.997821591   |
| 1       | Hand2    | 7.45E-125 | 0.803650494   |
| 1       | Figf     | 2.46E-124 | 1.479581895   |
| 1       | Cdh11    | 3.32E-124 | 0.703610037   |
| 1       | Itm2c    | 9.18E-124 | 0.807540855   |
| 1       | Sna1     | 4.93E-123 | 0.779286191   |
| 1       | Lpl      | 6.37E-123 | 1.286473819   |
| 1       | Ppib     | 1.44E-120 | 0.666415348   |
| 1       | Fgfr1    | 2.51E-120 | 0.742234439   |
| 1       | Kdelr3   | 4.37E-118 | 0.735034963   |
| 1       | Hsd11b1  | 8.46E-118 | 1.240204292   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value   | fold change * |
|---------|----------|-----------|---------------|
| 1       | Lix1l    | 4.38E-117 | 0.573224634   |
| 1       | Cnn2     | 1.98E-116 | 0.923464681   |
| 1       | Thy1     | 2.15E-115 | 1.272121078   |
| 1       | Pdpn     | 2.94E-114 | 0.840879948   |
| 1       | Hmox1    | 6.52E-114 | 1.194214954   |
| 1       | Igf1     | 8.94E-113 | 0.847002882   |
| 1       | Rspo3    | 1.15E-112 | 0.838615215   |
| 1       | Emilin1  | 1.17E-112 | 0.586386903   |
| 1       | Plod2    | 1.62E-112 | 0.741306546   |
| 1       | Ndn      | 8.51E-112 | 0.711366458   |
| 1       | Cebpb    | 1.07E-111 | 0.884446631   |
| 1       | Meg3     | 5.28E-111 | 1.997932511   |
| 1       | Ier3     | 7.36E-111 | 1.113974847   |
| 1       | Saa3     | 1.97E-110 | 2.902800309   |
| 1       | Tfpi     | 6.21E-110 | 0.564212392   |
| 1       | Tceb2    | 4.34E-108 | 0.550699874   |
| 1       | Tspan3   | 7.04E-108 | 0.744610822   |
| 1       | Gpx8     | 1.48E-106 | 0.753752613   |
| 1       | Serpine1 | 4.23E-106 | 1.034815079   |
| 1       | C1s1     | 6.53E-106 | 0.706323163   |
| 1       | Fkbp11   | 1.66E-105 | 0.733025609   |
| 1       | Bicc1    | 3.17E-105 | 0.626308162   |
| 1       | Islr     | 3.55E-105 | 0.584305163   |
| 1       | Tmed3    | 5.98E-104 | 0.727785105   |
| 1       | Maged1   | 1.04E-103 | 0.77721257    |
| 1       | Hexa     | 5.80E-103 | 0.816447334   |
| 1       | 7-Sep    | 4.52E-102 | 0.778605551   |
| 1       | Nr2f1    | 4.73E-102 | 0.641469151   |
| 1       | Ptgis    | 1.06E-100 | 0.628954955   |
| 1       | Fbn1     | 1.59E-100 | 0.662401291   |
| 1       | Snhg18   | 1.10E-99  | 0.729255963   |
| 1       | Dpysl3   | 1.46E-99  | 0.748317274   |
| 1       | Calr     | 3.50E-99  | 0.667997793   |
| 1       | Fxyd6    | 6.20E-99  | 1.065114166   |
| 1       | Gas1     | 1.08E-98  | 0.765901494   |
| 1       | Vcam1    | 7.37E-98  | 0.759192812   |
| 1       | Qpct     | 7.73E-98  | 0.652961692   |
| 1       | Fermt2   | 2.04E-97  | 0.660854086   |
| 1       | Tmem50a  | 2.95E-97  | 0.656956334   |
| 1       | Rcn2     | 6.69E-97  | 0.690610984   |
| 1       | Sec61b   | 4.66E-96  | 0.620948071   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 1       | Txndc5   | 8.10E-96 | 0.722729819   |
| 1       | Arxes2   | 9.10E-96 | 0.714804882   |
| 1       | Tgfb1    | 1.05E-95 | 0.850344407   |
| 1       | Ppic     | 1.32E-94 | 0.756223774   |
| 1       | Pde1a    | 1.87E-94 | 0.626470769   |
| 1       | Fln      | 3.44E-94 | 0.548087728   |
| 1       | Tmem119  | 6.27E-94 | 0.533034014   |
| 1       | Creb3l1  | 9.00E-94 | 0.477156553   |
| 1       | C1ra     | 1.95E-92 | 0.681042366   |
| 1       | Thbs1    | 2.06E-92 | 0.912104528   |
| 1       | Ngfrap1  | 2.68E-92 | 0.770905438   |
| 1       | Smim1    | 3.91E-92 | 0.583984718   |
| 1       | Ifi27    | 4.98E-92 | 0.709394371   |
| 1       | Flot1    | 5.35E-92 | 0.710079946   |
| 1       | Sdpr     | 1.15E-91 | 0.623141464   |
| 1       | Prdx4    | 4.66E-91 | 0.73096041    |
| 1       | Tnc      | 7.76E-91 | 0.951001424   |
| 1       | Thbd     | 1.82E-90 | 0.73723708    |
| 1       | Mdk      | 1.15E-89 | 0.961475631   |
| 1       | Tpm4     | 2.90E-89 | 0.755938973   |
| 1       | Tm4sf1   | 7.82E-88 | 0.646531627   |
| 1       | Nid1     | 8.49E-88 | 0.496880531   |
| 1       | Lgi2     | 2.59E-87 | 0.6823409     |
| 1       | Mmp23    | 3.46E-87 | 0.593120946   |
| 1       | Tmem45a  | 3.54E-87 | 0.490062565   |
| 1       | Arpc1b   | 5.68E-87 | 0.563994476   |
| 1       | Glipr2   | 8.49E-87 | 0.521599186   |
| 1       | Ak1      | 1.15E-86 | 0.493778808   |
| 1       | Hsp90b1  | 1.82E-86 | 0.670993569   |
| 1       | Has2     | 4.06E-86 | 0.635016133   |
| 1       | Adamts2  | 7.16E-86 | 0.554120009   |
| 1       | Eif4ebp1 | 9.33E-86 | 0.740707242   |
| 1       | Il6st    | 1.22E-85 | 0.739351978   |
| 1       | Fgf7     | 1.24E-85 | 0.608154375   |
| 1       | Renbp    | 3.08E-85 | 0.489196079   |
| 1       | Spp1     | 6.19E-85 | 1.681318203   |
| 1       | Loxl2    | 8.48E-85 | 0.500665477   |
| 1       | Osmr     | 1.50E-84 | 0.514196826   |
| 1       | Gdpd2    | 1.58E-84 | 0.72820607    |
| 1       | Pmp22    | 1.32E-83 | 0.682424745   |
| 1       | Pdgfra   | 3.58E-83 | 0.534292242   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 1       | Mmp19   | 4.22E-83 | 0.570409406   |
| 1       | Oaf     | 3.48E-82 | 0.56488903    |
| 1       | Lsp1    | 3.75E-82 | 0.515514781   |
| 1       | Apbb1ip | 4.52E-81 | 0.449880286   |
| 1       | Tenm3   | 1.69E-80 | 0.458136846   |
| 1       | Mmp3    | 3.09E-80 | 1.829315927   |
| 1       | Nrp1    | 7.84E-80 | 0.568426528   |
| 1       | Col4a1  | 8.09E-80 | 0.568645188   |
| 1       | Gadd45b | 1.04E-79 | 0.756358788   |
| 1       | Msn     | 9.50E-79 | 0.576553748   |
| 1       | Arxes1  | 1.13E-78 | 0.541659332   |
| 1       | Jam3    | 4.05E-78 | 0.463255798   |
| 1       | Rgs16   | 4.10E-77 | 0.619097933   |
| 1       | Mageh1  | 4.64E-77 | 0.446099501   |
| 1       | Tshz2   | 9.78E-77 | 0.822701755   |
| 1       | Plxdc2  | 3.45E-76 | 0.557799471   |
| 1       | Thbs2   | 1.98E-75 | 0.570922954   |
| 1       | Gem     | 4.84E-75 | 0.619670643   |
| 1       | Itgb1   | 1.03E-74 | 0.641521882   |
| 1       | Itga5   | 1.18E-74 | 0.521488485   |
| 1       | Npc2    | 1.19E-74 | 0.59094458    |
| 1       | Cpq     | 1.84E-74 | 0.413754296   |
| 1       | Lmcld1  | 2.16E-74 | 0.798741865   |
| 1       | P3h1    | 2.31E-74 | 0.401503028   |
| 1       | Plpp3   | 2.66E-74 | 0.578771718   |
| 1       | Nrn1    | 2.87E-74 | 0.577138252   |
| 1       | Lamp1   | 1.18E-73 | 0.539709729   |
| 1       | Grn     | 2.10E-73 | 0.6525983     |
| 1       | Ddr2    | 4.11E-73 | 0.440810252   |
| 1       | Gaa     | 6.93E-73 | 0.640001374   |
| 1       | Prdx5   | 7.11E-73 | 0.604093205   |
| 1       | Gadd45g | 1.86E-72 | 0.870634748   |
| 1       | Bdnf    | 2.00E-72 | 0.565930053   |
| 1       | Stear1  | 2.08E-72 | 0.627933401   |
| 1       | Gsn     | 2.43E-72 | 0.631978245   |
| 1       | Aspn    | 2.79E-72 | 0.574535082   |
| 1       | Clmp    | 1.70E-71 | 0.453543011   |
| 1       | Sod3    | 1.86E-71 | 0.559632981   |
| 1       | Mmp2    | 4.61E-71 | 0.532742095   |
| 1       | Ppp1r18 | 1.21E-70 | 0.424872215   |
| 1       | P3h3    | 1.30E-70 | 0.443591914   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 1       | Anxa6         | 2.21E-70 | 0.593251954   |
| 1       | Cfh           | 2.36E-70 | 0.455347268   |
| 1       | Rab31         | 2.92E-70 | 0.441842838   |
| 1       | Serpina3g     | 1.39E-69 | 0.538681193   |
| 1       | H6pd          | 2.06E-69 | 0.467681967   |
| 1       | Slc7a2        | 2.11E-69 | 0.578691321   |
| 1       | Sdf4          | 2.48E-69 | 0.54992905    |
| 1       | Slit3         | 3.14E-69 | 0.466003059   |
| 1       | Pde10a        | 1.10E-68 | 0.472493824   |
| 1       | Egr1          | 6.25E-68 | 0.64385119    |
| 1       | Lamp2         | 8.77E-68 | 0.606260581   |
| 1       | Phldb2        | 1.23E-67 | 0.482702784   |
| 1       | Vmp1          | 1.47E-67 | 0.583534449   |
| 1       | Barx1         | 4.96E-67 | 0.464162775   |
| 1       | Srp2          | 8.52E-67 | 0.514211709   |
| 1       | Tcea3         | 9.29E-67 | 0.470899516   |
| 1       | Cyba          | 1.95E-66 | 0.489606336   |
| 1       | Ikbip         | 5.60E-66 | 0.460135904   |
| 1       | 2210013O21Rik | 5.78E-66 | 0.553199899   |
| 1       | Slc16a2       | 6.37E-66 | 0.428421821   |
| 1       | Nell2         | 6.60E-66 | 0.546541126   |
| 1       | Ndufa2        | 1.23E-65 | 0.469009706   |
| 1       | Isl1          | 3.80E-65 | 0.4300693     |
| 1       | Fkbp9         | 4.08E-65 | 0.530876475   |
| 1       | Man2a1        | 5.93E-65 | 0.484314333   |
| 1       | Ltbp2         | 7.64E-65 | 0.487518002   |
| 1       | Axl           | 9.35E-65 | 0.507397159   |
| 1       | Hoxa5         | 1.70E-64 | 0.448518706   |
| 1       | Actg2         | 7.48E-64 | 0.887611195   |
| 1       | Crtap         | 1.12E-63 | 0.454546384   |
| 1       | Pdlim4        | 4.15E-63 | 0.462370909   |
| 1       | Slc43a3       | 1.74E-62 | 0.445430387   |
| 1       | Clta          | 1.78E-62 | 0.437694755   |
| 1       | Mmp14         | 2.04E-62 | 0.615452132   |
| 1       | Col4a2        | 2.55E-62 | 0.46554643    |
| 1       | Capzb         | 2.63E-62 | 0.497527753   |
| 1       | Myl6          | 7.72E-62 | 0.536573942   |
| 1       | Pros1         | 9.05E-62 | 0.454377125   |
| 1       | Ptx3          | 9.89E-62 | 0.881320301   |
| 1       | Inhba         | 1.46E-61 | 0.799514004   |
| 1       | Fn1           | 1.59E-61 | 0.662384359   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 1       | Flna     | 1.71E-61 | 0.619046561   |
| 1       | Sgce     | 3.13E-61 | 0.487731343   |
| 1       | Mgp      | 3.92E-61 | 1.200253147   |
| 1       | Svbp     | 1.18E-60 | 0.523627184   |
| 1       | Bex1     | 2.75E-60 | 0.851318316   |
| 1       | Cox7a2   | 1.37E-59 | 0.435678093   |
| 1       | Gpm6b    | 1.82E-59 | 0.624572235   |
| 1       | Mtch1    | 1.85E-59 | 0.505272208   |
| 1       | Bnip2    | 3.79E-59 | 0.499938171   |
| 1       | Ufc1     | 4.06E-59 | 0.53048799    |
| 1       | Slco3a1  | 5.48E-59 | 0.450373289   |
| 1       | Serf2    | 5.56E-59 | 0.522102729   |
| 1       | Isg15    | 1.76E-58 | 0.792556705   |
| 1       | B4galt5  | 1.80E-58 | 0.441856758   |
| 1       | Lpar1    | 2.42E-58 | 0.421880496   |
| 1       | Pea15a   | 3.03E-58 | 0.480595364   |
| 1       | Lman1    | 3.39E-58 | 0.557908794   |
| 1       | Ugdh     | 4.14E-58 | 0.736988087   |
| 1       | Vcan     | 5.28E-58 | 0.435288081   |
| 1       | Lxn      | 6.01E-58 | 0.662429103   |
| 1       | Angptl2  | 6.59E-58 | 0.421360993   |
| 1       | Hacd1    | 2.13E-57 | 0.522863971   |
| 1       | Tnfrsf1a | 2.33E-57 | 0.490796003   |
| 1       | Akr1b8   | 3.55E-57 | 0.475960504   |
| 1       | Creg1    | 4.87E-57 | 0.529594363   |
| 1       | Grina    | 1.17E-56 | 0.546614982   |
| 1       | Rab34    | 1.43E-56 | 0.527521446   |
| 1       | Nedd4    | 1.96E-56 | 0.475437638   |
| 1       | Timm8b   | 3.14E-56 | 0.506060146   |
| 1       | Ddah2    | 4.47E-56 | 0.532414476   |
| 1       | Derl1    | 5.62E-56 | 0.529296125   |
| 1       | Rrad     | 1.16E-55 | 0.772493983   |
| 1       | Plpp1    | 1.73E-55 | 0.44778835    |
| 1       | Atp6v0b  | 1.81E-55 | 0.454193847   |
| 1       | Srp14    | 2.63E-55 | 0.444211689   |
| 1       | Kdelr2   | 2.79E-55 | 0.510564801   |
| 1       | Vasn     | 5.00E-55 | 0.432230075   |
| 1       | Scpep1   | 6.48E-55 | 0.551470497   |
| 1       | Dad1     | 1.15E-54 | 0.405106975   |
| 1       | Snhg6    | 1.21E-54 | 0.4991987     |
| 1       | Macrod2  | 1.65E-54 | 0.420434618   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 1       | Ccdc107 | 1.77E-54 | 0.511929793   |
| 1       | Dap     | 3.04E-54 | 0.575938098   |
| 1       | Igfbp3  | 9.87E-54 | 1.0110424     |
| 1       | Surf4   | 1.76E-53 | 0.503653483   |
| 1       | Mif     | 1.76E-52 | 0.594396114   |
| 1       | Coppb2  | 3.43E-52 | 0.49031481    |
| 1       | Tnfaip6 | 4.74E-51 | 0.769636045   |
| 1       | Ssr2    | 9.50E-51 | 0.470195259   |
| 1       | Hdlbp   | 1.57E-50 | 0.487214476   |
| 1       | Ctsa    | 7.85E-50 | 0.520184738   |
| 1       | Srpr    | 1.38E-49 | 0.449298857   |
| 1       | Tmem258 | 1.00E-48 | 0.463332197   |
| 1       | Clic4   | 1.54E-48 | 0.43154613    |
| 1       | Ier5    | 1.87E-48 | 0.573847888   |
| 1       | Tmem59  | 2.04E-48 | 0.414979739   |
| 1       | Socs3   | 2.37E-48 | 0.549771542   |
| 1       | Ptgs1   | 2.61E-48 | 0.502539163   |
| 1       | Tbca    | 3.12E-48 | 0.42939578    |
| 1       | Creb3l2 | 4.12E-48 | 0.42373904    |
| 1       | Ddost   | 4.17E-48 | 0.46689201    |
| 1       | P4hb    | 4.68E-48 | 0.472796648   |
| 1       | Igfbp6  | 4.71E-48 | 0.569311512   |
| 1       | Ncam1   | 7.89E-48 | 0.42117123    |
| 1       | Asap1   | 1.78E-47 | 0.483624169   |
| 1       | P4ha1   | 1.88E-47 | 0.474821644   |
| 1       | Gpx3    | 1.98E-47 | 0.416138408   |
| 1       | Tubb3   | 3.16E-47 | 0.434642852   |
| 1       | Eprs    | 3.45E-47 | 0.501004579   |
| 1       | Degs1   | 5.86E-47 | 0.45152751    |
| 1       | Serf1   | 7.66E-47 | 0.472109988   |
| 1       | Fam162a | 1.02E-46 | 0.567765463   |
| 1       | Psma2   | 1.43E-46 | 0.413251186   |
| 1       | Sqstm1  | 2.02E-46 | 0.502851899   |
| 1       | Ssr4    | 2.08E-46 | 0.430209464   |
| 1       | Sod2    | 2.59E-46 | 0.497139463   |
| 1       | Adprh   | 3.19E-46 | 0.426622906   |
| 1       | Tmem167 | 3.38E-46 | 0.45902322    |
| 1       | Pkm     | 3.69E-46 | 0.459541346   |
| 1       | Rassf1  | 4.87E-46 | 0.45922825    |
| 1       | Ch25h   | 5.42E-46 | 0.431411425   |
| 1       | Manf    | 5.76E-46 | 0.49711349    |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 1       | Fabp4         | 7.89E-46 | 0.531301858   |
| 1       | Fibin         | 9.88E-46 | 0.487731782   |
| 1       | Vimp          | 1.13E-45 | 0.49756459    |
| 1       | Smad7         | 1.27E-45 | 0.472749753   |
| 1       | 11-Sep        | 1.35E-45 | 0.484369326   |
| 1       | Prnp          | 1.75E-45 | 0.512339094   |
| 1       | Nov           | 2.04E-45 | 0.637652076   |
| 1       | Myeov2        | 3.34E-45 | 0.446735575   |
| 1       | Eif1b         | 6.45E-45 | 0.458656425   |
| 1       | Serpinb6a     | 1.28E-44 | 0.476415944   |
| 1       | Gng12         | 4.86E-44 | 0.478216748   |
| 1       | Apoe          | 6.47E-44 | 0.87790581    |
| 1       | Rsrp1         | 6.93E-44 | 0.459391602   |
| 1       | Hexb          | 9.23E-44 | 0.445282234   |
| 1       | Penk          | 1.04E-43 | 0.552939106   |
| 1       | Vegfa         | 1.13E-43 | 0.509582688   |
| 1       | Gnai2         | 1.80E-43 | 0.442143179   |
| 1       | 2310022B05Rik | 3.67E-43 | 0.406908254   |
| 1       | Ddb1          | 4.78E-43 | 0.475028638   |
| 1       | Cnn1          | 5.38E-43 | 0.490645169   |
| 1       | Mrpl20        | 6.25E-43 | 0.436900177   |
| 1       | Pnp           | 9.28E-43 | 0.46223673    |
| 1       | Ndufb6        | 9.94E-43 | 0.428754384   |
| 1       | Sh3bgrl3      | 1.34E-42 | 0.445811275   |
| 1       | Htra1         | 1.74E-42 | 0.514468292   |
| 1       | Lyz2          | 2.32E-42 | 0.48415003    |
| 1       | 1110065P20Rik | 2.52E-42 | 0.435959721   |
| 1       | Tln1          | 2.78E-42 | 0.417196644   |
| 1       | Eno1          | 3.46E-42 | 0.466724324   |
| 1       | Arl2          | 3.88E-42 | 0.44306657    |
| 1       | Aprt          | 5.16E-42 | 0.434477144   |
| 1       | Vat1          | 2.77E-41 | 0.432418016   |
| 1       | Cdkn2b        | 6.14E-41 | 0.558795865   |
| 1       | Sepp1         | 1.89E-40 | 0.428516581   |
| 1       | Sar1a         | 2.97E-40 | 0.434606856   |
| 1       | Aga           | 4.19E-40 | 0.442429217   |
| 1       | Tomm5         | 6.05E-40 | 0.436317574   |
| 1       | Tspan6        | 1.04E-39 | 0.425631142   |
| 1       | Serpine2      | 1.14E-39 | 0.582117256   |
| 1       | Morf4l2       | 1.35E-39 | 0.441626351   |
| 1       | Pofut2        | 1.90E-39 | 0.417539194   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene      | p value  | fold change * |
|---------|-----------|----------|---------------|
| 1       | Txndc15   | 2.06E-39 | 0.408300866   |
| 1       | Cyb5r3    | 4.69E-39 | 0.426444868   |
| 1       | Ccnd3     | 4.89E-39 | 0.459487862   |
| 1       | Anxa5     | 5.69E-39 | 0.441092673   |
| 1       | Rexo2     | 3.13E-38 | 0.405338202   |
| 1       | Ahnak     | 5.47E-38 | 0.486661547   |
| 1       | Cd44      | 5.47E-38 | 0.419003314   |
| 1       | Mmp11     | 6.11E-38 | 0.439886159   |
| 1       | Srm       | 9.26E-38 | 0.437280885   |
| 1       | Nenf      | 1.06E-37 | 0.400002678   |
| 1       | Prelp     | 1.31E-37 | 0.462424076   |
| 1       | Clptm1l   | 1.78E-37 | 0.403065652   |
| 1       | Sec13     | 2.35E-37 | 0.406520426   |
| 1       | Marcks    | 2.37E-37 | 0.41393038    |
| 1       | Dbi       | 2.47E-37 | 0.41447517    |
| 1       | Igfbp2    | 1.36E-36 | 0.885806349   |
| 1       | 2-Mar     | 1.38E-36 | 0.430566984   |
| 1       | Il6       | 1.74E-36 | 0.419140515   |
| 1       | Zwint     | 2.79E-36 | 0.433832954   |
| 1       | Pdlim7    | 1.20E-35 | 0.411089934   |
| 1       | Cnn3      | 1.62E-35 | 0.4188935     |
| 1       | Fzd1      | 1.44E-34 | 0.471411118   |
| 1       | Rnase4    | 1.69E-34 | 0.426418042   |
| 1       | Cxcl1     | 1.79E-33 | 0.84908332    |
| 1       | Lamb1     | 5.37E-33 | 0.449672493   |
| 1       | Lum       | 1.26E-32 | 0.675943428   |
| 1       | Serpinb1a | 1.38E-32 | 0.637764833   |
| 1       | C3        | 1.13E-31 | 0.434114017   |
| 1       | Zfp36     | 1.42E-30 | 0.49647374    |
| 1       | Sfrp2     | 1.67E-30 | 0.452877944   |
| 1       | Sgk1      | 3.35E-29 | 0.57826925    |
| 1       | Itgb5     | 4.49E-29 | 0.402894078   |
| 1       | Cdkn1c    | 1.15E-28 | 0.460080665   |
| 1       | Csrp2     | 9.21E-28 | 0.436820857   |
| 1       | Higd1a    | 1.24E-26 | 0.408467598   |
| 1       | Dlk1      | 1.88E-26 | 0.501318824   |
| 1       | Ddit3     | 5.52E-26 | 0.401106626   |
| 1       | Hist1h2bc | 5.20E-25 | 0.535620829   |
| 1       | Ptn       | 9.50E-24 | 0.408202671   |
| 1       | Gadd45a   | 2.15E-23 | 0.410421817   |
| 1       | Ifi27l2a  | 7.61E-21 | 0.401332159   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 2       | Stmn1         | 2.79E-52 | 1.585766778   |
| 2       | Tuba1b        | 2.10E-43 | 1.272324602   |
| 2       | Ccnb1         | 2.67E-43 | 0.952595938   |
| 2       | Smc2          | 3.26E-43 | 1.168850342   |
| 2       | Ccna2         | 3.70E-43 | 0.785733773   |
| 2       | Birc5         | 6.13E-43 | 1.513741243   |
| 2       | Cdca8         | 1.43E-42 | 1.066515736   |
| 2       | Cenpa         | 2.20E-41 | 1.456242429   |
| 2       | Ube2c         | 7.26E-41 | 1.539011437   |
| 2       | Cks1b         | 1.87E-39 | 1.220824957   |
| 2       | Spc24         | 2.59E-39 | 0.99670743    |
| 2       | Cdca3         | 1.95E-38 | 0.954177835   |
| 2       | Pbk           | 2.00E-38 | 0.793156593   |
| 2       | 2810417H13Rik | 3.18E-38 | 1.289902728   |
| 2       | Cdc20         | 1.00E-37 | 1.088339964   |
| 2       | Lockd         | 8.05E-37 | 0.998941324   |
| 2       | Ccnb2         | 9.17E-36 | 1.03999761    |
| 2       | 2700094K13Rik | 1.05E-35 | 1.157561752   |
| 2       | Cenpm         | 2.93E-35 | 0.937468975   |
| 2       | Cenpw         | 9.93E-35 | 0.819405715   |
| 2       | Pttg1         | 1.08E-34 | 1.356035737   |
| 2       | Lgals1        | 4.44E-32 | 1.176506565   |
| 2       | Ckap2         | 2.05E-31 | 0.476932444   |
| 2       | Cdk1          | 1.12E-30 | 1.23689341    |
| 2       | Tubb5         | 1.75E-30 | 1.106031819   |
| 2       | Tpx2          | 7.84E-30 | 0.722553122   |
| 2       | Ube2t         | 1.60E-29 | 0.563126247   |
| 2       | Racgap1       | 2.28E-29 | 0.860437078   |
| 2       | Aurka         | 4.96E-29 | 0.659383597   |
| 2       | Cks2          | 5.46E-29 | 0.998715668   |
| 2       | Spc25         | 1.13E-28 | 0.694522307   |
| 2       | Knstrn        | 1.25E-28 | 0.752741555   |
| 2       | Cenpf         | 1.46E-28 | 0.801258035   |
| 2       | Fam64a        | 1.49E-28 | 0.685170425   |
| 2       | Cenph         | 1.75E-28 | 0.673421819   |
| 2       | Top2a         | 1.69E-27 | 1.107537763   |
| 2       | Cdkn3         | 1.71E-27 | 0.659893869   |
| 2       | Ran           | 1.47E-26 | 0.788746939   |
| 2       | Mns1          | 6.04E-26 | 0.46265413    |
| 2       | Ckap2l        | 1.05E-25 | 0.443355811   |
| 2       | Anln          | 1.15E-24 | 0.503316576   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 2       | Hmmr     | 1.70E-24 | 0.496384219   |
| 2       | Nusap1   | 4.13E-24 | 0.497628422   |
| 2       | Tubb6    | 4.91E-24 | 1.052864698   |
| 2       | Cenpe    | 7.22E-24 | 0.621477012   |
| 2       | Rad51    | 1.10E-23 | 0.622486414   |
| 2       | Rrm2     | 1.24E-21 | 0.690089742   |
| 2       | Cdca2    | 1.32E-21 | 0.494227514   |
| 2       | Ska1     | 2.22E-21 | 0.414970967   |
| 2       | Atad2    | 2.24E-21 | 0.534238417   |
| 2       | Ndc80    | 2.56E-21 | 0.52075181    |
| 2       | Smc4     | 2.72E-21 | 0.980901862   |
| 2       | Ncapd2   | 7.16E-21 | 0.491201038   |
| 2       | Hmgb2    | 8.09E-21 | 1.101706048   |
| 2       | Kif2c    | 1.39E-20 | 0.482224271   |
| 2       | Tk1      | 1.45E-20 | 0.730760412   |
| 2       | Tacc3    | 2.54E-20 | 0.480854479   |
| 2       | Dhfr     | 5.90E-20 | 0.613209948   |
| 2       | Gins2    | 1.09E-19 | 0.750168397   |
| 2       | Dtymk    | 3.77E-19 | 0.807825624   |
| 2       | Pmf1     | 8.09E-19 | 0.696330219   |
| 2       | Dbf4     | 2.51E-18 | 0.604570554   |
| 2       | Hmgn2    | 3.48E-18 | 0.502337231   |
| 2       | Bgn      | 6.71E-18 | 0.576337309   |
| 2       | Dek      | 6.97E-18 | 0.826537241   |
| 2       | H2afv    | 1.33E-17 | 0.690212013   |
| 2       | Kifc1    | 1.76E-17 | 0.441721177   |
| 2       | Asf1b    | 3.36E-17 | 0.446249589   |
| 2       | Ncl      | 4.11E-17 | 0.715498297   |
| 2       | Dut      | 4.13E-17 | 0.878814261   |
| 2       | H2afz    | 5.15E-17 | 0.710121185   |
| 2       | Tm4sf1   | 6.00E-17 | 0.522233944   |
| 2       | Slc29a1  | 8.03E-17 | 0.543165024   |
| 2       | Mcm3     | 9.01E-17 | 0.488320307   |
| 2       | Serpinf1 | 1.16E-16 | 0.416228889   |
| 2       | Plk1     | 1.42E-16 | 0.418384087   |
| 2       | Tyms     | 1.65E-16 | 0.737872629   |
| 2       | Nsg1     | 2.79E-16 | 0.448553      |
| 2       | Kif23    | 3.42E-16 | 0.486128553   |
| 2       | Vim      | 4.38E-16 | 0.867177059   |
| 2       | Aurkb    | 4.68E-16 | 0.489862582   |
| 2       | Wisp1    | 5.94E-16 | 0.538951276   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 2       | Srm           | 6.13E-16 | 0.786335933   |
| 2       | Psat1         | 6.56E-16 | 0.694833512   |
| 2       | Prkg2         | 9.03E-16 | 0.748702671   |
| 2       | Cald1         | 1.01E-15 | 0.555400832   |
| 2       | Kif20a        | 1.11E-15 | 0.429970053   |
| 2       | Gmnn          | 1.91E-15 | 0.535056318   |
| 2       | Nt5dc2        | 2.55E-15 | 0.602935161   |
| 2       | Rpa2          | 3.36E-15 | 0.525513371   |
| 2       | 2700029M09Rik | 4.03E-15 | 0.524695555   |
| 2       | Cmtm3         | 4.33E-15 | 0.432653167   |
| 2       | Bcat1         | 4.37E-15 | 0.495871575   |
| 2       | Prc1          | 1.11E-14 | 0.458393648   |
| 2       | Ranbp1        | 2.19E-14 | 0.750817198   |
| 2       | Serpinh1      | 2.70E-14 | 0.48680713    |
| 2       | Mthfd2        | 2.76E-14 | 0.714289501   |
| 2       | Tcf19         | 4.65E-14 | 0.451262768   |
| 2       | Mki67         | 6.84E-14 | 0.41566602    |
| 2       | Pcna          | 1.09E-13 | 0.607921225   |
| 2       | Ezh2          | 1.21E-13 | 0.484396323   |
| 2       | Tipin         | 1.94E-13 | 0.550467719   |
| 2       | Hn1           | 2.04E-13 | 0.665689494   |
| 2       | Dnajc9        | 2.12E-13 | 0.43045014    |
| 2       | Lsm2          | 2.18E-13 | 0.625644588   |
| 2       | Usp1          | 3.12E-13 | 0.472059505   |
| 2       | Anp32b        | 5.11E-13 | 0.640099092   |
| 2       | Rad21         | 5.47E-13 | 0.499535998   |
| 2       | Rrm1          | 6.52E-13 | 0.405792962   |
| 2       | Prrx1         | 7.14E-13 | 0.486435803   |
| 2       | Pkm           | 1.02E-12 | 0.590196703   |
| 2       | Rangap1       | 1.15E-12 | 0.534614015   |
| 2       | Prdx4         | 1.15E-12 | 0.736429675   |
| 2       | Ak6           | 1.33E-12 | 0.561419787   |
| 2       | Tmpo          | 3.11E-12 | 0.494778455   |
| 2       | Tuba1a        | 3.54E-12 | 0.704972594   |
| 2       | Wdr12         | 3.99E-12 | 0.407733172   |
| 2       | Tubb3         | 9.28E-12 | 0.43127579    |
| 2       | Txn1          | 9.87E-12 | 0.497245728   |
| 2       | Steap1        | 1.28E-11 | 0.495926924   |
| 2       | Hmga2         | 1.73E-11 | 0.701439264   |
| 2       | Eif4ebp1      | 1.85E-11 | 0.629670205   |
| 2       | D030056L22Rik | 1.98E-11 | 0.424581081   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 2       | Terf1   | 2.04E-11 | 0.459314483   |
| 2       | Nop56   | 2.44E-11 | 0.638437302   |
| 2       | Nudcd2  | 2.44E-11 | 0.550805329   |
| 2       | Fbln2   | 2.71E-11 | 0.457236923   |
| 2       | Alyref  | 2.74E-11 | 0.542218225   |
| 2       | Yaf2    | 3.39E-11 | 0.588616034   |
| 2       | Msn     | 4.27E-11 | 0.438692326   |
| 2       | Peak1   | 4.39E-11 | 0.470415227   |
| 2       | Cdkn2d  | 7.01E-11 | 0.463006004   |
| 2       | Mif     | 7.37E-11 | 0.632420689   |
| 2       | Cox7a2  | 9.92E-11 | 0.496840831   |
| 2       | Psip1   | 1.07E-10 | 0.591587084   |
| 2       | Oaf     | 1.31E-10 | 0.452864648   |
| 2       | Pin1    | 1.57E-10 | 0.546954664   |
| 2       | Hat1    | 1.74E-10 | 0.497954393   |
| 2       | Syce2   | 2.03E-10 | 0.474399981   |
| 2       | Cmc2    | 2.36E-10 | 0.565230683   |
| 2       | Shmt2   | 2.38E-10 | 0.597144286   |
| 2       | Tmem97  | 3.63E-10 | 0.422075063   |
| 2       | Phgdh   | 3.78E-10 | 0.536877877   |
| 2       | Nhp2    | 5.66E-10 | 0.580347989   |
| 2       | Mcm6    | 7.33E-10 | 0.459829418   |
| 2       | Ssr1    | 9.92E-10 | 0.435525962   |
| 2       | Mrpl18  | 1.02E-09 | 0.486740618   |
| 2       | Pole4   | 1.10E-09 | 0.492286111   |
| 2       | Lsm3    | 1.19E-09 | 0.440777205   |
| 2       | Ppa1    | 1.33E-09 | 0.436734125   |
| 2       | Pabpc1  | 1.40E-09 | 0.487542749   |
| 2       | Ndufaf2 | 1.42E-09 | 0.430626644   |
| 2       | Ak2     | 1.61E-09 | 0.544310589   |
| 2       | Ncaph2  | 1.65E-09 | 0.474451663   |
| 2       | Cth     | 1.75E-09 | 0.552855603   |
| 2       | Dkc1    | 1.87E-09 | 0.494909264   |
| 2       | Rhoc    | 2.15E-09 | 0.44958788    |
| 2       | Nucks1  | 2.18E-09 | 0.492308823   |
| 2       | Pole3   | 2.50E-09 | 0.434473534   |
| 2       | Ssrp1   | 2.92E-09 | 0.515426938   |
| 2       | Clic4   | 3.36E-09 | 0.406417529   |
| 2       | Spp1    | 3.41E-09 | 0.786362303   |
| 2       | Aars    | 3.65E-09 | 0.538684165   |
| 2       | Nsmce2  | 4.22E-09 | 0.457808436   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 2       | Mrpl13   | 4.84E-09 | 0.46245379    |
| 2       | Banf1    | 4.86E-09 | 0.507605102   |
| 2       | Emp3     | 5.91E-09 | 0.554428863   |
| 2       | Fam92a   | 5.96E-09 | 0.488004105   |
| 2       | Angptl6  | 8.23E-09 | 0.450541333   |
| 2       | Dctpp1   | 8.53E-09 | 0.498241355   |
| 2       | Cep57    | 9.39E-09 | 0.456878779   |
| 2       | Pspf     | 1.01E-08 | 0.569263126   |
| 2       | Nme1     | 1.08E-08 | 0.537633072   |
| 2       | Hmga1    | 1.32E-08 | 0.427230551   |
| 2       | Anapc11  | 1.59E-08 | 0.520435313   |
| 2       | Fkbp2    | 1.99E-08 | 0.452830411   |
| 2       | Ppil1    | 2.04E-08 | 0.421018684   |
| 2       | Ddx39    | 2.06E-08 | 0.498274762   |
| 2       | Rrp15    | 2.07E-08 | 0.436033094   |
| 2       | Fkbp1a   | 2.37E-08 | 0.462411023   |
| 2       | Snrpd1   | 2.82E-08 | 0.479566892   |
| 2       | Ebna1bp2 | 2.95E-08 | 0.405784597   |
| 2       | Orc6     | 3.86E-08 | 0.477967006   |
| 2       | Cbx5     | 6.32E-08 | 0.421981969   |
| 2       | Cox6a2   | 6.66E-08 | 0.404567751   |
| 2       | Hmgb1    | 6.99E-08 | 0.500103796   |
| 2       | Cnih1    | 7.13E-08 | 0.435193131   |
| 2       | Serbp1   | 8.90E-08 | 0.462882893   |
| 2       | H2afx    | 9.14E-08 | 0.579839148   |
| 2       | G3bp1    | 1.14E-07 | 0.494074531   |
| 2       | Ddx18    | 1.17E-07 | 0.415578432   |
| 2       | Pgp      | 1.17E-07 | 0.444779737   |
| 2       | Polr2f   | 1.43E-07 | 0.449282739   |
| 2       | Eno1     | 1.54E-07 | 0.461508212   |
| 2       | Rps19bp1 | 1.72E-07 | 0.430370178   |
| 2       | Ccnd1    | 1.94E-07 | 0.488514271   |
| 2       | Manf     | 3.10E-07 | 0.446479797   |
| 2       | Dcn      | 3.72E-07 | 0.459339096   |
| 2       | Zcrb1    | 4.00E-07 | 0.41760872    |
| 2       | Phf5a    | 4.27E-07 | 0.494359586   |
| 2       | Mrpl49   | 4.54E-07 | 0.427951195   |
| 2       | Ccl7     | 4.74E-07 | 0.401557485   |
| 2       | Cyb5r1   | 4.98E-07 | 0.432072392   |
| 2       | Mrto4    | 6.49E-07 | 0.438072545   |
| 2       | Eef1e1   | 6.59E-07 | 0.439546288   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value   | fold change * |
|---------|---------------|-----------|---------------|
| 2       | Zfos1         | 6.72E-07  | 0.527722845   |
| 2       | Srsf7         | 1.42E-06  | 0.511249878   |
| 2       | Zfp706        | 1.59E-06  | 0.416566722   |
| 2       | Gapdh         | 1.63E-06  | 0.421677802   |
| 2       | Cnih4         | 1.69E-06  | 0.443960488   |
| 2       | Timm17a       | 1.94E-06  | 0.417976719   |
| 2       | Hspa9         | 2.16E-06  | 0.451721534   |
| 2       | Dap           | 2.49E-06  | 0.42699002    |
| 2       | Dlk1          | 3.09E-06  | 0.52806399    |
| 2       | Mrps30        | 4.12E-06  | 0.428794958   |
| 2       | Lrrc59        | 4.95E-06  | 0.412620308   |
| 2       | Nap1l1        | 6.23E-06  | 0.401929062   |
| 2       | Lyar          | 6.72E-06  | 0.444762068   |
| 2       | Gars          | 7.52E-06  | 0.402341493   |
| 2       | Tpm2          | 9.32E-06  | 0.477991853   |
| 2       | Mrpl51        | 9.68E-06  | 0.420881229   |
| 2       | Arpp19        | 1.42E-05  | 0.404682031   |
| 2       | Asns          | 2.47E-05  | 0.430844236   |
| 2       | Tspo          | 4.85E-05  | 0.452533903   |
| 2       | Tpm1          | 0.001126  | 0.435035359   |
| 2       | Ptn           | 0.009524  | 0.418968182   |
| 3       | Elof1         | 1.63E-115 | 2.047977978   |
| 3       | Chchd10       | 1.67E-93  | 2.55615977    |
| 3       | Ift172        | 3.17E-93  | 2.593299503   |
| 3       | 1700016K19Rik | 1.17E-76  | 2.555619536   |
| 3       | Cfap126       | 2.26E-76  | 2.416804586   |
| 3       | Tppp3         | 4.79E-73  | 2.724652206   |
| 3       | Ccdc153       | 3.45E-72  | 2.579859463   |
| 3       | 1700088E04Rik | 8.05E-71  | 1.921528797   |
| 3       | Tmem212       | 4.96E-68  | 2.574395408   |
| 3       | Pifo          | 5.42E-66  | 2.359817497   |
| 3       | Mlf1          | 4.04E-65  | 2.075547331   |
| 3       | Meig1         | 6.22E-65  | 2.307228694   |
| 3       | Lrrc51        | 6.43E-63  | 1.918428137   |
| 3       | 1700007K13Rik | 6.48E-61  | 2.102926924   |
| 3       | Fam183b       | 7.06E-61  | 2.488691138   |
| 3       | Tmem107       | 1.40E-60  | 1.752096808   |
| 3       | Ift43         | 1.24E-58  | 1.589900565   |
| 3       | Ccdc189       | 7.05E-58  | 1.793031492   |
| 3       | Rspn1         | 8.55E-58  | 2.008079083   |
| 3       | Arhdg1        | 1.24E-56  | 1.772585561   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | 1110004E09Rik | 1.47E-56 | 1.535835502   |
| 3       | Prr29         | 1.14E-55 | 1.918647146   |
| 3       | Tctex1d4      | 1.03E-54 | 1.665581873   |
| 3       | Cfap206       | 9.21E-54 | 1.422667294   |
| 3       | Spef1         | 2.05E-53 | 1.67707032    |
| 3       | 2410004P03Rik | 2.05E-53 | 1.648694289   |
| 3       | AU040972      | 2.30E-53 | 3.032962153   |
| 3       | Bola1         | 4.36E-51 | 1.416952234   |
| 3       | 1700026L06Rik | 3.71E-50 | 1.830329597   |
| 3       | Dpcd          | 1.88E-48 | 1.455534976   |
| 3       | BC051019      | 6.55E-48 | 1.540618792   |
| 3       | Foxj1         | 1.42E-47 | 1.842427318   |
| 3       | Erich2        | 2.78E-47 | 1.631885808   |
| 3       | Morn5         | 6.67E-47 | 1.653555242   |
| 3       | Chchd6        | 3.67E-45 | 1.446489889   |
| 3       | Nme5          | 1.53E-44 | 1.555206465   |
| 3       | Fam92b        | 1.58E-44 | 1.552148094   |
| 3       | Capsl         | 3.75E-44 | 1.675687207   |
| 3       | 1110017D15Rik | 5.40E-44 | 1.658491714   |
| 3       | Ccdc113       | 8.93E-44 | 1.530073382   |
| 3       | Cetn4         | 1.87E-42 | 1.500036607   |
| 3       | Cep83         | 2.43E-41 | 1.472853986   |
| 3       | Ccpg1os       | 2.45E-41 | 1.403310909   |
| 3       | Ccdc34        | 2.68E-41 | 1.536010899   |
| 3       | Ezr           | 8.20E-41 | 1.586184293   |
| 3       | 4933434E20Rik | 5.28E-40 | 1.422748967   |
| 3       | Gtsf1l        | 5.75E-40 | 1.270765625   |
| 3       | Tekt1         | 2.63E-39 | 1.51627138    |
| 3       | Gtf2b         | 4.03E-39 | 1.328391893   |
| 3       | Smim5         | 4.75E-39 | 1.582841457   |
| 3       | Nudc          | 7.42E-39 | 1.289877856   |
| 3       | Rsp9          | 1.30E-38 | 1.370566528   |
| 3       | 1700013F07Rik | 1.36E-38 | 1.330407391   |
| 3       | Mycbp         | 1.46E-38 | 1.314509373   |
| 3       | Sntn          | 4.86E-38 | 1.346895419   |
| 3       | Lrrc23        | 7.97E-38 | 1.31890668    |
| 3       | Cfap77        | 1.17E-37 | 1.129633657   |
| 3       | Dnali1        | 1.72E-37 | 1.140897496   |
| 3       | Lrrc48        | 1.85E-37 | 1.382642227   |
| 3       | Cfap36        | 3.72E-37 | 1.312704543   |
| 3       | Cfap52        | 4.99E-37 | 1.211945927   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Dnah12        | 1.19E-36 | 1.527263581   |
| 3       | Ift22         | 1.33E-36 | 1.293385331   |
| 3       | Ccdc146       | 1.84E-36 | 1.110296964   |
| 3       | Calm3         | 1.98E-36 | 1.257830087   |
| 3       | 2610028H24Rik | 2.50E-36 | 1.395826322   |
| 3       | Gde1          | 5.30E-36 | 1.31707006    |
| 3       | Dnajb13       | 9.27E-36 | 1.081795418   |
| 3       | 1700007G11Rik | 2.43E-35 | 1.227063803   |
| 3       | Cib1          | 2.55E-35 | 1.310219747   |
| 3       | Mapk15        | 5.50E-35 | 0.978310241   |
| 3       | Ccdc17        | 5.59E-35 | 1.015842281   |
| 3       | Ndufaf3       | 1.38E-34 | 1.282593114   |
| 3       | Cyp2s1        | 1.55E-34 | 1.133007823   |
| 3       | Gm867         | 2.03E-34 | 1.27825278    |
| 3       | 1110032A03Rik | 4.61E-34 | 1.232522852   |
| 3       | Ccdc39        | 5.48E-34 | 1.372106505   |
| 3       | Crip2         | 5.85E-34 | 1.401719175   |
| 3       | Fank1         | 7.04E-34 | 1.047397175   |
| 3       | Tspan1        | 7.60E-34 | 1.672277071   |
| 3       | Tekt4         | 9.92E-34 | 1.060344452   |
| 3       | Eml2          | 1.12E-33 | 1.272530421   |
| 3       | Ift46         | 1.24E-33 | 1.195717097   |
| 3       | Mns1          | 1.85E-33 | 1.069613341   |
| 3       | Cldn3         | 4.91E-33 | 1.644314643   |
| 3       | Tm4sf1        | 5.24E-33 | 1.843686359   |
| 3       | Vpreb3        | 1.79E-32 | 1.654192823   |
| 3       | Cfap45        | 2.68E-32 | 1.166602772   |
| 3       | Ctxn1         | 3.64E-32 | 1.274897284   |
| 3       | Ccdc181       | 3.88E-32 | 1.297080978   |
| 3       | Fam47e        | 4.32E-32 | 1.006829354   |
| 3       | Cetn2         | 1.02E-31 | 1.193806125   |
| 3       | Kif19a        | 2.78E-31 | 1.135981993   |
| 3       | Ccdc96        | 3.19E-31 | 0.937706242   |
| 3       | Smim22        | 4.65E-31 | 1.37469908    |
| 3       | Acox2         | 5.63E-31 | 1.207835194   |
| 3       | Smim6         | 7.78E-31 | 1.326878146   |
| 3       | Basp1         | 9.52E-31 | 1.370678576   |
| 3       | Pih1d2        | 9.94E-31 | 1.069538755   |
| 3       | 1700001C02Rik | 1.14E-30 | 1.212266806   |
| 3       | Tubb4b        | 1.65E-30 | 1.307449741   |
| 3       | Ttc25         | 1.74E-30 | 0.994356556   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Spef2         | 2.42E-30 | 1.035073279   |
| 3       | Fbxo36        | 5.47E-30 | 1.236414633   |
| 3       | Saxo2         | 5.49E-30 | 1.172057347   |
| 3       | Ttc16         | 6.79E-30 | 0.8661098     |
| 3       | Cxcl17        | 7.67E-30 | 1.76963025    |
| 3       | Uckl1os       | 9.61E-30 | 1.193986832   |
| 3       | Lrrc71        | 1.16E-29 | 0.700925401   |
| 3       | Cyb561        | 1.52E-29 | 1.218875062   |
| 3       | Gas8          | 1.54E-29 | 1.129303785   |
| 3       | Ubxn11        | 2.84E-29 | 1.044381849   |
| 3       | Morn3         | 3.07E-29 | 0.917159682   |
| 3       | Dnah6         | 3.65E-29 | 0.776565498   |
| 3       | Enkur         | 4.32E-29 | 1.0516868     |
| 3       | Lrrc46        | 4.96E-29 | 1.034541268   |
| 3       | Ccdc65        | 5.01E-29 | 0.931811355   |
| 3       | B9d1          | 5.05E-29 | 1.193620354   |
| 3       | Ccdc78        | 5.94E-29 | 0.902640644   |
| 3       | Dnaaf3        | 6.87E-29 | 1.001640869   |
| 3       | Sri           | 8.30E-29 | 1.037906164   |
| 3       | Cfap70        | 1.06E-28 | 0.951391331   |
| 3       | Dnajc15       | 1.11E-28 | 1.102753447   |
| 3       | Gm29538       | 2.81E-28 | 0.965154154   |
| 3       | 3300002A11Rik | 7.73E-28 | 1.378196937   |
| 3       | Spag17        | 9.55E-28 | 0.725697826   |
| 3       | Ppfia3        | 1.34E-27 | 1.161196786   |
| 3       | Ccdc40        | 2.25E-27 | 0.905702365   |
| 3       | Mok           | 2.41E-27 | 1.048446863   |
| 3       | Cystm1        | 4.37E-27 | 1.281472093   |
| 3       | 1810037I17Rik | 1.18E-26 | 1.122935943   |
| 3       | Iqcg          | 1.73E-26 | 0.820459527   |
| 3       | Fam179a       | 2.88E-26 | 0.787998468   |
| 3       | Tuba1a        | 3.63E-26 | 1.411634349   |
| 3       | Nhlrc4        | 6.30E-26 | 0.547354274   |
| 3       | Ak9           | 7.59E-26 | 0.733430747   |
| 3       | Dnah9         | 1.04E-25 | 0.798879757   |
| 3       | 4931406C07Rik | 1.19E-25 | 1.104691698   |
| 3       | Cby1          | 1.30E-25 | 1.12196023    |
| 3       | Wdr60         | 1.31E-25 | 1.093250674   |
| 3       | Mak           | 2.56E-25 | 0.741675295   |
| 3       | Ift27         | 3.39E-25 | 1.098916517   |
| 3       | 1700028P14Rik | 3.75E-25 | 0.860546874   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Pacrg         | 4.52E-25 | 0.924119259   |
| 3       | Dynlrb2       | 1.07E-24 | 1.594440413   |
| 3       | Znhit1        | 1.13E-24 | 0.968224353   |
| 3       | Swi5          | 1.24E-24 | 0.965024636   |
| 3       | Ttc21a        | 1.42E-24 | 0.805943817   |
| 3       | Vwa3a         | 1.61E-24 | 0.567259161   |
| 3       | Rabl2         | 1.75E-24 | 1.040654438   |
| 3       | Dusp14        | 1.89E-24 | 1.213179609   |
| 3       | Cdhr4         | 2.25E-24 | 0.954541757   |
| 3       | Eif2b2        | 2.62E-24 | 1.052555626   |
| 3       | Cfap44        | 2.88E-24 | 0.581339123   |
| 3       | Bphl          | 4.41E-24 | 1.043009289   |
| 3       | Dalrd3        | 5.39E-24 | 1.137495143   |
| 3       | Cd24a         | 5.82E-24 | 1.430247705   |
| 3       | Tmc5          | 6.15E-24 | 0.870571835   |
| 3       | Ak7           | 6.84E-24 | 0.708053092   |
| 3       | Ift88         | 8.66E-24 | 0.916493732   |
| 3       | Zmynd12       | 1.95E-23 | 0.724828563   |
| 3       | Lgals3        | 2.54E-23 | 1.725386814   |
| 3       | Fam81b        | 3.41E-23 | 0.778928621   |
| 3       | 1700037C18Rik | 4.37E-23 | 0.91264269    |
| 3       | Ccdc103       | 4.43E-23 | 0.933054808   |
| 3       | Aldh1a1       | 4.67E-23 | 1.338606919   |
| 3       | Ift74         | 4.68E-23 | 1.000240575   |
| 3       | Gm15402       | 5.77E-23 | 0.701109909   |
| 3       | Ruvbl2        | 1.12E-22 | 1.052864378   |
| 3       | Lhb           | 1.13E-22 | 0.504852229   |
| 3       | Bbof1         | 1.13E-22 | 0.844404607   |
| 3       | Las1l         | 1.39E-22 | 1.12898068    |
| 3       | Myh14         | 1.40E-22 | 1.214362248   |
| 3       | Agc2          | 1.54E-22 | 1.643386939   |
| 3       | 1700029J07Rik | 1.67E-22 | 0.844078765   |
| 3       | Gpx4          | 1.73E-22 | 0.887171593   |
| 3       | Ankrd42       | 2.18E-22 | 0.887363731   |
| 3       | Dydc2         | 2.35E-22 | 0.661622155   |
| 3       | Kcnh3         | 3.57E-22 | 0.743439807   |
| 3       | Ccdc151       | 4.57E-22 | 0.676805384   |
| 3       | Enkd1         | 4.76E-22 | 0.913638892   |
| 3       | Wdr66         | 5.55E-22 | 0.628809873   |
| 3       | Fhad1         | 8.53E-22 | 0.74265168    |
| 3       | Rspn4a        | 1.51E-21 | 0.53847201    |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Armc4         | 1.86E-21 | 0.704831483   |
| 3       | Cep126        | 2.07E-21 | 0.759926166   |
| 3       | Kif3a         | 2.55E-21 | 0.990367006   |
| 3       | Wdr63         | 4.75E-21 | 0.490862715   |
| 3       | Ino80b        | 9.42E-21 | 1.016069384   |
| 3       | Adam8         | 1.48E-20 | 0.824212916   |
| 3       | Cfap69        | 1.55E-20 | 0.861052818   |
| 3       | Hydin         | 1.87E-20 | 0.527089609   |
| 3       | Hspa2         | 2.10E-20 | 1.019753777   |
| 3       | Tomm7         | 2.20E-20 | 0.862220678   |
| 3       | Hdc           | 2.44E-20 | 0.871128733   |
| 3       | Sptlc3        | 2.61E-20 | 0.75957123    |
| 3       | Clic3         | 3.18E-20 | 1.050222611   |
| 3       | BC022687      | 3.96E-20 | 0.93067376    |
| 3       | Dnah3         | 5.65E-20 | 0.572878509   |
| 3       | Arhgef28      | 6.96E-20 | 1.016745079   |
| 3       | Cfap46        | 9.18E-20 | 0.442327194   |
| 3       | Lrriq1        | 1.00E-19 | 0.659227245   |
| 3       | Gng5          | 1.11E-19 | 0.807488947   |
| 3       | Ifitm1        | 1.34E-19 | 1.7730778     |
| 3       | Efhc1         | 1.35E-19 | 0.659413006   |
| 3       | Cbr2          | 1.60E-19 | 1.662611877   |
| 3       | Ankrd54       | 1.62E-19 | 0.994300242   |
| 3       | Dnah11        | 4.43E-19 | 0.492770916   |
| 3       | Cfap100       | 4.56E-19 | 0.829870129   |
| 3       | Fam216a       | 4.67E-19 | 0.982817142   |
| 3       | Cmtm8         | 5.25E-19 | 0.983967835   |
| 3       | Dnaaf1        | 6.53E-19 | 0.605187539   |
| 3       | Adipor2       | 7.75E-19 | 0.982938076   |
| 3       | Maats1        | 8.06E-19 | 0.504746447   |
| 3       | Kif9          | 1.03E-18 | 0.618470576   |
| 3       | Cisd3         | 1.05E-18 | 1.009805793   |
| 3       | Cfap161       | 1.16E-18 | 0.452593247   |
| 3       | Ttc39a        | 1.47E-18 | 0.68065919    |
| 3       | Akip1         | 2.04E-18 | 0.921711542   |
| 3       | Oscp1         | 2.57E-18 | 0.822974071   |
| 3       | Prr15l        | 2.79E-18 | 0.930645218   |
| 3       | Krt8          | 3.00E-18 | 1.223037349   |
| 3       | Tctex1d2      | 3.09E-18 | 0.914685892   |
| 3       | Rspn14        | 4.09E-18 | 0.407683643   |
| 3       | 2200002D01Rik | 4.09E-18 | 1.138473878   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Cds1          | 4.49E-18 | 0.733166336   |
| 3       | Cnp           | 4.91E-18 | 0.925169021   |
| 3       | Strbp         | 4.92E-18 | 0.973030577   |
| 3       | Ulk4          | 5.11E-18 | 0.671305458   |
| 3       | Ctsh          | 5.42E-18 | 1.014656539   |
| 3       | Lrrc56        | 6.33E-18 | 0.656234419   |
| 3       | Lrrc10b       | 7.34E-18 | 0.631042015   |
| 3       | Sec14l3       | 7.60E-18 | 0.687244387   |
| 3       | Ppil6         | 8.44E-18 | 0.756716147   |
| 3       | Ccdc74a       | 1.08E-17 | 0.628338112   |
| 3       | Dcxr          | 1.10E-17 | 1.313506649   |
| 3       | Ndufb5        | 1.16E-17 | 0.814403923   |
| 3       | 2010109I03Rik | 1.45E-17 | 0.632313853   |
| 3       | Fam161b       | 1.63E-17 | 0.584780595   |
| 3       | Gm42722       | 1.76E-17 | 0.542989755   |
| 3       | Ccdc180       | 1.80E-17 | 0.490659078   |
| 3       | Ldlrad1       | 1.80E-17 | 0.476904532   |
| 3       | Sys1          | 2.25E-17 | 0.866480231   |
| 3       | Catip         | 2.31E-17 | 0.612764975   |
| 3       | Mt1           | 3.08E-17 | 1.085645687   |
| 3       | Traf3ip1      | 3.16E-17 | 0.800000152   |
| 3       | Spa17         | 3.49E-17 | 0.846999999   |
| 3       | Adck4         | 4.36E-17 | 0.894157246   |
| 3       | Rfc2          | 4.79E-17 | 0.900460632   |
| 3       | Dusp18        | 4.97E-17 | 0.919529278   |
| 3       | 6820408C15Rik | 6.65E-17 | 0.677079432   |
| 3       | Efcab10       | 6.81E-17 | 0.733604712   |
| 3       | Cntrl         | 7.13E-17 | 0.796857368   |
| 3       | Mdh1b         | 8.49E-17 | 0.417963943   |
| 3       | Nek11         | 8.98E-17 | 0.575550452   |
| 3       | Nphp1         | 1.03E-16 | 0.846064922   |
| 3       | Dnah1         | 1.05E-16 | 0.433869858   |
| 3       | Pbx4          | 1.15E-16 | 0.811259431   |
| 3       | Wdr54         | 1.43E-16 | 0.851795846   |
| 3       | Riiad1        | 1.46E-16 | 0.794244906   |
| 3       | Ribc1         | 1.55E-16 | 0.616397021   |
| 3       | Ckap2l        | 1.76E-16 | 0.912242669   |
| 3       | Dnaaf2        | 1.93E-16 | 0.826097467   |
| 3       | Cfap20        | 2.00E-16 | 0.847095357   |
| 3       | Gm26717       | 2.81E-16 | 0.65582891    |
| 3       | Ift81         | 2.81E-16 | 0.848356212   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Pcnxl4        | 2.92E-16 | 0.836295237   |
| 3       | Syt5          | 2.93E-16 | 0.642432905   |
| 3       | Slc9a3r1      | 3.92E-16 | 0.953974227   |
| 3       | Ccdc67        | 4.04E-16 | 0.869960697   |
| 3       | Fam227a       | 4.50E-16 | 0.454908661   |
| 3       | Tsnaxip1      | 4.71E-16 | 0.577948246   |
| 3       | Zmynd10       | 6.51E-16 | 0.813396191   |
| 3       | B230118H07Rik | 7.05E-16 | 0.916405936   |
| 3       | Bbs7          | 7.55E-16 | 0.599225702   |
| 3       | Fam134b       | 9.60E-16 | 0.959755058   |
| 3       | Ppp5c         | 9.71E-16 | 0.852684509   |
| 3       | Nat9          | 1.16E-15 | 0.868097135   |
| 3       | Styxl1        | 1.18E-15 | 0.620995136   |
| 3       | Wdr34         | 1.30E-15 | 0.832826267   |
| 3       | Akap14        | 1.35E-15 | 0.565976116   |
| 3       | Ccdc60        | 1.35E-15 | 0.413920135   |
| 3       | Lrwd1         | 1.37E-15 | 0.87335647    |
| 3       | Dpy30         | 1.40E-15 | 0.833960962   |
| 3       | Ddr1          | 1.65E-15 | 0.948705254   |
| 3       | Morn2         | 2.09E-15 | 0.92213713    |
| 3       | Prom1         | 2.36E-15 | 0.928208248   |
| 3       | Cep290        | 2.56E-15 | 0.894243462   |
| 3       | D430036J16Rik | 2.74E-15 | 0.452763797   |
| 3       | 1700024G13Rik | 2.79E-15 | 0.718625259   |
| 3       | Hes6          | 2.84E-15 | 1.223564647   |
| 3       | Hipk1         | 2.88E-15 | 0.829084007   |
| 3       | Smkr-ps       | 3.19E-15 | 0.421628119   |
| 3       | Sugt1         | 3.30E-15 | 0.815359795   |
| 3       | Pglyrp1       | 3.56E-15 | 1.156578507   |
| 3       | Ccdc173       | 3.70E-15 | 0.700056004   |
| 3       | Wdr78         | 3.91E-15 | 0.623983254   |
| 3       | Rfk           | 4.05E-15 | 0.87329244    |
| 3       | Krt18         | 4.26E-15 | 1.166202399   |
| 3       | Josd2         | 4.36E-15 | 0.817550371   |
| 3       | Acyp1         | 4.39E-15 | 0.947084946   |
| 3       | 1810008I18Rik | 4.64E-15 | 0.425392748   |
| 3       | D430042009Rik | 4.96E-15 | 0.921859686   |
| 3       | Dynlt1f       | 5.12E-15 | 0.858453315   |
| 3       | Ina           | 5.92E-15 | 0.704380527   |
| 3       | Lrrc73        | 7.27E-15 | 0.731674268   |
| 3       | 2210407C18Rik | 7.35E-15 | 0.762586142   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | 1810043G02Rik | 1.11E-14 | 0.876633513   |
| 3       | Hspa4l        | 1.16E-14 | 1.154845183   |
| 3       | 1700003E16Rik | 1.22E-14 | 0.405740896   |
| 3       | Lekr1         | 1.63E-14 | 0.765024236   |
| 3       | Pkig          | 1.70E-14 | 0.819773836   |
| 3       | Ccdc30        | 2.00E-14 | 0.566184588   |
| 3       | Gm33050       | 2.31E-14 | 0.447017529   |
| 3       | Cfap57        | 3.00E-14 | 0.431312325   |
| 3       | Fhit          | 3.24E-14 | 0.641440304   |
| 3       | Snrnp25       | 3.54E-14 | 0.783112274   |
| 3       | Ccdc191       | 4.07E-14 | 0.842627154   |
| 3       | Mdm1          | 6.44E-14 | 0.762898576   |
| 3       | Psmd9         | 9.82E-14 | 0.798770798   |
| 3       | Iqck          | 1.08E-13 | 0.517559045   |
| 3       | Odf2l         | 1.16E-13 | 0.810526413   |
| 3       | Spag6l        | 1.22E-13 | 0.553024953   |
| 3       | 1700086L19Rik | 1.40E-13 | 0.539551722   |
| 3       | BC005624      | 1.61E-13 | 0.785824005   |
| 3       | Nudt4         | 2.92E-13 | 0.881823529   |
| 3       | Ruvbl1        | 3.03E-13 | 0.758261269   |
| 3       | Wdr35         | 4.07E-13 | 0.819608678   |
| 3       | B9d2          | 4.25E-13 | 0.801002464   |
| 3       | Ndufab1       | 5.01E-13 | 0.761743314   |
| 3       | Fbxo32        | 6.37E-13 | 0.941711911   |
| 3       | Ppp1r16a      | 6.38E-13 | 0.684515877   |
| 3       | Mrpl34        | 6.52E-13 | 0.694598994   |
| 3       | Ift57         | 7.89E-13 | 0.847731828   |
| 3       | Efcab11       | 8.56E-13 | 0.619419257   |
| 3       | Rph3al        | 9.00E-13 | 0.50763156    |
| 3       | Med31         | 9.35E-13 | 0.73994836    |
| 3       | Wwc1          | 1.49E-12 | 0.787953827   |
| 3       | Glod4         | 1.61E-12 | 0.817614935   |
| 3       | Ccp110        | 2.00E-12 | 0.574267448   |
| 3       | Tmem231       | 2.01E-12 | 0.53854261    |
| 3       | Cep131        | 2.07E-12 | 0.572332861   |
| 3       | Elf3          | 2.19E-12 | 0.914744947   |
| 3       | Lrrc45        | 2.47E-12 | 0.803199333   |
| 3       | Pcyt1b        | 2.64E-12 | 0.543005767   |
| 3       | Bag1          | 2.72E-12 | 0.673380114   |
| 3       | Acot13        | 2.73E-12 | 0.792367916   |
| 3       | PISD          | 3.37E-12 | 0.902733104   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 3       | Ppp1r14c | 3.44E-12 | 0.740632226   |
| 3       | Mea1     | 3.69E-12 | 0.669184941   |
| 3       | Gga1     | 3.72E-12 | 0.767377028   |
| 3       | Ahsa1    | 3.74E-12 | 0.776741044   |
| 3       | Serpina9 | 4.86E-12 | 0.955146999   |
| 3       | Fam167a  | 5.09E-12 | 0.518309203   |
| 3       | Fbxo16   | 5.39E-12 | 0.434246705   |
| 3       | Plip     | 5.53E-12 | 0.617343539   |
| 3       | Ly6c1    | 6.38E-12 | 1.345831691   |
| 3       | Arl6     | 6.81E-12 | 0.776118563   |
| 3       | Rassf7   | 7.23E-12 | 0.806375976   |
| 3       | Zc2hc1c  | 7.38E-12 | 0.545806034   |
| 3       | Prr13    | 8.07E-12 | 0.768017576   |
| 3       | Rilpl2   | 8.63E-12 | 0.728987537   |
| 3       | Gm16537  | 1.50E-11 | 0.456584011   |
| 3       | Nelfe    | 1.57E-11 | 0.715750451   |
| 3       | Thop1    | 1.72E-11 | 0.74494959    |
| 3       | Cmbl     | 1.77E-11 | 0.650626481   |
| 3       | Cluap1   | 1.81E-11 | 0.754808005   |
| 3       | Bad      | 2.07E-11 | 0.605683744   |
| 3       | Churc1   | 2.66E-11 | 0.785860357   |
| 3       | Dnal4    | 3.09E-11 | 0.764078932   |
| 3       | Spire2   | 3.21E-11 | 0.478290505   |
| 3       | Rwdd3    | 4.18E-11 | 0.482691191   |
| 3       | Ift20    | 4.47E-11 | 0.750111429   |
| 3       | Gm17586  | 6.58E-11 | 0.487440643   |
| 3       | Mrpl24   | 6.59E-11 | 0.66972194    |
| 3       | Nudt17   | 7.00E-11 | 0.459162836   |
| 3       | Diras2   | 7.05E-11 | 0.474181248   |
| 3       | Mrpl57   | 7.45E-11 | 0.716371097   |
| 3       | Rpgrip1l | 7.60E-11 | 0.595345982   |
| 3       | Lrrc34   | 7.91E-11 | 0.444579701   |
| 3       | Ift52    | 8.01E-11 | 0.692005005   |
| 3       | Ttc36    | 8.12E-11 | 0.522332749   |
| 3       | Gdpd1    | 8.48E-11 | 0.693848628   |
| 3       | Ogg1     | 1.02E-10 | 0.571855185   |
| 3       | Ndufc2   | 1.04E-10 | 0.677792318   |
| 3       | Pla2g16  | 1.26E-10 | 0.721613784   |
| 3       | Mrps17   | 1.31E-10 | 0.688969258   |
| 3       | Znhit2   | 1.37E-10 | 0.635600908   |
| 3       | Ceacam1  | 1.38E-10 | 0.793017203   |

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| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 3       | Isyna1  | 1.64E-10 | 0.810404443   |
| 3       | Cd82    | 1.74E-10 | 0.705510359   |
| 3       | Rfx2    | 1.90E-10 | 0.530431903   |
| 3       | Spint2  | 2.19E-10 | 0.561831168   |
| 3       | Gm11992 | 2.26E-10 | 0.439519311   |
| 3       | Polr3k  | 2.72E-10 | 0.716624448   |
| 3       | Pdxk    | 2.82E-10 | 0.659745187   |
| 3       | Celsr1  | 2.83E-10 | 0.549064387   |
| 3       | Tmem17  | 2.88E-10 | 0.573198715   |
| 3       | Abcb6   | 3.04E-10 | 0.507802948   |
| 3       | Wars    | 4.72E-10 | 0.666464211   |
| 3       | Ly6g6c  | 6.09E-10 | 0.741245022   |
| 3       | Cdpf1   | 6.14E-10 | 0.690747157   |
| 3       | Fam84b  | 6.64E-10 | 0.489901663   |
| 3       | Myo5b   | 6.82E-10 | 0.416632488   |
| 3       | Shisa8  | 6.86E-10 | 0.819759825   |
| 3       | Gm1673  | 9.74E-10 | 0.707878087   |
| 3       | Odf2    | 1.00E-09 | 0.606775099   |
| 3       | Spns1   | 1.13E-09 | 0.70875836    |
| 3       | Scd2    | 1.19E-09 | 0.746364168   |
| 3       | Carkd   | 1.20E-09 | 0.653057413   |
| 3       | Phtf1   | 1.22E-09 | 0.687683088   |
| 3       | Sirt3   | 1.43E-09 | 0.579165216   |
| 3       | Naga    | 1.46E-09 | 0.671937205   |
| 3       | Plxnb2  | 1.69E-09 | 0.734900634   |
| 3       | Mid1ip1 | 1.83E-09 | 0.742115924   |
| 3       | Dnajb2  | 2.03E-09 | 0.673337077   |
| 3       | Sec11c  | 2.20E-09 | 0.708648037   |
| 3       | Sec14l1 | 2.51E-09 | 0.69678572    |
| 3       | Asrgl1  | 2.56E-09 | 0.630459767   |
| 3       | Cep164  | 2.61E-09 | 0.725648998   |
| 3       | Oit1    | 2.63E-09 | 0.642679315   |
| 3       | Cipc    | 2.92E-09 | 0.526320936   |
| 3       | Hsbp1   | 2.96E-09 | 0.625822439   |
| 3       | Txnip   | 3.08E-09 | 0.816450315   |
| 3       | Wdr73   | 3.11E-09 | 0.545853226   |
| 3       | Nr2c2ap | 3.25E-09 | 0.651980442   |
| 3       | Cdkl2   | 3.41E-09 | 0.400949723   |
| 3       | Flt3l   | 3.61E-09 | 0.429383129   |
| 3       | Ropn1l  | 3.77E-09 | 0.432794086   |
| 3       | Cspp1   | 4.39E-09 | 0.650704086   |

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| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 3       | Misp     | 5.42E-09 | 0.556008268   |
| 3       | Mcee     | 5.51E-09 | 0.63968702    |
| 3       | Rpap3    | 5.53E-09 | 0.60282557    |
| 3       | Ift122   | 5.95E-09 | 0.563150349   |
| 3       | Fgfr1op  | 6.31E-09 | 0.650410608   |
| 3       | Tpd52l2  | 6.62E-09 | 0.61742398    |
| 3       | Phf10    | 7.99E-09 | 0.6916081     |
| 3       | Aes      | 8.05E-09 | 0.583398218   |
| 3       | Tesc     | 8.78E-09 | 0.459746161   |
| 3       | Gm26542  | 9.24E-09 | 0.420776896   |
| 3       | Ccdc157  | 9.76E-09 | 0.456961448   |
| 3       | Zdhhc1   | 1.01E-08 | 0.471728994   |
| 3       | Ttc30b   | 1.01E-08 | 0.435996635   |
| 3       | Baiap2l1 | 1.05E-08 | 0.525819469   |
| 3       | Chchd4   | 1.12E-08 | 0.66488058    |
| 3       | Ndufa12  | 1.13E-08 | 0.537187807   |
| 3       | Lfng     | 1.13E-08 | 0.524697672   |
| 3       | Ccno     | 1.28E-08 | 0.801045158   |
| 3       | Fbxw9    | 1.30E-08 | 0.596200097   |
| 3       | Gm42418  | 1.50E-08 | 0.650957869   |
| 3       | Lztf1    | 1.52E-08 | 0.664756018   |
| 3       | Pddc1    | 1.61E-08 | 0.701389631   |
| 3       | Vps13d   | 1.69E-08 | 0.538927206   |
| 3       | Wnt7b    | 2.05E-08 | 0.637327224   |
| 3       | Osbpl3   | 2.12E-08 | 0.684110222   |
| 3       | Ephx4    | 2.24E-08 | 0.459271432   |
| 3       | Nek2     | 2.35E-08 | 0.459148608   |
| 3       | Suds3    | 2.42E-08 | 0.633819106   |
| 3       | Abcb8    | 2.61E-08 | 0.624955748   |
| 3       | Papola   | 2.88E-08 | 0.624382019   |
| 3       | Cracr2b  | 3.02E-08 | 0.607570139   |
| 3       | Bbs5     | 3.37E-08 | 0.53079794    |
| 3       | Mipep    | 3.42E-08 | 0.486288537   |
| 3       | Rab25    | 3.49E-08 | 0.50991237    |
| 3       | Dync2li1 | 3.50E-08 | 0.657485739   |
| 3       | Mien1    | 3.57E-08 | 0.633393537   |
| 3       | Iqce     | 3.79E-08 | 0.49506886    |
| 3       | Tagln2   | 4.15E-08 | 0.574884915   |
| 3       | Pcnt     | 4.16E-08 | 0.571544161   |
| 3       | Pex11g   | 5.12E-08 | 0.552935127   |
| 3       | Frem2    | 5.13E-08 | 0.452973703   |

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| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Cep19         | 5.30E-08 | 0.564551628   |
| 3       | Fam229b       | 5.68E-08 | 0.565004164   |
| 3       | Dgcr6         | 6.31E-08 | 0.567325874   |
| 3       | Glx5          | 6.58E-08 | 0.5417873     |
| 3       | Zc3h14        | 6.85E-08 | 0.664704147   |
| 3       | Gm20661       | 7.01E-08 | 0.534240012   |
| 3       | Arhgap39      | 8.19E-08 | 0.545496139   |
| 3       | R3hdm4        | 8.23E-08 | 0.626323      |
| 3       | Tmc4          | 9.38E-08 | 0.760216813   |
| 3       | Qsox1         | 9.49E-08 | 0.643569237   |
| 3       | Pfkp          | 1.08E-07 | 0.62219752    |
| 3       | Rab36         | 1.15E-07 | 0.409993101   |
| 3       | Slf1          | 1.29E-07 | 0.501286141   |
| 3       | Bcl2l12       | 1.31E-07 | 0.542579826   |
| 3       | Bok           | 1.37E-07 | 0.691656947   |
| 3       | Pxk           | 1.41E-07 | 0.569791604   |
| 3       | Nin           | 1.47E-07 | 0.437435076   |
| 3       | Fkbp8         | 1.47E-07 | 0.548537533   |
| 3       | Ube2m         | 1.62E-07 | 0.560119718   |
| 3       | Epn3          | 1.70E-07 | 0.560445318   |
| 3       | Med19         | 1.81E-07 | 0.561568866   |
| 3       | Wfdc2         | 1.92E-07 | 0.86773041    |
| 3       | Mdm2          | 2.00E-07 | 0.707737475   |
| 3       | Dhx16         | 2.32E-07 | 0.466917675   |
| 3       | Spata24       | 2.60E-07 | 0.469211348   |
| 3       | Wdr19         | 2.67E-07 | 0.418638011   |
| 3       | Ank3          | 2.78E-07 | 0.64206601    |
| 3       | Heatr5a       | 2.90E-07 | 0.436071341   |
| 3       | 4932443I19Rik | 2.94E-07 | 0.429138409   |
| 3       | Arl2bp        | 3.02E-07 | 0.627683573   |
| 3       | Fdps          | 3.07E-07 | 0.678623323   |
| 3       | Nek1          | 3.43E-07 | 0.556205401   |
| 3       | Nme7          | 3.46E-07 | 0.531053633   |
| 3       | Psmc3ip       | 3.56E-07 | 0.523957582   |
| 3       | Smc4          | 3.68E-07 | 0.618362521   |
| 3       | Gnb2          | 3.71E-07 | 0.485780191   |
| 3       | 1500009L16Rik | 3.74E-07 | 0.536008204   |
| 3       | Slc44a4       | 4.09E-07 | 0.45762948    |
| 3       | Ech1          | 4.57E-07 | 0.582867015   |
| 3       | Sclt1         | 4.74E-07 | 0.612363118   |
| 3       | Mul1          | 4.76E-07 | 0.544230731   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Dnaaf5        | 5.06E-07 | 0.468897478   |
| 3       | Arl3          | 5.10E-07 | 0.570621362   |
| 3       | Ric8          | 5.23E-07 | 0.535261702   |
| 3       | Col27a1       | 5.32E-07 | 0.55949471    |
| 3       | Gm5617        | 5.39E-07 | 0.586321276   |
| 3       | Dtx3          | 6.95E-07 | 0.63064997    |
| 3       | Cdc14a        | 7.29E-07 | 0.47318792    |
| 3       | Mrpl39        | 7.32E-07 | 0.551042199   |
| 3       | Alms1         | 7.65E-07 | 0.539426037   |
| 3       | 2310030G06Rik | 7.67E-07 | 0.44075123    |
| 3       | Acot7         | 7.74E-07 | 0.607284043   |
| 3       | Stk11         | 7.83E-07 | 0.56603956    |
| 3       | Myb           | 7.91E-07 | 0.472860187   |
| 3       | Cldn7         | 8.07E-07 | 0.519895075   |
| 3       | Pex7          | 8.17E-07 | 0.605512127   |
| 3       | Erlin2        | 8.87E-07 | 0.435826635   |
| 3       | Casz1         | 9.70E-07 | 0.498538696   |
| 3       | Apbb1         | 9.91E-07 | 0.520725779   |
| 3       | Cuta          | 1.01E-06 | 0.514404042   |
| 3       | Pak4          | 1.06E-06 | 0.40107185    |
| 3       | Adrbk2        | 1.07E-06 | 0.475271079   |
| 3       | Dgat2         | 1.08E-06 | 0.436942495   |
| 3       | mt-Co1        | 1.12E-06 | 0.680319151   |
| 3       | Rnf181        | 1.13E-06 | 0.563493556   |
| 3       | Akap9         | 1.16E-06 | 0.623601044   |
| 3       | Cep89         | 1.20E-06 | 0.420700471   |
| 3       | Rogdi         | 1.20E-06 | 0.496594653   |
| 3       | Isoc2b        | 1.24E-06 | 0.54298924    |
| 3       | Irak1bp1      | 1.26E-06 | 0.557242338   |
| 3       | Gprc5c        | 1.26E-06 | 0.46192814    |
| 3       | Dxo           | 1.30E-06 | 0.442289307   |
| 3       | Fads3         | 1.32E-06 | 0.518267688   |
| 3       | Slc9a8        | 1.33E-06 | 0.482550729   |
| 3       | Galk1         | 1.34E-06 | 0.575497386   |
| 3       | Wrap53        | 1.38E-06 | 0.4481079     |
| 3       | Atp1a1        | 1.44E-06 | 0.550612791   |
| 3       | Spata7        | 1.55E-06 | 0.433176572   |
| 3       | Taf11         | 1.56E-06 | 0.560863024   |
| 3       | Tmem216       | 1.65E-06 | 0.536730414   |
| 3       | Six1          | 1.81E-06 | 0.54631317    |
| 3       | Ccnc          | 1.84E-06 | 0.433817954   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Pltp          | 1.85E-06 | 0.507795925   |
| 3       | H2afx         | 1.92E-06 | 0.663538948   |
| 3       | 1810043H04Rik | 2.13E-06 | 0.480032782   |
| 3       | Sox2          | 2.25E-06 | 0.577021196   |
| 3       | Cops5         | 2.55E-06 | 0.509485658   |
| 3       | Mt2           | 2.56E-06 | 0.721916288   |
| 3       | Calml4        | 2.57E-06 | 0.411742129   |
| 3       | Fkbp1         | 2.70E-06 | 0.400207735   |
| 3       | Hyls1         | 2.70E-06 | 0.490533417   |
| 3       | Aig1          | 2.76E-06 | 0.602868696   |
| 3       | 0610011F06Rik | 3.12E-06 | 0.57737583    |
| 3       | Kbtbd4        | 3.26E-06 | 0.402131218   |
| 3       | Wbp2          | 3.46E-06 | 0.555736973   |
| 3       | Ccdc61        | 3.59E-06 | 0.522308318   |
| 3       | 1110008L16Rik | 3.60E-06 | 0.557863671   |
| 3       | Zc3h6         | 3.84E-06 | 0.508025788   |
| 3       | Eif4g3        | 3.90E-06 | 0.518958218   |
| 3       | Nubpl         | 4.04E-06 | 0.484528186   |
| 3       | Fam161a       | 4.05E-06 | 0.497870176   |
| 3       | Ppp1r11       | 4.07E-06 | 0.502882777   |
| 3       | Lamtor2       | 4.28E-06 | 0.482227533   |
| 3       | Plet1         | 4.39E-06 | 0.608135707   |
| 3       | Pop5          | 4.56E-06 | 0.573387512   |
| 3       | Slc4a2        | 4.75E-06 | 0.557234271   |
| 3       | Grhpr         | 4.88E-06 | 0.510157494   |
| 3       | Suclg1        | 4.91E-06 | 0.532512733   |
| 3       | Ubald2        | 5.19E-06 | 0.55798901    |
| 3       | Ypel3         | 5.48E-06 | 0.5680993     |
| 3       | Yipf1         | 5.61E-06 | 0.498514613   |
| 3       | Blzf1         | 5.92E-06 | 0.500852941   |
| 3       | Myo1d         | 6.30E-06 | 0.447959999   |
| 3       | Me2           | 6.43E-06 | 0.466893749   |
| 3       | Cct7          | 6.68E-06 | 0.493525028   |
| 3       | Lgals4        | 6.80E-06 | 0.512460625   |
| 3       | Ahcyl1        | 7.50E-06 | 0.492809696   |
| 3       | Abcc1         | 7.97E-06 | 0.521604567   |
| 3       | Coq10a        | 8.11E-06 | 0.457478661   |
| 3       | Ccdc148       | 8.62E-06 | 0.486134608   |
| 3       | Sptan1        | 8.92E-06 | 0.591336275   |
| 3       | Tspan13       | 9.09E-06 | 0.45562822    |
| 3       | Cars          | 9.30E-06 | 0.548539678   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Usp22         | 9.63E-06 | 0.507184044   |
| 3       | Wdyhv1        | 9.67E-06 | 0.522521967   |
| 3       | Dyrk3         | 1.06E-05 | 0.479604179   |
| 3       | Cav2          | 1.09E-05 | 0.622013742   |
| 3       | Cdk2ap2       | 1.18E-05 | 0.471984285   |
| 3       | Hist1h2bc     | 1.18E-05 | 0.595146781   |
| 3       | Epb41l4b      | 1.27E-05 | 0.408821372   |
| 3       | Rita1         | 1.29E-05 | 0.428178545   |
| 3       | Hgs           | 1.32E-05 | 0.527053721   |
| 3       | 0610009B22Rik | 1.33E-05 | 0.534888385   |
| 3       | Ptges3        | 1.34E-05 | 0.542317764   |
| 3       | Atp1b1        | 1.39E-05 | 0.675998124   |
| 3       | Pebp1         | 1.40E-05 | 0.443856348   |
| 3       | Rassf9        | 1.40E-05 | 0.548831455   |
| 3       | Abr           | 1.65E-05 | 0.460944196   |
| 3       | Rrp7a         | 1.71E-05 | 0.490095352   |
| 3       | Eif3c         | 1.76E-05 | 0.484628736   |
| 3       | Ckmt1         | 1.78E-05 | 0.481509332   |
| 3       | Plvap         | 1.92E-05 | 0.540478808   |
| 3       | Wbp11         | 1.98E-05 | 0.53435809    |
| 3       | Mgst2         | 2.01E-05 | 0.613485412   |
| 3       | Rab11fip1     | 2.18E-05 | 0.428812293   |
| 3       | Itpr2         | 2.19E-05 | 0.453846938   |
| 3       | Sec23b        | 2.20E-05 | 0.50345631    |
| 3       | Tmem194       | 2.22E-05 | 0.405917978   |
| 3       | Etnk1         | 2.32E-05 | 0.509139061   |
| 3       | Anapc11       | 2.32E-05 | 0.468284242   |
| 3       | Gpx2          | 2.39E-05 | 0.642847404   |
| 3       | B4galt4       | 2.41E-05 | 0.422330367   |
| 3       | Cenpb         | 2.65E-05 | 0.534541468   |
| 3       | Hid1          | 2.76E-05 | 0.439074165   |
| 3       | Tpgs1         | 2.76E-05 | 0.435932243   |
| 3       | Tefm          | 2.78E-05 | 0.408132265   |
| 3       | Krcc1         | 2.83E-05 | 0.493790237   |
| 3       | Zmynd8        | 2.93E-05 | 0.488549236   |
| 3       | Trip4         | 2.93E-05 | 0.409077907   |
| 3       | Ndufc1        | 2.98E-05 | 0.451881259   |
| 3       | Ppdpf         | 3.17E-05 | 0.485614495   |
| 3       | Lrp10         | 3.17E-05 | 0.517487319   |
| 3       | Coasy         | 3.21E-05 | 0.459110461   |
| 3       | Ssna1         | 3.23E-05 | 0.512205908   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 3       | Trib3    | 3.31E-05 | 0.56329054    |
| 3       | Fam98c   | 3.33E-05 | 0.470468035   |
| 3       | Myl12b   | 3.58E-05 | 0.537358843   |
| 3       | Mrpl54   | 3.77E-05 | 0.477354675   |
| 3       | Gm38037  | 3.86E-05 | 0.423963771   |
| 3       | Napg     | 3.98E-05 | 0.452031357   |
| 3       | Fam83h   | 4.03E-05 | 0.49823045    |
| 3       | Cryz     | 4.11E-05 | 0.482482947   |
| 3       | Dicer1   | 4.16E-05 | 0.514059489   |
| 3       | Tmem138  | 4.32E-05 | 0.444627145   |
| 3       | Rcbtb2   | 4.60E-05 | 0.481859945   |
| 3       | Ndufaf7  | 4.62E-05 | 0.432222163   |
| 3       | Fam102a  | 4.73E-05 | 0.42051729    |
| 3       | Dmkn     | 4.90E-05 | 0.427905579   |
| 3       | Csde1    | 4.95E-05 | 0.459298164   |
| 3       | Plk4     | 5.02E-05 | 0.486476515   |
| 3       | Mettl20  | 5.24E-05 | 0.423813247   |
| 3       | Brd8     | 5.50E-05 | 0.497420377   |
| 3       | Appl2    | 5.69E-05 | 0.412355751   |
| 3       | Stard10  | 6.40E-05 | 0.460965404   |
| 3       | Gtf2i    | 6.45E-05 | 0.508386049   |
| 3       | Gas2l1   | 6.94E-05 | 0.440948399   |
| 3       | Gemin7   | 7.17E-05 | 0.459961163   |
| 3       | Ict1     | 7.39E-05 | 0.4709606     |
| 3       | Sod1     | 7.86E-05 | 0.488638281   |
| 3       | Endog    | 7.97E-05 | 0.433243627   |
| 3       | Rab3ip   | 8.26E-05 | 0.492420697   |
| 3       | Paf1     | 8.44E-05 | 0.419163242   |
| 3       | Mif4gd   | 8.70E-05 | 0.541565166   |
| 3       | Med25    | 9.10E-05 | 0.455226053   |
| 3       | Fam213a  | 9.85E-05 | 0.527543593   |
| 3       | Smim20   | 9.86E-05 | 0.464697938   |
| 3       | Slc25a46 | 0.000101 | 0.416385462   |
| 3       | Alkbh6   | 0.000101 | 0.415365863   |
| 3       | Zfp704   | 0.000102 | 0.448979811   |
| 3       | Hax1     | 0.000106 | 0.416630101   |
| 3       | Atxn2    | 0.000113 | 0.437760273   |
| 3       | Cox14    | 0.000117 | 0.405026253   |
| 3       | Minos1   | 0.00012  | 0.415054102   |
| 3       | BC029214 | 0.000122 | 0.432375796   |
| 3       | Syne2    | 0.000124 | 0.532662989   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 3       | Daam1    | 0.000124 | 0.433697697   |
| 3       | Tanc2    | 0.000124 | 0.581068223   |
| 3       | Skiv2l   | 0.000127 | 0.461682531   |
| 3       | Amdhd2   | 0.000131 | 0.417138398   |
| 3       | Dynll2   | 0.000135 | 0.438022235   |
| 3       | Oaz2     | 0.00014  | 0.475362704   |
| 3       | Cbap     | 0.000141 | 0.484176468   |
| 3       | Fam32a   | 0.000141 | 0.495944294   |
| 3       | Slc25a10 | 0.000146 | 0.425901844   |
| 3       | Yif1b    | 0.000149 | 0.426223918   |
| 3       | Rhoq     | 0.000149 | 0.456077841   |
| 3       | Cs       | 0.00015  | 0.426848653   |
| 3       | Npnt     | 0.000154 | 0.416667383   |
| 3       | Pitpna   | 0.000157 | 0.426767569   |
| 3       | Ppp1r35  | 0.000157 | 0.475710442   |
| 3       | Haghl    | 0.000162 | 0.459495224   |
| 3       | Crb3     | 0.000164 | 0.490669459   |
| 3       | Nrd1     | 0.000168 | 0.436947377   |
| 3       | Ildr1    | 0.000171 | 0.426394141   |
| 3       | Nr2f6    | 0.000172 | 0.497513192   |
| 3       | Nfe2l1   | 0.000177 | 0.449888241   |
| 3       | Tmem218  | 0.000183 | 0.412867871   |
| 3       | Tes      | 0.000187 | 0.423266607   |
| 3       | Fam234a  | 0.000211 | 0.486713166   |
| 3       | Med8     | 0.000214 | 0.432457748   |
| 3       | Macrod1  | 0.000219 | 0.427349908   |
| 3       | Bsdc1    | 0.00022  | 0.410538378   |
| 3       | Ralgds   | 0.000225 | 0.403564857   |
| 3       | Bola3    | 0.000225 | 0.446057782   |
| 3       | Card19   | 0.000236 | 0.446392365   |
| 3       | Ttc8     | 0.000243 | 0.446648183   |
| 3       | Mvb12a   | 0.000243 | 0.453428804   |
| 3       | Eps8l2   | 0.000255 | 0.431525868   |
| 3       | Fzr1     | 0.000257 | 0.439564133   |
| 3       | Stx18    | 0.000261 | 0.436718026   |
| 3       | Pir      | 0.000267 | 0.436154939   |
| 3       | Pnkp     | 0.000268 | 0.459692163   |
| 3       | Babam1   | 0.000269 | 0.435035699   |
| 3       | Nxt1     | 0.00028  | 0.413818024   |
| 3       | Cmtm4    | 0.000281 | 0.407370715   |
| 3       | Ebp      | 0.000282 | 0.485372991   |

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| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Tmem126b      | 0.000285 | 0.405004855   |
| 3       | Gle1          | 0.00029  | 0.467193785   |
| 3       | Pcm1          | 0.000296 | 0.513803856   |
| 3       | Usp19         | 0.000301 | 0.418653822   |
| 3       | Uhrf1bp1l     | 0.000319 | 0.439427638   |
| 3       | Mrpl43        | 0.000325 | 0.426920612   |
| 3       | Spop          | 0.00033  | 0.471150052   |
| 3       | Lgals3bp      | 0.000343 | 0.448750041   |
| 3       | Hspbp1        | 0.000356 | 0.435924608   |
| 3       | Slc25a1       | 0.00039  | 0.423288599   |
| 3       | Caml          | 0.000392 | 0.401394455   |
| 3       | Rif1          | 0.000401 | 0.410817953   |
| 3       | Sptbn1        | 0.000413 | 0.497218333   |
| 3       | 2510002D24Rik | 0.00043  | 0.439717659   |
| 3       | Ddx42         | 0.000431 | 0.442759644   |
| 3       | Pbxip1        | 0.000492 | 0.440394173   |
| 3       | Dnajb14       | 0.000514 | 0.404070128   |
| 3       | Pigyl         | 0.000514 | 0.434446603   |
| 3       | Slc31a1       | 0.000525 | 0.428211152   |
| 3       | Lsm10         | 0.000561 | 0.435122098   |
| 3       | Ubn2          | 0.000562 | 0.471320334   |
| 3       | Tmem109       | 0.000592 | 0.44748964    |
| 3       | Scrib         | 0.000592 | 0.459086952   |
| 3       | Tmem53        | 0.000608 | 0.42608826    |
| 3       | Pafah1b3      | 0.000647 | 0.461297373   |
| 3       | Wwox          | 0.000661 | 0.411547497   |
| 3       | Cdkn1a        | 0.000694 | 0.540651746   |
| 3       | Ndufv3        | 0.000697 | 0.407511537   |
| 3       | Krtcap3       | 0.000703 | 0.483382956   |
| 3       | Hacd1         | 0.000767 | 0.499031553   |
| 3       | Wbp1          | 0.000821 | 0.422357694   |
| 3       | Sgsm3         | 0.000833 | 0.408905994   |
| 3       | Mphosph8      | 0.000887 | 0.469284854   |
| 3       | Coq4          | 0.000908 | 0.417531426   |
| 3       | Btbd9         | 0.000939 | 0.425227249   |
| 3       | Ascc1         | 0.001007 | 0.419155517   |
| 3       | Adh7          | 0.001156 | 0.402091043   |
| 3       | Trmt1l        | 0.001168 | 0.426529958   |
| 3       | Cbr1          | 0.00117  | 0.441150913   |
| 3       | Traf4         | 0.001222 | 0.433589985   |
| 3       | Fabp5         | 0.001231 | 0.533172963   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 3       | Gak           | 0.001387 | 0.419830528   |
| 3       | Rbck1         | 0.001422 | 0.412391524   |
| 3       | Dnajc7        | 0.001505 | 0.437942715   |
| 3       | Slc35e4       | 0.001622 | 0.404909228   |
| 3       | Cttn          | 0.001622 | 0.431974532   |
| 3       | Pin1          | 0.00201  | 0.40705329    |
| 3       | Fasn          | 0.00221  | 0.421241318   |
| 3       | Agpat4        | 0.002612 | 0.42491386    |
| 3       | Hook2         | 0.002644 | 0.404938866   |
| 3       | Slc39a4       | 0.003177 | 0.412498764   |
| 3       | Ten1          | 0.003334 | 0.404935243   |
| 3       | Irf2bp1       | 0.004816 | 0.417606662   |
| 3       | Gclm          | 0.009502 | 0.412797608   |
| 4       | Hmgb2         | 2.09E-76 | 1.699244725   |
| 4       | Birc5         | 1.65E-62 | 1.641672639   |
| 4       | Smc4          | 5.75E-62 | 1.484280452   |
| 4       | Ube2c         | 3.79E-56 | 2.145619256   |
| 4       | Cdca3         | 2.11E-55 | 1.292562962   |
| 4       | H2afz         | 9.11E-53 | 1.172542347   |
| 4       | Cenpa         | 2.59E-52 | 1.7170923     |
| 4       | Ccna2         | 2.79E-52 | 1.040211181   |
| 4       | Stmn1         | 9.62E-52 | 1.427301848   |
| 4       | Top2a         | 1.90E-47 | 1.520530513   |
| 4       | Cdc20         | 3.51E-47 | 1.466847645   |
| 4       | Cks1b         | 8.99E-45 | 1.212859639   |
| 4       | Cdk1          | 1.19E-43 | 1.328129099   |
| 4       | Nusap1        | 3.94E-43 | 0.929336071   |
| 4       | Cenpf         | 7.04E-41 | 1.209351196   |
| 4       | Cenpe         | 1.32E-40 | 1.083750354   |
| 4       | Pttg1         | 2.38E-40 | 1.312802817   |
| 4       | Ccnb1         | 2.80E-39 | 1.073262882   |
| 4       | Esco2         | 1.33E-38 | 0.745089676   |
| 4       | H2afv         | 3.83E-38 | 0.957504051   |
| 4       | Knstrn        | 6.69E-38 | 0.981151294   |
| 4       | Arl6ip1       | 7.42E-38 | 1.1084841     |
| 4       | Spc24         | 1.18E-36 | 0.912265672   |
| 4       | Mki67         | 3.97E-34 | 0.677271983   |
| 4       | Prc1          | 5.40E-34 | 0.802104957   |
| 4       | Ect2          | 9.95E-34 | 0.802543931   |
| 4       | 2810417H13Rik | 4.80E-33 | 1.073304129   |
| 4       | Ccdc34        | 5.39E-33 | 1.056669241   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 4       | Cdca8   | 7.08E-32 | 0.91968694    |
| 4       | Ccnb2   | 1.39E-31 | 0.946485335   |
| 4       | Pbk     | 2.69E-31 | 0.840251451   |
| 4       | Tpx2    | 1.40E-30 | 0.704853439   |
| 4       | Aurkb   | 2.42E-30 | 0.564672233   |
| 4       | Hmgb1   | 6.67E-29 | 0.832928414   |
| 4       | Tacc3   | 2.04E-28 | 0.766270217   |
| 4       | Racgap1 | 5.05E-28 | 0.842732397   |
| 4       | Cdca2   | 2.09E-27 | 0.539399647   |
| 4       | Hmmr    | 3.54E-27 | 0.535060762   |
| 4       | Lockd   | 9.15E-27 | 0.821200604   |
| 4       | Plk1    | 2.93E-26 | 0.60980922    |
| 4       | Dlgap5  | 4.12E-25 | 0.514311856   |
| 4       | Kifc1   | 6.02E-25 | 0.497555767   |
| 4       | Mad2l1  | 1.45E-24 | 0.613423965   |
| 4       | Psnc1   | 1.45E-24 | 0.510152638   |
| 4       | Rrm2    | 1.54E-24 | 0.822118966   |
| 4       | Cdkn3   | 3.17E-24 | 0.739250495   |
| 4       | Fbxo5   | 7.15E-24 | 0.452746683   |
| 4       | Tubb5   | 8.25E-24 | 0.880668197   |
| 4       | Rfc4    | 9.74E-24 | 0.715262925   |
| 4       | Anp32e  | 2.11E-23 | 0.809230483   |
| 4       | H2afx   | 3.91E-23 | 0.891375594   |
| 4       | Ckap2l  | 4.09E-23 | 0.475537269   |
| 4       | Kif22   | 5.49E-23 | 0.5324948     |
| 4       | Hdgf    | 1.13E-22 | 0.72726775    |
| 4       | Spc25   | 1.48E-22 | 0.521015744   |
| 4       | Smc2    | 5.57E-22 | 0.689956614   |
| 4       | Pmf1    | 5.79E-22 | 0.761024655   |
| 4       | Fam64a  | 6.34E-22 | 0.55254808    |
| 4       | Gmnn    | 8.81E-22 | 0.631540842   |
| 4       | Bub1    | 1.21E-21 | 0.402988057   |
| 4       | Kif23   | 1.42E-21 | 0.562783304   |
| 4       | Wfdc2   | 1.63E-21 | 0.560326307   |
| 4       | Bub3    | 8.01E-21 | 0.80932574    |
| 4       | Tmpo    | 1.09E-20 | 0.8305883     |
| 4       | Ezh2    | 1.37E-20 | 0.666374801   |
| 4       | Aurka   | 1.95E-20 | 0.726288904   |
| 4       | Hn1     | 3.96E-20 | 0.749133567   |
| 4       | Kpna2   | 6.95E-20 | 0.636332505   |
| 4       | Tk1     | 1.79E-19 | 0.5913502     |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 4       | Sapcd2        | 2.31E-19 | 0.443964898   |
| 4       | Tuba1b        | 2.36E-19 | 0.741359857   |
| 4       | Casc5         | 2.91E-19 | 0.522459345   |
| 4       | Ckap2         | 5.31E-19 | 0.557454753   |
| 4       | Cks2          | 5.84E-19 | 0.711129728   |
| 4       | Cit           | 6.10E-19 | 0.519957868   |
| 4       | Rad51         | 1.31E-18 | 0.478546828   |
| 4       | Shcbp1        | 1.97E-18 | 0.466219459   |
| 4       | Mcm7          | 2.55E-18 | 0.680175698   |
| 4       | Nrm           | 6.97E-18 | 0.542738752   |
| 4       | Mcm5          | 7.88E-18 | 0.562603032   |
| 4       | Uhrf1         | 1.77E-17 | 0.431453255   |
| 4       | Hells         | 1.93E-17 | 0.474905129   |
| 4       | Gpsm2         | 2.11E-17 | 0.605665196   |
| 4       | Ube2t         | 3.90E-17 | 0.436348523   |
| 4       | Epcam         | 5.21E-17 | 0.65242094    |
| 4       | H1f0          | 8.49E-17 | 0.879063833   |
| 4       | 2700094K13Rik | 9.88E-17 | 0.735375317   |
| 4       | Aspm          | 2.55E-16 | 0.457011115   |
| 4       | Sgol2a        | 3.55E-16 | 0.471193553   |
| 4       | Ncapg         | 7.78E-16 | 0.425473994   |
| 4       | Rfc5          | 1.23E-15 | 0.567217078   |
| 4       | Prim1         | 1.98E-15 | 0.477658118   |
| 4       | Hmgb3         | 5.71E-15 | 0.56879187    |
| 4       | Krt19         | 7.77E-15 | 0.780988682   |
| 4       | Hmgn5         | 1.36E-14 | 0.543727346   |
| 4       | Lsm4          | 1.47E-14 | 0.555978794   |
| 4       | H1fx          | 1.65E-14 | 0.686049828   |
| 4       | Spag5         | 6.92E-14 | 0.405461877   |
| 4       | Terf1         | 7.56E-14 | 0.470274229   |
| 4       | Cenpm         | 8.05E-14 | 0.500563859   |
| 4       | Lmnb1         | 9.98E-14 | 0.476121593   |
| 4       | Krtcap2       | 1.08E-13 | 0.606182508   |
| 4       | Nucks1        | 1.44E-13 | 0.647200476   |
| 4       | Dnajc9        | 1.65E-13 | 0.627394732   |
| 4       | Lig1          | 2.14E-13 | 0.596810826   |
| 4       | Vrk1          | 2.99E-13 | 0.581853356   |
| 4       | Krt8          | 6.30E-13 | 0.580620051   |
| 4       | Nup37         | 9.67E-13 | 0.517286683   |
| 4       | Rrm1          | 1.28E-12 | 0.565198753   |
| 4       | Sap30         | 2.69E-12 | 0.697641474   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 4       | Cldn3    | 2.85E-12 | 0.41933633    |
| 4       | Mis18a   | 2.86E-12 | 0.423113963   |
| 4       | Ccdc18   | 3.74E-12 | 0.411524881   |
| 4       | Cldn7    | 3.97E-12 | 0.715331598   |
| 4       | Hmgn2    | 6.60E-12 | 0.411527405   |
| 4       | Reep6    | 1.06E-11 | 0.43603883    |
| 4       | Rangap1  | 2.42E-11 | 0.437507509   |
| 4       | Actl6a   | 5.61E-11 | 0.580875282   |
| 4       | Trib3    | 6.92E-11 | 0.516903483   |
| 4       | Lsm2     | 8.49E-11 | 0.573707647   |
| 4       | Rad21    | 1.34E-10 | 0.504004988   |
| 4       | Ubald2   | 1.54E-10 | 0.562865272   |
| 4       | Srsf6    | 1.65E-10 | 0.534373209   |
| 4       | Cdk4     | 1.96E-10 | 0.461786661   |
| 4       | Parp2    | 2.49E-10 | 0.450319511   |
| 4       | Rnaseh2c | 3.12E-10 | 0.476536234   |
| 4       | Dazap1   | 3.98E-10 | 0.491409829   |
| 4       | Mcm3     | 4.50E-10 | 0.459699736   |
| 4       | Reep4    | 5.41E-10 | 0.469055836   |
| 4       | Serbp1   | 7.85E-10 | 0.427905229   |
| 4       | Dbf4     | 9.41E-10 | 0.403237003   |
| 4       | Set      | 1.02E-09 | 0.497447173   |
| 4       | Arpc5l   | 1.05E-09 | 0.504898872   |
| 4       | Usp1     | 1.19E-09 | 0.41814722    |
| 4       | Aspa     | 1.54E-09 | 0.556612843   |
| 4       | Cbx1     | 1.83E-09 | 0.504729317   |
| 4       | Ewsr1    | 2.98E-09 | 0.41190292    |
| 4       | Dek      | 3.05E-09 | 0.495684889   |
| 4       | Ncaph2   | 3.51E-09 | 0.493220371   |
| 4       | Msln     | 8.31E-09 | 0.801570079   |
| 4       | Tubb4b   | 8.69E-09 | 0.540969378   |
| 4       | Gltp     | 9.97E-09 | 0.497241395   |
| 4       | Ddx39b   | 1.28E-08 | 0.469279398   |
| 4       | Sae1     | 1.44E-08 | 0.48347756    |
| 4       | Hnrnpa3  | 1.66E-08 | 0.499183106   |
| 4       | Sf3b4    | 1.76E-08 | 0.46778374    |
| 4       | Lsm5     | 2.12E-08 | 0.431917464   |
| 4       | Ilf2     | 2.26E-08 | 0.484909557   |
| 4       | Hnrnpf   | 2.58E-08 | 0.468105583   |
| 4       | Apobec3  | 2.69E-08 | 0.524774036   |
| 4       | Mrpl24   | 2.73E-08 | 0.437192994   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene      | p value  | fold change * |
|---------|-----------|----------|---------------|
| 4       | Slrp      | 3.85E-08 | 0.442164327   |
| 4       | Srsf1     | 3.91E-08 | 0.420153869   |
| 4       | Hnrnpa2b1 | 3.92E-08 | 0.429073299   |
| 4       | Trim28    | 4.39E-08 | 0.543605952   |
| 4       | Rfc2      | 4.84E-08 | 0.428180082   |
| 4       | Srsf3     | 6.25E-08 | 0.406717648   |
| 4       | Trim2     | 7.30E-08 | 0.486836006   |
| 4       | Ckap5     | 7.55E-08 | 0.400618847   |
| 4       | Larp7     | 8.42E-08 | 0.450065345   |
| 4       | Crabp2    | 9.19E-08 | 0.466057947   |
| 4       | Pnn       | 9.88E-08 | 0.417284896   |
| 4       | Asf1a     | 1.18E-07 | 0.407121823   |
| 4       | Rbm8a     | 1.85E-07 | 0.414288162   |
| 4       | Exosc8    | 2.02E-07 | 0.42842817    |
| 4       | Krt18     | 2.03E-07 | 0.429847807   |
| 4       | Ssrp1     | 2.15E-07 | 0.423177878   |
| 4       | Prpf40a   | 2.19E-07 | 0.415243073   |
| 4       | Taf15     | 2.60E-07 | 0.427822443   |
| 4       | Atf5      | 2.65E-07 | 0.42302881    |
| 4       | Rpf1      | 2.66E-07 | 0.412258556   |
| 4       | Phgdh     | 3.04E-07 | 0.463619671   |
| 4       | Dctpp1    | 3.40E-07 | 0.452639479   |
| 4       | Sptssb    | 3.40E-07 | 0.493972756   |
| 4       | Sypl      | 4.14E-07 | 0.493791752   |
| 4       | Dut       | 4.21E-07 | 0.437339746   |
| 4       | Alyref    | 4.67E-07 | 0.405100164   |
| 4       | Ngdn      | 4.76E-07 | 0.418391235   |
| 4       | Ranbp1    | 4.87E-07 | 0.446774765   |
| 4       | Anxa3     | 5.52E-07 | 0.537326836   |
| 4       | Krcc1     | 5.61E-07 | 0.401785359   |
| 4       | Cebpg     | 7.82E-07 | 0.419391864   |
| 4       | Eif2s1    | 1.02E-06 | 0.456357007   |
| 4       | Tyms      | 1.13E-06 | 0.42963662    |
| 4       | Lsm8      | 1.30E-06 | 0.427493331   |
| 4       | Gipc1     | 1.46E-06 | 0.424072031   |
| 4       | Nop56     | 1.63E-06 | 0.417032726   |
| 4       | Tspan8    | 2.06E-06 | 0.449022736   |
| 4       | Pcna      | 3.16E-06 | 0.416637388   |
| 4       | Psmd14    | 5.15E-06 | 0.404940768   |
| 4       | Sptssa    | 5.19E-06 | 0.427337688   |
| 4       | Papola    | 5.39E-06 | 0.406416533   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value   | fold change * |
|---------|---------|-----------|---------------|
| 4       | Smc6    | 1.15E-05  | 0.429235754   |
| 4       | Hat1    | 1.61E-05  | 0.404263578   |
| 4       | Cldn6   | 2.60E-05  | 0.433237121   |
| 5       | Ly6d    | 0         | 1.823742329   |
| 5       | Gsta4   | 0         | 1.799718775   |
| 5       | Wfdc2   | 0         | 1.407448719   |
| 5       | Epcam   | 5.52E-306 | 1.495413613   |
| 5       | Spint2  | 2.06E-303 | 1.29957543    |
| 5       | Krt7    | 5.44E-274 | 1.406820162   |
| 5       | Fxyd3   | 2.91E-253 | 1.2022928     |
| 5       | Krt19   | 3.33E-246 | 1.6637729     |
| 5       | Eif3f   | 1.19E-237 | 0.99878454    |
| 5       | Cyp2f2  | 4.94E-235 | 1.636193459   |
| 5       | Gsto1   | 5.89E-234 | 1.099143993   |
| 5       | Sfn     | 1.13E-224 | 1.372514743   |
| 5       | Clu     | 5.33E-220 | 1.688248324   |
| 5       | Klf5    | 8.95E-218 | 1.292656809   |
| 5       | Avpi1   | 8.50E-197 | 1.33007236    |
| 5       | S100a14 | 8.40E-184 | 1.090024812   |
| 5       | Rab25   | 8.54E-181 | 1.113232469   |
| 5       | Krt8    | 1.13E-180 | 1.067120122   |
| 5       | Bcam    | 5.56E-180 | 1.044792553   |
| 5       | Perp    | 1.05E-176 | 0.862367161   |
| 5       | Cd24a   | 4.98E-174 | 1.064994348   |
| 5       | Cldn7   | 2.29E-172 | 1.139356004   |
| 5       | Sprr1a  | 4.79E-170 | 1.924404217   |
| 5       | Fam3c   | 5.53E-169 | 1.030392425   |
| 5       | Foxq1   | 4.84E-165 | 1.202565787   |
| 5       | S100a16 | 1.39E-163 | 1.002635772   |
| 5       | Ezr     | 3.43E-162 | 0.811223963   |
| 5       | Anxa8   | 1.00E-158 | 1.068981423   |
| 5       | Gpx2    | 1.66E-154 | 1.075093028   |
| 5       | Pthlh   | 5.96E-153 | 1.675147473   |
| 5       | Lmo7    | 2.51E-150 | 1.16236807    |
| 5       | Cd9     | 1.75E-146 | 0.893497625   |
| 5       | Ahr     | 1.14E-140 | 1.040423783   |
| 5       | Areg    | 4.11E-140 | 1.441688972   |
| 5       | Krt18   | 5.03E-140 | 1.023428241   |
| 5       | Ces1d   | 7.77E-139 | 1.377788507   |
| 5       | Ywhaq   | 1.34E-138 | 0.769488738   |
| 5       | Aqp5    | 8.63E-134 | 1.096581051   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value   | fold change * |
|---------|---------------|-----------|---------------|
| 5       | Krt14         | 2.19E-133 | 0.762988309   |
| 5       | Col25a1       | 2.78E-129 | 0.974606673   |
| 5       | Dnajb4        | 1.50E-128 | 1.049293589   |
| 5       | Tacstd2       | 8.11E-127 | 0.894595737   |
| 5       | Cldn4         | 3.17E-125 | 1.187242058   |
| 5       | Cdkn1a        | 5.52E-120 | 1.066194182   |
| 5       | Hes6          | 2.63E-118 | 1.073897135   |
| 5       | Sprr2a3       | 3.02E-117 | 1.59824558    |
| 5       | Krt15         | 1.09E-116 | 1.603205892   |
| 5       | Anxa1         | 3.65E-115 | 0.798617909   |
| 5       | Msln          | 9.95E-115 | 1.449103797   |
| 5       | 2200002D01Rik | 3.64E-114 | 0.789004614   |
| 5       | Cdh13         | 2.18E-113 | 0.796460936   |
| 5       | Ccnd2         | 6.57E-113 | 0.683789951   |
| 5       | Fam107b       | 2.01E-112 | 0.899799481   |
| 5       | Tmc4          | 3.54E-110 | 0.775377894   |
| 5       | Shroom3       | 2.99E-108 | 0.973780211   |
| 5       | Gprc5a        | 1.48E-106 | 0.873727387   |
| 5       | Tspan1        | 2.37E-105 | 0.705290038   |
| 5       | Jup           | 1.76E-102 | 0.807700488   |
| 5       | Ppp2r2b       | 1.12E-100 | 0.765641105   |
| 5       | Ckmt1         | 3.06E-100 | 0.731857249   |
| 5       | Adam28        | 2.45E-99  | 0.734593886   |
| 5       | Ifrd1         | 1.09E-97  | 0.960610004   |
| 5       | Hspa4l        | 1.86E-97  | 0.836645834   |
| 5       | F3            | 1.30E-93  | 0.950336658   |
| 5       | Lsr           | 1.76E-93  | 0.624576766   |
| 5       | Aspa          | 1.09E-90  | 0.743207326   |
| 5       | Atp1b1        | 3.83E-90  | 0.784706966   |
| 5       | Fbxo2         | 7.18E-90  | 0.747419244   |
| 5       | Tspan8        | 2.18E-87  | 0.712289665   |
| 5       | Eya2          | 6.78E-87  | 0.631733398   |
| 5       | Homer2        | 2.66E-86  | 0.621848439   |
| 5       | Pdzk1ip1      | 2.76E-84  | 0.803179974   |
| 5       | Adh7          | 4.29E-84  | 0.850832014   |
| 5       | Aqp4          | 1.01E-83  | 0.704061924   |
| 5       | Plaur         | 1.05E-83  | 0.925931629   |
| 5       | Kcnk1         | 8.85E-83  | 0.631167608   |
| 5       | Krt6a         | 1.43E-82  | 1.179052619   |
| 5       | Noct          | 6.89E-82  | 0.796200429   |
| 5       | Trim2         | 3.27E-81  | 0.972738499   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene     | p value  | fold change * |
|---------|----------|----------|---------------|
| 5       | Urah     | 9.59E-81 | 0.535647957   |
| 5       | Gstm1    | 1.44E-79 | 0.905144709   |
| 5       | Ifitm1   | 2.63E-79 | 0.617802304   |
| 5       | Socs2    | 1.04E-78 | 0.739816349   |
| 5       | Taldo1   | 1.48E-78 | 0.643827317   |
| 5       | Pax9     | 3.67E-78 | 0.638048297   |
| 5       | Mapk13   | 2.56E-77 | 0.646654469   |
| 5       | Mgst2    | 2.36E-76 | 0.620835376   |
| 5       | Fam110c  | 1.56E-74 | 0.773549283   |
| 5       | Tpd52    | 4.31E-74 | 0.647999536   |
| 5       | Cdh1     | 9.93E-74 | 0.58127111    |
| 5       | Ly6e     | 2.71E-73 | 0.600721478   |
| 5       | Sox2     | 8.69E-73 | 0.570803499   |
| 5       | Elf3     | 2.66E-70 | 0.649554368   |
| 5       | Aig1     | 3.66E-70 | 0.622694527   |
| 5       | H2afj    | 1.39E-69 | 0.517490833   |
| 5       | Sox11    | 8.96E-69 | 0.694528798   |
| 5       | Krtcap3  | 2.24E-68 | 0.524221183   |
| 5       | Pmm1     | 3.48E-68 | 0.601376693   |
| 5       | Tsc22d1  | 1.36E-67 | 0.590012629   |
| 5       | Fermt1   | 3.75E-67 | 0.607104597   |
| 5       | Trappc6a | 1.65E-66 | 0.579276252   |
| 5       | Ube2d3   | 2.58E-66 | 0.462726859   |
| 5       | Nr4a1    | 3.43E-66 | 0.582892282   |
| 5       | Gclm     | 5.88E-66 | 0.670770257   |
| 5       | Tmem238  | 7.81E-66 | 0.597482297   |
| 5       | Ltbp4    | 1.16E-65 | 0.63008075    |
| 5       | Sypl     | 1.32E-65 | 0.590418761   |
| 5       | Klf13    | 1.38E-65 | 0.668064407   |
| 5       | Zfand6   | 2.53E-65 | 0.62477615    |
| 5       | Arl4a    | 2.76E-65 | 0.752022485   |
| 5       | Fgfbp1   | 1.26E-64 | 0.669872668   |
| 5       | Sox21    | 2.56E-64 | 0.537840195   |
| 5       | Syne4    | 3.47E-64 | 0.485808201   |
| 5       | Gltscr2  | 4.95E-64 | 0.553881575   |
| 5       | Serpinb5 | 9.60E-64 | 0.603707865   |
| 5       | Ripk4    | 2.44E-63 | 0.4344643     |
| 5       | Slc26a2  | 2.62E-61 | 0.614182987   |
| 5       | Tst      | 2.24E-60 | 0.838183829   |
| 5       | Lgals3   | 2.44E-60 | 0.460175307   |
| 5       | Rps29    | 4.79E-60 | 0.439224226   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 5       | Foxg1         | 1.25E-59 | 0.54418898    |
| 5       | Nudt14        | 1.63E-59 | 0.560800987   |
| 5       | Hspa1a        | 1.69E-59 | 0.566004702   |
| 5       | Tspan15       | 2.23E-59 | 0.516002989   |
| 5       | Adrb2         | 2.81E-59 | 0.578373688   |
| 5       | Alcam         | 3.09E-59 | 0.56401702    |
| 5       | Ehf           | 4.92E-59 | 0.456617423   |
| 5       | Mdh1          | 7.12E-59 | 0.479313179   |
| 5       | Ccnl1         | 1.76E-58 | 0.542134187   |
| 5       | Cystm1        | 1.83E-58 | 0.587334605   |
| 5       | Pitx1         | 2.10E-58 | 0.455578745   |
| 5       | Aldh3a1       | 6.18E-58 | 0.646308231   |
| 5       | Cbr2          | 8.83E-58 | 0.679583679   |
| 5       | Itgb4         | 1.15E-57 | 0.446384943   |
| 5       | Emp1          | 1.18E-57 | 0.637506789   |
| 5       | Rpl36al       | 2.49E-57 | 0.444724838   |
| 5       | SftpD         | 2.67E-57 | 0.821126351   |
| 5       | Rpl22l1       | 3.23E-57 | 0.654662092   |
| 5       | Klc3          | 1.01E-56 | 0.472485288   |
| 5       | Baz1a         | 3.25E-56 | 0.582798003   |
| 5       | Eif5          | 3.66E-56 | 0.505854904   |
| 5       | Msmo1         | 3.17E-55 | 0.675978131   |
| 5       | Tra2a         | 7.47E-54 | 0.519841171   |
| 5       | Plek2         | 1.44E-53 | 0.513315451   |
| 5       | Onecut2       | 2.10E-52 | 0.419023664   |
| 5       | Siva1         | 2.47E-52 | 0.569447979   |
| 5       | Tprg          | 5.15E-52 | 0.458403609   |
| 5       | Vill          | 5.53E-52 | 0.405087216   |
| 5       | Echs1         | 7.98E-52 | 0.516713908   |
| 5       | Hbegf         | 3.96E-51 | 0.708893827   |
| 5       | Cisd1         | 1.16E-50 | 0.455400569   |
| 5       | Nr4a2         | 1.20E-50 | 0.677983527   |
| 5       | 4930523C07Rik | 1.23E-50 | 0.482270676   |
| 5       | Srsf5         | 1.28E-50 | 0.498198786   |
| 5       | Tkt           | 3.30E-50 | 0.472776895   |
| 5       | Skil          | 1.28E-49 | 0.570850302   |
| 5       | Cldn3         | 1.89E-49 | 0.432574639   |
| 5       | Neat1         | 2.44E-49 | 0.545788157   |
| 5       | Dusp1         | 8.33E-49 | 0.744616758   |
| 5       | Ttc9          | 1.11E-48 | 0.501259888   |
| 5       | Crb3          | 2.36E-48 | 0.403532352   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene      | p value  | fold change * |
|---------|-----------|----------|---------------|
| 5       | Dedd2     | 3.63E-48 | 0.447072153   |
| 5       | Crabp2    | 5.90E-48 | 0.511949063   |
| 5       | Fkbp4     | 2.58E-47 | 0.443096846   |
| 5       | Vamp8     | 9.59E-47 | 0.411950435   |
| 5       | Slc39a4   | 1.16E-46 | 0.403338501   |
| 5       | Sdc1      | 1.22E-46 | 0.471129762   |
| 5       | Serpinb11 | 1.63E-46 | 0.496243971   |
| 5       | Rac3      | 2.58E-46 | 0.452807007   |
| 5       | Sf3b6     | 4.87E-46 | 0.457461267   |
| 5       | Anxa3     | 7.17E-46 | 0.559426601   |
| 5       | Epas1     | 9.63E-46 | 0.452833005   |
| 5       | Bhlhe40   | 1.29E-45 | 0.562917278   |
| 5       | Gpr87     | 1.35E-45 | 0.521678511   |
| 5       | Bace2     | 1.82E-45 | 0.4692982     |
| 5       | Osbpl3    | 3.78E-45 | 0.465178923   |
| 5       | Dcxr      | 9.06E-45 | 0.672287057   |
| 5       | Kcnq1ot1  | 4.74E-44 | 0.536988101   |
| 5       | Wnt4      | 1.40E-43 | 0.413804289   |
| 5       | Krt20     | 1.99E-43 | 0.618807541   |
| 5       | Basp1     | 1.11E-42 | 0.499327344   |
| 5       | Ahsa1     | 1.47E-42 | 0.463698614   |
| 5       | Id2       | 3.57E-42 | 0.556134007   |
| 5       | Krt23     | 4.85E-42 | 0.615104861   |
| 5       | Cirbp     | 9.52E-42 | 0.47314332    |
| 5       | Atp6v1d   | 5.86E-41 | 0.453453062   |
| 5       | Ffar4     | 7.41E-41 | 0.480120726   |
| 5       | Krt17     | 1.38E-40 | 0.89130566    |
| 5       | Stard10   | 1.79E-40 | 0.417009424   |
| 5       | Ythdc1    | 2.70E-40 | 0.497619451   |
| 5       | Taf10     | 1.28E-39 | 0.422822438   |
| 5       | Ptprf     | 1.58E-39 | 0.445409529   |
| 5       | Crip2     | 1.97E-39 | 0.404957852   |
| 5       | Tubb4b    | 5.20E-39 | 0.424714072   |
| 5       | Cav2      | 7.15E-39 | 0.466475616   |
| 5       | Tgif1     | 7.62E-39 | 0.517843747   |
| 5       | Fuca2     | 2.35E-38 | 0.414862067   |
| 5       | Klf3      | 1.29E-37 | 0.489393873   |
| 5       | Larp1b    | 3.84E-37 | 0.409555219   |
| 5       | Ces1f     | 5.51E-37 | 0.664659383   |
| 5       | Zfp36l1   | 7.78E-37 | 0.448269892   |
| 5       | Sh3yl1    | 1.17E-36 | 0.408547222   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value   | fold change * |
|---------|---------------|-----------|---------------|
| 5       | Pgap2         | 1.27E-36  | 0.414988997   |
| 5       | Grasp         | 1.55E-36  | 0.473683042   |
| 5       | Pmaip1        | 2.06E-36  | 0.441415136   |
| 5       | Ttc14         | 6.91E-36  | 0.437815966   |
| 5       | Rab10         | 1.31E-35  | 0.413027455   |
| 5       | Pnrc1         | 1.67E-35  | 0.437132969   |
| 5       | Lypd2         | 1.71E-35  | 0.460247181   |
| 5       | Limk2         | 5.24E-35  | 0.412945914   |
| 5       | Rbm25         | 8.15E-35  | 0.416736317   |
| 5       | Egln3         | 9.24E-35  | 0.46293       |
| 5       | Isg20         | 2.50E-34  | 0.41866963    |
| 5       | Hras          | 4.87E-34  | 0.426117724   |
| 5       | 2010111I01Rik | 3.14E-33  | 0.453622238   |
| 5       | Cmip          | 4.23E-33  | 0.431550406   |
| 5       | Lmo4          | 4.41E-33  | 0.409316773   |
| 5       | Atf3          | 8.73E-33  | 0.574906675   |
| 5       | Tnfaip8       | 8.79E-33  | 0.496419666   |
| 5       | Cd14          | 3.33E-32  | 0.437825816   |
| 5       | Srxn1         | 7.18E-31  | 0.505193637   |
| 5       | Lurap1l       | 2.06E-30  | 0.458032088   |
| 5       | Tuba4a        | 3.08E-30  | 0.443768815   |
| 5       | Gpd2          | 5.90E-30  | 0.400374097   |
| 5       | Alkbh1        | 7.14E-30  | 0.416258748   |
| 5       | Bpgm          | 2.55E-28  | 0.48403594    |
| 5       | Fam213a       | 1.42E-27  | 0.413876048   |
| 5       | Sema3c        | 2.04E-27  | 0.402883861   |
| 5       | Btg1          | 6.87E-27  | 0.409404998   |
| 5       | Ltf           | 1.16E-26  | 1.127846318   |
| 5       | 8430408G22Rik | 3.08E-24  | 0.400525108   |
| 5       | Klf6          | 8.51E-24  | 0.453172451   |
| 5       | Dnaja4        | 8.89E-23  | 0.412636914   |
| 5       | Reg3g         | 5.85E-17  | 0.816313433   |
| 5       | Nppc          | 1.42E-14  | 0.435486781   |
| 5       | Hp            | 6.72E-11  | 0.54110486    |
| 5       | Lcn2          | 1.22E-06  | 0.40051354    |
| 6       | Krt5          | 1.73E-160 | 2.70169159    |
| 6       | Hspb1         | 4.03E-102 | 2.352654542   |
| 6       | Krt14         | 1.16E-80  | 1.861942819   |
| 6       | Ecm1          | 4.03E-57  | 1.283212506   |
| 6       | Hspb8         | 1.45E-48  | 1.193185125   |
| 6       | Sfn           | 1.51E-46  | 1.208900876   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 6       | Fxyd3         | 2.03E-46 | 1.188783905   |
| 6       | Lmo1          | 2.66E-42 | 1.0482416     |
| 6       | Ucp2          | 5.66E-41 | 0.969347328   |
| 6       | Perp          | 1.76E-39 | 1.060742747   |
| 6       | Urah          | 8.92E-39 | 1.022160071   |
| 6       | Krt17         | 1.28E-34 | 1.538286299   |
| 6       | Ociad2        | 6.75E-34 | 0.861583524   |
| 6       | Mt2           | 2.95E-33 | 1.179799001   |
| 6       | Hcar2         | 6.92E-33 | 1.14246861    |
| 6       | S100a10       | 1.36E-32 | 0.86248736    |
| 6       | Glul          | 1.84E-32 | 1.004749956   |
| 6       | Palmd         | 1.19E-30 | 0.662876847   |
| 6       | Cat           | 4.19E-30 | 0.770632009   |
| 6       | Mt1           | 6.90E-30 | 1.010100191   |
| 6       | Vsnl1         | 1.34E-29 | 0.748300885   |
| 6       | Pycard        | 5.09E-28 | 0.641749445   |
| 6       | Rab27b        | 4.61E-27 | 0.764431584   |
| 6       | Ly6a          | 4.72E-27 | 1.256282604   |
| 6       | Dusp6         | 7.15E-27 | 0.944542107   |
| 6       | App           | 7.00E-25 | 0.735958439   |
| 6       | Lgals3        | 1.32E-23 | 0.970603435   |
| 6       | Ifitm10       | 1.46E-23 | 0.560275709   |
| 6       | Anxa3         | 9.37E-23 | 0.774080625   |
| 6       | Pitx1         | 2.84E-22 | 0.777985542   |
| 6       | Phlda3        | 1.30E-21 | 0.654972738   |
| 6       | Hbegf         | 2.88E-20 | 0.814119199   |
| 6       | Serpinb5      | 3.78E-20 | 0.780318302   |
| 6       | Sostdc1       | 4.49E-20 | 0.531542218   |
| 6       | Anxa1         | 1.18E-19 | 0.726204859   |
| 6       | Gpx2          | 1.87E-19 | 0.842846027   |
| 6       | Anxa8         | 2.13E-19 | 0.64698534    |
| 6       | Slc25a5       | 5.22E-19 | 0.547523139   |
| 6       | Ramp3         | 1.10E-18 | 0.870583271   |
| 6       | Upk3bl        | 4.68E-18 | 0.824493095   |
| 6       | Krt7          | 2.84E-17 | 0.609909275   |
| 6       | Stra6         | 7.44E-17 | 0.412823249   |
| 6       | 4930523C07Rik | 7.98E-17 | 0.76489862    |
| 6       | Lypd3         | 1.36E-16 | 0.598813942   |
| 6       | Ppp2r2c       | 1.71E-16 | 0.516668251   |
| 6       | Tacstd2       | 2.44E-16 | 0.717621174   |
| 6       | Atf3          | 4.35E-16 | 0.805879665   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene          | p value  | fold change * |
|---------|---------------|----------|---------------|
| 6       | Kif21a        | 4.43E-16 | 0.600197857   |
| 6       | Lad1          | 8.32E-16 | 0.529739919   |
| 6       | F11r          | 8.92E-16 | 0.561874315   |
| 6       | Ctsc          | 1.36E-15 | 0.642391313   |
| 6       | Tuba4a        | 1.82E-15 | 0.605311681   |
| 6       | Ackr3         | 3.25E-15 | 0.679141426   |
| 6       | Ube2f         | 5.02E-15 | 0.444797805   |
| 6       | Pdlim1        | 7.40E-15 | 0.549094039   |
| 6       | Golim4        | 1.02E-14 | 0.511986894   |
| 6       | Yrdc          | 1.17E-14 | 0.473819644   |
| 6       | Moxd1         | 1.30E-14 | 0.404377203   |
| 6       | Serpinb10     | 1.67E-14 | 0.535691601   |
| 6       | Plk2          | 2.10E-14 | 0.574277784   |
| 6       | Arrdc4        | 2.52E-14 | 0.522173748   |
| 6       | Vps37b        | 4.14E-14 | 0.531471042   |
| 6       | Arhgdin       | 4.81E-14 | 0.556256228   |
| 6       | Krt6a         | 5.02E-14 | 0.834887315   |
| 6       | Gsr           | 8.63E-14 | 0.516382833   |
| 6       | Ly6d          | 2.07E-13 | 0.449578828   |
| 6       | 4833423E24Rik | 2.80E-13 | 0.429423241   |
| 6       | Lrrkip1       | 3.93E-13 | 0.519202158   |
| 6       | Col17a1       | 4.03E-13 | 0.579740033   |
| 6       | Vwa1          | 4.60E-13 | 0.412993852   |
| 6       | Dsp           | 5.53E-13 | 0.479454787   |
| 6       | Lurap1l       | 1.10E-12 | 0.608959793   |
| 6       | Trim29        | 1.59E-12 | 0.57623139    |
| 6       | S100a14       | 1.68E-12 | 0.595859093   |
| 6       | Lgals7        | 2.38E-12 | 0.649004239   |
| 6       | Sdc1          | 7.19E-12 | 0.450036667   |
| 6       | Avpi1         | 7.43E-12 | 0.406648268   |
| 6       | Klf4          | 1.54E-11 | 0.565079882   |
| 6       | Runx1         | 1.61E-11 | 0.415458682   |
| 6       | Bcl11b        | 2.00E-11 | 0.468412659   |
| 6       | Krt13         | 2.28E-11 | 1.003836193   |
| 6       | Arl13b        | 2.34E-11 | 0.476262798   |
| 6       | Itga6         | 2.50E-11 | 0.55962991    |
| 6       | Areg          | 3.25E-11 | 0.661198968   |
| 6       | Icam1         | 5.52E-11 | 0.534631556   |
| 6       | Gabrp         | 8.14E-11 | 0.589977198   |
| 6       | Ly6e          | 8.61E-11 | 0.507594294   |
| 6       | Arl4c         | 1.37E-10 | 0.541357766   |

Table S2: Cluster specific genes identified by the differential analysis in the Organoid.

| cluster | gene    | p value  | fold change * |
|---------|---------|----------|---------------|
| 6       | Flrt3   | 1.48E-10 | 0.466178683   |
| 6       | Cnot6l  | 1.51E-10 | 0.475989263   |
| 6       | Ifitm1  | 1.75E-10 | 0.719885128   |
| 6       | Wnt10a  | 1.86E-10 | 0.454621744   |
| 6       | Cyp4b1  | 2.32E-10 | 0.410247258   |
| 6       | Irx5    | 2.75E-10 | 0.43702258    |
| 6       | Cpne8   | 3.25E-10 | 0.402605298   |
| 6       | Coq10b  | 3.98E-10 | 0.467785657   |
| 6       | Ets2    | 4.34E-10 | 0.427612991   |
| 6       | Rras2   | 6.77E-10 | 0.403817736   |
| 6       | Dnaja1  | 7.38E-10 | 0.471449538   |
| 6       | Gpr87   | 1.29E-09 | 0.51605069    |
| 6       | Pltp    | 2.13E-09 | 0.428198535   |
| 6       | Osr2    | 2.22E-09 | 0.47861804    |
| 6       | Emp2    | 2.41E-09 | 0.408645029   |
| 6       | Tns4    | 2.67E-09 | 0.430436239   |
| 6       | Ehf     | 6.37E-09 | 0.460849163   |
| 6       | Gltscr2 | 6.76E-09 | 0.412091472   |
| 6       | Pthlh   | 8.32E-09 | 0.525894148   |
| 6       | Serinc2 | 1.25E-08 | 0.411984368   |
| 6       | Klf5    | 1.73E-08 | 0.439197594   |
| 6       | Ifi202b | 1.79E-08 | 0.462310932   |
| 6       | Trp63   | 2.47E-08 | 0.483953156   |
| 6       | Cav2    | 3.90E-08 | 0.405539251   |
| 6       | Id4     | 3.91E-08 | 0.406099324   |
| 6       | Emp1    | 4.44E-08 | 0.450827154   |
| 6       | Acsl3   | 5.77E-08 | 0.410278803   |
| 6       | Tnfaip8 | 9.24E-08 | 0.433261253   |
| 6       | Cbr2    | 1.62E-07 | 0.500896843   |
| 6       | Nrip1   | 3.84E-07 | 0.408480517   |
| 6       | Lamc2   | 4.30E-07 | 0.404450092   |
| 6       | Dusp14  | 7.15E-07 | 0.427487973   |
| 6       | Gsto1   | 1.09E-06 | 0.693475535   |
| 6       | Ltf     | 1.39E-06 | 0.659725534   |
| 6       | Sgk1    | 1.69E-06 | 0.517439731   |
| 6       | Prss23  | 3.00E-06 | 0.407644186   |
| 6       | Plek2   | 5.44E-06 | 0.403550912   |
| 6       | Fst     | 8.80E-06 | 0.655697395   |
| 6       | Fgfbp1  | 5.69E-05 | 0.578848018   |
| 6       | Krt16   | 0.002544 | 0.477537959   |
| 6       | Cldn4   | 0.006403 | 0.455986765   |

Table S3. Differentially expressed genes between Lgr5\_1 and Lgr5\_2

| gene     | fold change * | p value  | Adjusted p value |
|----------|---------------|----------|------------------|
| Lgals1   | -3.933507993  | 1.19E-23 | 1.80E-19         |
| Sparc    | -3.311605515  | 8.50E-17 | 1.28E-12         |
| Dcn      | -3.145369214  | 2.72E-11 | 4.10E-07         |
| Col3a1   | -3.115959694  | 6.31E-14 | 9.50E-10         |
| Ctla2a   | -2.703667543  | 9.40E-09 | 1.42E-04         |
| Bgn      | -2.696418013  | 1.89E-16 | 2.84E-12         |
| Col1a1   | -2.644233003  | 7.39E-15 | 1.11E-10         |
| Igfbp3   | -2.485017539  | 1.38E-07 | 2.08E-03         |
| Serpinh1 | -2.462043746  | 1.22E-11 | 1.84E-07         |
| Serpinf1 | -2.449164351  | 2.55E-13 | 3.84E-09         |
| Col1a2   | -2.383334282  | 1.51E-13 | 2.28E-09         |
| Igfbp7   | -2.33686282   | 6.08E-09 | 9.17E-05         |
| Vim      | -2.296674529  | 9.34E-10 | 1.41E-05         |
| Timp3    | -2.204728746  | 1.41E-08 | 2.13E-04         |
| Sfrp1    | -2.159555637  | 9.94E-08 | 1.50E-03         |
| Klf2     | -2.127980984  | 1.24E-07 | 1.86E-03         |
| Col5a2   | -2.085115373  | 2.86E-11 | 4.31E-07         |
| Id3      | -2.044335654  | 1.21E-08 | 1.82E-04         |
| Rcn3     | -1.996299999  | 1.23E-11 | 1.85E-07         |
| Aebp1    | -1.937583694  | 9.14E-11 | 1.38E-06         |
| B2m      | -1.863180825  | 5.85E-16 | 8.82E-12         |
| Timp1    | -1.859544689  | 6.56E-10 | 9.89E-06         |
| Igfbp4   | -1.774322692  | 1.15E-07 | 1.73E-03         |
| Wbp5     | -1.744268061  | 2.90E-11 | 4.37E-07         |
| Cpxm1    | -1.731016617  | 1.54E-05 | 2.31E-01         |
| Selm     | -1.661642553  | 4.60E-10 | 6.92E-06         |
| Tceal8   | -1.63665571   | 2.04E-09 | 3.07E-05         |
| Cxcl12   | -1.629281246  | 1.45E-06 | 2.18E-02         |
| Cald1    | -1.622908226  | 1.51E-11 | 2.27E-07         |
| Sdc2     | -1.603558565  | 3.77E-07 | 5.68E-03         |
| Ccl7     | -1.556483232  | 4.76E-06 | 7.17E-02         |
| Ccdc80   | -1.553517777  | 1.44E-05 | 2.17E-01         |
| Postn    | -1.51433019   | 9.31E-08 | 1.40E-03         |
| Pcolce   | -1.509460638  | 1.14E-07 | 1.72E-03         |
| Cdkn2a   | -1.501499782  | 4.63E-09 | 6.98E-05         |
| Rasl11a  | -1.459399716  | 2.86E-05 | 4.31E-01         |
| Nov      | -1.45069933   | 1.67E-06 | 2.51E-02         |
| Gng11    | -1.445587687  | 5.10E-09 | 7.68E-05         |
| Fbln2    | -1.436744772  | 5.46E-08 | 8.22E-04         |
| Nsg1     | -1.430892805  | 1.14E-08 | 1.71E-04         |
| Mif      | -1.39557716   | 1.25E-07 | 1.88E-03         |

Table S3. Differentially expressed genes between Lgr5\_1 and Lgr5\_2

| gene     | fold change * | p value  | Adjusted p value |
|----------|---------------|----------|------------------|
| Myl9     | -1.386630671  | 2.50E-05 | 3.76E-01         |
| Plac8    | -1.354033347  | 1.22E-07 | 1.84E-03         |
| Cst3     | -1.350747955  | 3.68E-07 | 5.54E-03         |
| Grem1    | -1.327497424  | 6.40E-08 | 9.64E-04         |
| Efemp2   | -1.314370574  | 2.97E-08 | 4.48E-04         |
| Ngfrap1  | -1.291234465  | 2.18E-08 | 3.28E-04         |
| Lrp1     | -1.260921713  | 3.90E-08 | 5.88E-04         |
| Loxl1    | -1.255623869  | 4.97E-11 | 7.49E-07         |
| Tmsb10   | -1.244032611  | 3.70E-07 | 5.57E-03         |
| Cmtm3    | -1.232241829  | 4.37E-10 | 6.59E-06         |
| Col6a1   | -1.227051286  | 2.83E-07 | 4.26E-03         |
| Mxra8    | -1.220722439  | 3.49E-06 | 5.25E-02         |
| Lhfp     | -1.199633293  | 1.79E-07 | 2.70E-03         |
| Pdlim2   | -1.196746414  | 3.18E-05 | 4.79E-01         |
| Timp2    | -1.191294124  | 1.44E-06 | 2.16E-02         |
| Fam162a  | -1.189048038  | 2.13E-06 | 3.21E-02         |
| Cd302    | -1.178399798  | 6.72E-06 | 1.01E-01         |
| Tubb6    | -1.172764921  | 1.22E-05 | 1.83E-01         |
| Col12a1  | -1.166954559  | 1.16E-06 | 1.74E-02         |
| Emp3     | -1.134346907  | 6.47E-06 | 9.75E-02         |
| Csf1     | -1.133642051  | 2.12E-06 | 3.20E-02         |
| Nudt4    | -1.09960902   | 1.25E-07 | 1.88E-03         |
| Eva1b    | -1.086625163  | 1.26E-06 | 1.90E-02         |
| Ctsz     | -1.077181056  | 5.26E-07 | 7.93E-03         |
| Cdc42ep3 | -1.077014363  | 3.92E-06 | 5.90E-02         |
| Map1lc3a | -1.071689564  | 2.28E-06 | 3.44E-02         |
| Lbh      | -1.054211443  | 1.49E-06 | 2.24E-02         |
| Prrx1    | -1.013627606  | 5.10E-09 | 7.68E-05         |
| Pde1a    | -0.989365337  | 5.10E-09 | 7.68E-05         |
| Wisp1    | -0.977155312  | 4.15E-08 | 6.25E-04         |
| Has2     | -0.972452553  | 8.74E-06 | 1.32E-01         |
| Mfap2    | -0.964101319  | 2.19E-06 | 3.29E-02         |
| Fstl1    | -0.943913823  | 1.22E-07 | 1.84E-03         |
| Nr2f1    | -0.942654875  | 1.67E-06 | 2.52E-02         |
| Calu     | -0.931663582  | 5.34E-06 | 8.04E-02         |
| Pdgfrb   | -0.9271987    | 1.67E-06 | 2.52E-02         |
| Fbln1    | -0.920710523  | 5.14E-06 | 7.75E-02         |
| Fhl2     | -0.915380446  | 2.94E-05 | 4.42E-01         |
| Olfml3   | -0.90752279   | 1.67E-06 | 2.52E-02         |
| Slc7a2   | -0.86789767   | 6.43E-06 | 9.69E-02         |
| Lgi2     | -0.867138283  | 8.95E-06 | 1.35E-01         |

Table S3. Differentially expressed genes between Lgr5\_1 and Lgr5\_2

| gene    | fold change * | p value  | Adjusted p value |
|---------|---------------|----------|------------------|
| Ptgs1   | -0.859029386  | 1.21E-05 | 1.82E-01         |
| Plod2   | -0.836713919  | 1.66E-06 | 2.50E-02         |
| Pdlim4  | -0.81599942   | 8.74E-06 | 1.32E-01         |
| Cdh11   | -0.807624682  | 4.15E-08 | 6.25E-04         |
| Ctsk    | -0.800363412  | 8.74E-06 | 1.32E-01         |
| Dpysl3  | -0.791210488  | 5.77E-06 | 8.69E-02         |
| Psmd5   | -0.744240167  | 1.50E-07 | 2.26E-03         |
| Phldb2  | -0.730963361  | 8.74E-06 | 1.32E-01         |
| S100a1  | -0.724680758  | 1.29E-05 | 1.95E-01         |
| Rab34   | -0.711155006  | 3.10E-05 | 4.68E-01         |
| Lama4   | -0.708976763  | 1.67E-06 | 2.52E-02         |
| Plpp3   | -0.683348996  | 8.74E-06 | 1.32E-01         |
| Myeov2  | -0.682177996  | 2.53E-05 | 3.82E-01         |
| Kdelr3  | -0.679283329  | 6.57E-06 | 9.90E-02         |
| Tomm5   | -0.675096251  | 2.61E-05 | 3.93E-01         |
| Scarf2  | -0.63974762   | 8.74E-06 | 1.32E-01         |
| Map4    | -0.622943559  | 1.42E-05 | 2.14E-01         |
| Qpct    | -0.60556909   | 8.74E-06 | 1.32E-01         |
| Gem     | -0.524298072  | 6.44E-06 | 9.71E-02         |
| Slc30a5 | -0.420916332  | 1.04E-05 | 1.57E-01         |
| Psme1   | 0.843882334   | 1.37E-05 | 2.07E-01         |
| Tuba4a  | 0.948936605   | 1.54E-05 | 2.32E-01         |
| Gltscr2 | 0.968232152   | 2.78E-05 | 4.18E-01         |
| Cirbp   | 0.995095114   | 6.35E-06 | 9.56E-02         |
| Aig1    | 1.033823533   | 3.10E-06 | 4.67E-02         |
| H2-D1   | 1.095027446   | 3.82E-07 | 5.76E-03         |
| Pitx1   | 1.109255302   | 1.61E-05 | 2.42E-01         |
| Ezr     | 1.13588339    | 2.60E-05 | 3.92E-01         |
| Anxa1   | 1.1586122     | 1.38E-06 | 2.07E-02         |
| Tmc4    | 1.167227289   | 5.47E-06 | 8.24E-02         |
| Eif3f   | 1.204483522   | 1.93E-08 | 2.91E-04         |
| Ly6e    | 1.318418726   | 2.52E-06 | 3.80E-02         |
| Krt8    | 1.378755843   | 1.15E-06 | 1.73E-02         |
| Krt18   | 1.382895674   | 4.20E-07 | 6.33E-03         |
| Anxa8   | 1.394677198   | 9.45E-07 | 1.42E-02         |
| Lmo7    | 1.397189572   | 1.08E-05 | 1.63E-01         |
| Tacstd2 | 1.403784564   | 3.49E-08 | 5.26E-04         |
| Trim2   | 1.420821066   | 4.52E-06 | 6.81E-02         |
| Perp    | 1.425856709   | 3.26E-08 | 4.91E-04         |
| Rab25   | 1.44441173    | 8.96E-06 | 1.35E-01         |
| Hes6    | 1.513525565   | 1.09E-05 | 1.64E-01         |

Table S3. Differentially expressed genes between Lgr5\_1 and Lgr5\_2

| gene    | fold change * | p value  | Adjusted p value |
|---------|---------------|----------|------------------|
| S100a16 | 1.547725061   | 3.59E-07 | 5.41E-03         |
| Cd24a   | 1.631796389   | 1.87E-07 | 2.82E-03         |
| Avpi1   | 1.728311437   | 5.73E-08 | 8.63E-04         |
| Sprr1a  | 1.763943958   | 1.93E-05 | 2.91E-01         |
| Gsto1   | 1.795945872   | 7.93E-07 | 1.20E-02         |
| S100a14 | 1.833403534   | 6.10E-10 | 9.19E-06         |
| Spint2  | 2.001677383   | 1.74E-12 | 2.62E-08         |
| Klf5    | 2.031702639   | 1.65E-11 | 2.48E-07         |
| Gpx2    | 2.05373539    | 7.96E-09 | 1.20E-04         |
| Krt19   | 2.093457581   | 1.01E-07 | 1.53E-03         |
| Clu     | 2.111669841   | 1.58E-06 | 2.38E-02         |
| Krt7    | 2.206029512   | 2.46E-09 | 3.71E-05         |
| Cyp2f2  | 2.304594388   | 2.07E-10 | 3.13E-06         |
| Epcam   | 2.324802668   | 1.39E-10 | 2.10E-06         |
| Gsta4   | 2.445766921   | 1.49E-13 | 2.24E-09         |
| Wfdc2   | 2.562240003   | 2.60E-16 | 3.92E-12         |
| Fxyd3   | 2.600897447   | 4.96E-11 | 7.48E-07         |
| Sfn     | 2.771746625   | 8.38E-09 | 1.26E-04         |
| Krt14   | 2.877080886   | 3.45E-09 | 5.20E-05         |
| Ly6d    | 2.998619786   | 2.66E-15 | 4.00E-11         |

\* fold change for differentially expressed genes between epithelial cluster and fibroblast cluster is na

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene     | p value   | Adjusted p value | fold change * |
|----------|-----------|------------------|---------------|
| Col1a1   | 0         | 0                | -2.417279479  |
| Sfrp1    | 5.93E-216 | 8.9335E-212      | -2.050607432  |
| Grem1    | 3.80E-209 | 5.7247E-205      | -1.326195833  |
| Wisp1    | 2.04E-206 | 3.0733E-202      | -1.034760698  |
| Lrp1     | 2.59E-178 | 3.9018E-174      | -1.080624682  |
| Krt6a    | 1.70E-141 | 2.5611E-137      | 1.734564734   |
| Rspo3    | 5.12E-128 | 7.7133E-124      | -0.854205222  |
| Bicc1    | 2.70E-119 | 4.0676E-115      | -0.627935942  |
| Sox2     | 7.05E-115 | 1.0621E-110      | 0.730680136   |
| Cdh1     | 1.25E-105 | 1.8831E-101      | 0.685627869   |
| Fermt2   | 5.20E-105 | 7.8338E-101      | -0.670145046  |
| Tgfb1i1  | 3.05E-91  | 4.59483E-87      | -0.406135268  |
| Barx1    | 1.09E-88  | 1.64209E-84      | -0.494256723  |
| Nkd1     | 1.89E-82  | 2.84729E-78      | -0.403924455  |
| Zeb2     | 4.56E-80  | 6.86964E-76      | -0.386152116  |
| Plpp3    | 1.05E-79  | 1.58183E-75      | -0.577786008  |
| Isl1     | 2.45E-79  | 3.69093E-75      | -0.442622614  |
| Wnt4     | 4.73E-71  | 7.12575E-67      | 0.503058554   |
| Sdc1     | 4.88E-67  | 7.35172E-63      | 0.650822984   |
| Egr1     | 5.49E-63  | 8.27069E-59      | -0.623132231  |
| Sulf1    | 3.33E-62  | 5.01665E-58      | -0.388753969  |
| Dkk3     | 4.93E-61  | 7.42705E-57      | -0.390418704  |
| Celsr2   | 2.84E-56  | 4.27846E-52      | 0.407509855   |
| Hic1     | 1.28E-53  | 1.92832E-49      | -0.280492456  |
| Wnt7b    | 2.93E-51  | 4.41405E-47      | 0.353789992   |
| Cd44     | 5.02E-48  | 7.56263E-44      | -0.44968687   |
| Slc9a3r1 | 2.92E-47  | 4.39898E-43      | 0.509971116   |
| Dab2     | 8.79E-46  | 1.32421E-41      | -0.242275728  |
| Dkk2     | 1.92E-44  | 2.89248E-40      | -0.363645129  |
| Ddb1     | 5.12E-44  | 7.71328E-40      | -0.473092731  |
| Ryk      | 5.40E-43  | 8.1351E-39       | -0.40274682   |
| Apoe     | 2.09E-42  | 3.14859E-38      | -0.845713006  |
| Cdh2     | 3.67E-42  | 5.52886E-38      | -0.198896953  |
| Celsr1   | 4.36E-41  | 6.56834E-37      | 0.257165445   |
| Hmga2    | 5.16E-41  | 7.77354E-37      | -0.436220037  |
| Nfatc4   | 7.27E-40  | 1.09523E-35      | -0.272372705  |
| Pin1     | 2.56E-38  | 3.85664E-34      | -0.419157068  |
| Macf1    | 1.17E-37  | 1.76261E-33      | -0.317061243  |
| Grb10    | 1.31E-37  | 1.97352E-33      | -0.379438099  |
| Wnt5b    | 4.74E-37  | 7.14081E-33      | 0.249084125   |
| Mark1    | 9.67E-36  | 1.45679E-31      | -0.264954223  |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene     | p value  | Adjusted p value | fold change * |
|----------|----------|------------------|---------------|
| Thra     | 4.08E-33 | 6.14652E-29      | -0.341759039  |
| Sfrp2    | 3.72E-32 | 5.60418E-28      | -0.444073376  |
| Wnt5a    | 4.15E-32 | 6.25198E-28      | -0.229987584  |
| Wisp2    | 6.85E-32 | 1.03195E-27      | -0.278648466  |
| Ror2     | 7.80E-32 | 1.17507E-27      | -0.169814016  |
| Amotl2   | 8.64E-32 | 1.30162E-27      | -0.304828052  |
| Cdc42    | 1.50E-31 | 2.25975E-27      | -0.321796466  |
| Fzd1     | 7.10E-31 | 1.06962E-26      | -0.442886045  |
| Nrarp    | 7.91E-31 | 1.19164E-26      | 0.22491565    |
| Ift20    | 1.55E-30 | 2.33508E-26      | -0.348695342  |
| Ddit3    | 8.25E-30 | 1.24286E-25      | -0.430943586  |
| Fgf10    | 3.42E-29 | 5.15223E-25      | -0.152134687  |
| Fgf2     | 5.11E-29 | 7.69822E-25      | -0.122412679  |
| Ndrg2    | 1.18E-28 | 1.77767E-24      | -0.192032154  |
| Lats2    | 3.23E-28 | 4.866E-24        | -0.195186234  |
| Hoxb9    | 4.33E-27 | 6.52315E-23      | -0.150486117  |
| Frat2    | 1.24E-26 | 1.86806E-22      | 0.361014923   |
| Pfdn5    | 2.43E-26 | 3.6608E-22       | 0.266938178   |
| Cpe      | 2.36E-25 | 3.55534E-21      | -0.331713893  |
| Gli3     | 6.31E-25 | 9.50602E-21      | -0.166624355  |
| Fzd2     | 3.02E-23 | 4.54963E-19      | -0.248391977  |
| Aes      | 3.09E-23 | 4.65509E-19      | 0.223429383   |
| Rbpj     | 1.44E-22 | 2.16936E-18      | -0.223764532  |
| Tbl1x    | 2.21E-22 | 3.32937E-18      | -0.273468921  |
| Itga3    | 2.29E-22 | 3.44989E-18      | 0.195630047   |
| Mdfic    | 2.66E-22 | 4.00729E-18      | -0.174773969  |
| Fgfr2    | 4.24E-22 | 6.38756E-18      | 0.212687772   |
| Wnt10a   | 5.36E-22 | 8.07484E-18      | 0.244819878   |
| Cela1    | 8.15E-22 | 1.2278E-17       | -0.126230919  |
| Dact3    | 1.80E-21 | 2.7117E-17       | -0.104079969  |
| Tbx18    | 2.02E-21 | 3.04313E-17      | -0.10092606   |
| Tmem237  | 2.87E-21 | 4.32366E-17      | -0.238283434  |
| Mgat3    | 5.78E-21 | 8.70757E-17      | 0.23832028    |
| Gpc3     | 1.69E-20 | 2.54599E-16      | -0.214025262  |
| Mdfi     | 7.81E-20 | 1.17658E-15      | 0.257787219   |
| Siah2    | 1.36E-19 | 2.04884E-15      | 0.312883507   |
| Bambi    | 3.68E-19 | 5.54392E-15      | -0.296468378  |
| Grk5     | 3.60E-18 | 5.4234E-14       | -0.085501132  |
| Prickle1 | 1.51E-17 | 2.27482E-13      | -0.121539401  |
| Foxo1    | 3.22E-17 | 4.85093E-13      | 0.274652345   |
| Lrrk2    | 3.58E-17 | 5.39327E-13      | -0.099864181  |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene     | p value  | Adjusted p value | fold change * |
|----------|----------|------------------|---------------|
| Jade1    | 5.89E-17 | 8.87329E-13      | 0.228514563   |
| Notch1   | 6.38E-17 | 9.61147E-13      | 0.169478053   |
| Wls      | 1.41E-16 | 2.12417E-12      | 0.241246489   |
| Mesdc2   | 2.10E-16 | 3.16365E-12      | -0.189623031  |
| Myc      | 3.70E-16 | 5.57405E-12      | -0.140662223  |
| Tle1     | 1.00E-15 | 1.5065E-11       | -0.217873228  |
| Lef1     | 3.19E-15 | 4.80574E-11      | -0.050941156  |
| Mark2    | 1.91E-14 | 2.87742E-10      | 0.222153377   |
| Ctnnd1   | 2.07E-14 | 3.11846E-10      | 0.254802347   |
| Nfkb1    | 5.83E-14 | 8.7829E-10       | -0.307350099  |
| Dact1    | 6.12E-14 | 9.21978E-10      | -0.085365     |
| Sox9     | 6.19E-14 | 9.32524E-10      | -0.205147347  |
| Cby1     | 1.42E-13 | 2.13923E-09      | -0.048461522  |
| Leo1     | 2.57E-13 | 3.87171E-09      | -0.160187699  |
| Zranb1   | 5.44E-13 | 8.19536E-09      | 0.207734333   |
| Wnt2     | 1.25E-12 | 1.88313E-08      | -0.094587216  |
| Hnf1b    | 1.65E-12 | 2.48573E-08      | 0.07483575    |
| Frzb     | 3.32E-12 | 5.00158E-08      | -0.06627257   |
| Ptpnu    | 9.16E-12 | 1.37995E-07      | 0.103105686   |
| Mitf     | 1.74E-11 | 2.62131E-07      | -0.05739222   |
| Wdr61    | 1.97E-11 | 2.96781E-07      | -0.081460082  |
| Rnf43    | 1.01E-10 | 1.52157E-06      | 0.066628535   |
| Bmp2     | 2.74E-10 | 4.12781E-06      | -0.185847093  |
| Cul3     | 2.86E-10 | 4.30859E-06      | -0.131242655  |
| Lzts2    | 3.07E-10 | 4.62496E-06      | -0.163820725  |
| Arl6     | 4.63E-10 | 6.9751E-06       | 0.147176807   |
| Fgfr3    | 5.79E-10 | 8.72264E-06      | 0.084323394   |
| Fzd6     | 7.15E-10 | 1.07715E-05      | 0.081749737   |
| Rtf1     | 8.52E-10 | 1.28354E-05      | 0.167125558   |
| Cpz      | 1.06E-09 | 1.59689E-05      | -0.052267872  |
| Csnk1a1  | 1.55E-09 | 2.33508E-05      | 0.169838207   |
| Rnf146   | 1.71E-09 | 2.57612E-05      | 0.167324547   |
| Brd7     | 3.14E-09 | 4.73041E-05      | 0.163507728   |
| Dapk3    | 3.83E-09 | 5.7699E-05       | -0.13469034   |
| Yap1     | 4.87E-09 | 7.33666E-05      | -0.141855645  |
| Bcl7b    | 1.85E-08 | 0.000278703      | -0.115950244  |
| Scyl2    | 2.58E-08 | 0.000388677      | 0.120768975   |
| Snai2    | 3.11E-08 | 0.000468522      | 0.062689869   |
| Cthrc1   | 3.52E-08 | 0.000530288      | -0.128516155  |
| Dlx5     | 8.01E-08 | 0.001206707      | 0.056965971   |
| Ctnnbip1 | 8.99E-08 | 0.001354344      | 0.036223499   |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene    | p value  | Adjusted p value | fold change * |
|---------|----------|------------------|---------------|
| Lrrkip2 | 9.23E-08 | 0.0013905        | -0.105309299  |
| Tmem64  | 9.52E-08 | 0.001434188      | 0.090315285   |
| Cav1    | 1.47E-07 | 0.002214555      | -0.051032733  |
| Amer1   | 2.08E-07 | 0.00313352       | -0.088446486  |
| Znrf3   | 2.61E-07 | 0.003931965      | 0.070201801   |
| Csnk2a1 | 2.80E-07 | 0.0042182        | 0.007946896   |
| Csnk1e  | 2.82E-07 | 0.00424833       | 0.120188685   |
| Ctnnb1  | 3.17E-07 | 0.004775605      | -0.052174692  |
| Pygo1   | 3.21E-07 | 0.004835865      | -0.041827844  |
| Lgr6    | 4.09E-07 | 0.006161585      | 0.043947399   |
| Ccne1   | 4.37E-07 | 0.006583405      | -0.057992969  |
| Wwtr1   | 4.73E-07 | 0.007125745      | -0.152225013  |
| Tnks2   | 5.59E-07 | 0.008421335      | 0.037144848   |
| Apc2    | 7.14E-07 | 0.01075641       | -0.026729328  |
| Sulf2   | 7.79E-07 | 0.011735635      | -0.08311142   |
| Nxn     | 1.11E-06 | 0.01672215       | -0.082020971  |
| Prkaa2  | 1.20E-06 | 0.018078         | 0.057890821   |
| Pitx2   | 1.73E-06 | 0.02606245       | -0.046251241  |
| Grk6    | 1.86E-06 | 0.0280209        | -0.060314905  |
| Rac1    | 2.21E-06 | 0.03329365       | -0.122547277  |
| Hdac2   | 2.22E-06 | 0.03344443       | 0.094308498   |
| Sdhaf2  | 2.27E-06 | 0.03419755       | -0.050852087  |
| Fzd9    | 2.82E-06 | 0.0424833        | 0.004458985   |
| Zbed3   | 3.44E-06 | 1                | -0.045022167  |
| Ccny    | 3.68E-06 | 1                | -0.003919382  |
| Rapgef1 | 3.83E-06 | 1                | -0.091136814  |
| Stk11   | 3.94E-06 | 1                | 0.068838472   |
| Csnk2b  | 4.05E-06 | 1                | -0.114546653  |
| Spin1   | 4.66E-06 | 1                | -0.074678397  |
| Tsc2    | 5.43E-06 | 1                | -0.108050268  |
| Csnk1d  | 6.16E-06 | 1                | -0.05169917   |
| Smarca4 | 6.84E-06 | 1                | 0.121338748   |
| Rab5a   | 7.34E-06 | 1                | -0.027589762  |
| Fuz     | 8.47E-06 | 1                | 0.108637648   |
| Stk3    | 1.17E-05 | 1                | -0.084757707  |
| Nkd2    | 1.20E-05 | 1                | -0.089899039  |
| Ptk7    | 1.42E-05 | 1                | -0.134187373  |
| Usp34   | 1.65E-05 | 1                | 0.076338795   |
| Vps35   | 1.71E-05 | 1                | -0.05744949   |
| Porcn   | 1.83E-05 | 1                | 0.110977464   |
| Emd     | 2.28E-05 | 1                | 0.021164651   |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene    | p value    | Adjusted p value | fold change * |
|---------|------------|------------------|---------------|
| Lgr4    | 2.37E-05   | 1                | 0.06642679    |
| Cxxc4   | 2.58E-05   | 1                | 0.063717357   |
| Fbxw4   | 2.86E-05   | 1                | 0.078385115   |
| Fzd7    | 4.06E-05   | 1                | -0.03730797   |
| Ubr5    | 4.08E-05   | 1                | -0.113145126  |
| Tsku    | 4.21E-05   | 1                | -0.020428155  |
| Ankrd10 | 6.29E-05   | 1                | 0.101557441   |
| Tlr2    | 6.57E-05   | 1                | -0.055188942  |
| Sall1   | 8.85E-05   | 1                | 0.025324497   |
| Dixdc1  | 8.95E-05   | 1                | -0.036681037  |
| Tbl1xr1 | 9.54E-05   | 1                | 0.087626162   |
| Sostdc1 | 0.000104   | 1                | 0.074587285   |
| Abl2    | 0.00012059 | 1                | 0.074690087   |
| Tcf7l1  | 0.00012906 | 1                | 0.093160312   |
| Nle1    | 0.00014944 | 1                | 0.074386474   |
| Wwox    | 0.00015859 | 1                | 0.089419296   |
| Csnk1g3 | 0.00016839 | 1                | 0.023078542   |
| Trpm4   | 0.00021108 | 1                | 0.063699468   |
| Psen1   | 0.00022286 | 1                | 0.09829427    |
| Vax2    | 0.00028417 | 1                | -0.02386274   |
| Mapk14  | 0.00031616 | 1                | 0.090239092   |
| Otulin  | 0.00033122 | 1                | 0.024367665   |
| Hdac1   | 0.00038486 | 1                | -0.021267021  |
| Nkx2-5  | 0.00042167 | 1                | -0.019961361  |
| Rspo1   | 0.00048441 | 1                | 0.022761686   |
| Atp6ap2 | 0.0004851  | 1                | -0.064110236  |
| Caprin2 | 0.00068611 | 1                | -0.038781858  |
| Trabd2b | 0.00092294 | 1                | -0.015032806  |
| Ube2b   | 0.00092569 | 1                | 0.086211341   |
| Dvl2    | 0.00093744 | 1                | -0.059385282  |
| Sox4    | 0.00106926 | 1                | -0.114822694  |
| Abl1    | 0.0011186  | 1                | -0.08366194   |
| Prkaa1  | 0.00116852 | 1                | -0.046110112  |
| Fzd3    | 0.00120823 | 1                | 0.06236498    |
| Sfrp4   | 0.0012433  | 1                | -0.040209253  |
| Amotl1  | 0.00145182 | 1                | 0.028986574   |
| Mbd2    | 0.00159507 | 1                | -0.073097285  |
| Ctr9    | 0.00163659 | 1                | 0.096035546   |
| Fbxw11  | 0.00170686 | 1                | 0.060969713   |
| Draxin  | 0.00201063 | 1                | -0.021057574  |
| Gsc     | 0.00205909 | 1                | -0.00483016   |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene     | p value    | Adjusted p value | fold change * |
|----------|------------|------------------|---------------|
| Pias4    | 0.00218513 | 1                | 0.102036716   |
| Paf1     | 0.00276107 | 1                | 0.087900118   |
| Limd1    | 0.0030196  | 1                | 0.035416968   |
| Ddx3x    | 0.00343283 | 1                | -0.013738181  |
| Uty      | 0.00351923 | 1                | 0.048749741   |
| Klf4     | 0.0037502  | 1                | -0.102242394  |
| Dvl1     | 0.00396404 | 1                | -0.032856209  |
| Gsk3b    | 0.00453161 | 1                | 0.063315946   |
| Xiap     | 0.00463015 | 1                | 0.077914288   |
| Tmem198  | 0.00483477 | 1                | -0.03981833   |
| Ilk      | 0.00503374 | 1                | -0.076754831  |
| Snx3     | 0.00549417 | 1                | -0.027514186  |
| Cdh3     | 0.00549621 | 1                | 0.029779749   |
| Ankrd6   | 0.00618002 | 1                | 0.025651019   |
| Chd8     | 0.00683122 | 1                | 0.087213955   |
| Calcoco1 | 0.00786322 | 1                | -0.022313222  |
| Csnk2a2  | 0.00823044 | 1                | -0.056982695  |
| Zfp703   | 0.00891291 | 1                | -0.065388706  |
| Ror1     | 0.01008176 | 1                | -0.016047226  |
| Pygo2    | 0.0114283  | 1                | 0.010489079   |
| Cdc73    | 0.01186762 | 1                | 0.048984726   |
| Hbp1     | 0.01196868 | 1                | 0.064060667   |
| Aspm     | 0.01392319 | 1                | 0.019374713   |
| Ldb1     | 0.01475674 | 1                | 0.025900348   |
| Naip2    | 0.0149579  | 1                | 0.0093315     |
| Wnt7a    | 0.0149579  | 1                | 0.010225992   |
| Fzd10    | 0.0149579  | 1                | 0.018959307   |
| Shisa2   | 0.01591465 | 1                | -0.017566202  |
| Stk4     | 0.01612986 | 1                | 0.035509028   |
| Tcf7     | 0.01791038 | 1                | 0.019966643   |
| G3bp1    | 0.01823693 | 1                | -0.030564453  |
| Pten     | 0.01836483 | 1                | -0.068320346  |
| Med12    | 0.02111411 | 1                | -0.04918339   |
| Tax1bp3  | 0.02480969 | 1                | 0.00528615    |
| Kdm6a    | 0.02828886 | 1                | 0.034115465   |
| Hhex     | 0.02855046 | 1                | 0.023354833   |
| Senp2    | 0.03008416 | 1                | -0.055125294  |
| Gli1     | 0.03034247 | 1                | -0.001780326  |
| Ppm1a    | 0.03332061 | 1                | 0.067439637   |
| Fzd5     | 0.03349694 | 1                | -0.011541053  |
| Kank1    | 0.03438915 | 1                | -0.017331951  |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene    | p value    | Adjusted p value | fold change * |
|---------|------------|------------------|---------------|
| Axin2   | 0.03946118 | 1                | -0.022545858  |
| Tnks    | 0.04031097 | 1                | 0.021434674   |
| Sox7    | 0.04223134 | 1                | -0.005385194  |
| Tiam1   | 0.04315055 | 1                | 0.059861428   |
| Arntl   | 0.04385047 | 1                | 0.007523399   |
| Wnt9a   | 0.04923634 | 1                | -0.01757598   |
| Gsk3a   | 0.0513927  | 1                | 0.0621353     |
| Eda     | 0.05249952 | 1                | -0.021427623  |
| Rnf138  | 0.05508831 | 1                | 0.048413618   |
| Lrp6    | 0.06447433 | 1                | -0.055066801  |
| Lats1   | 0.07192667 | 1                | 0.018196299   |
| Apc     | 0.07417088 | 1                | 0.058867228   |
| Park2   | 0.08275677 | 1                | -0.000390483  |
| Nog     | 0.08280885 | 1                | -0.02753193   |
| Tcf7l2  | 0.08561023 | 1                | 0.060397479   |
| Axin1   | 0.09408773 | 1                | -0.054253646  |
| Bcl9    | 0.09971873 | 1                | 0.05256694    |
| Ccar2   | 0.10187454 | 1                | 0.027034351   |
| Tmem88  | 0.10227135 | 1                | 0.001618228   |
| Csnk1g1 | 0.11220255 | 1                | 0.01570548    |
| Fzd8    | 0.12134457 | 1                | -0.018023561  |
| Ccdc88c | 0.12167533 | 1                | 0.007841937   |
| Sox17   | 0.12167533 | 1                | 0.008290613   |
| Lgr5    | 0.12587765 | 1                | 0.015579089   |
| Csnk1g2 | 0.12873887 | 1                | 0.029543061   |
| Lrrk1   | 0.13133465 | 1                | 0.066591302   |
| Wnt6    | 0.13364641 | 1                | 0.022724968   |
| Invs    | 0.14069419 | 1                | -0.026452533  |
| Bcl9l   | 0.14451088 | 1                | -0.015301848  |
| Mad2l2  | 0.14851633 | 1                | -0.023587458  |
| Mllt3   | 0.15435939 | 1                | 0.06238386    |
| Tle4    | 0.1636389  | 1                | 0.029045883   |
| Celsr3  | 0.17913684 | 1                | -0.005023602  |
| Smad3   | 0.17961683 | 1                | -0.045975293  |
| Ccnd1   | 0.18020117 | 1                | 0.024563149   |
| Fgf9    | 0.18204407 | 1                | -0.004744227  |
| Cyld    | 0.19226783 | 1                | 0.013097711   |
| Six3    | 0.22462014 | 1                | -0.005745769  |
| Ctnnd2  | 0.23209037 | 1                | -0.025029647  |
| NIk     | 0.23244543 | 1                | -0.024732111  |
| Rnf220  | 0.24037291 | 1                | 0.031606625   |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| gene       | p value    | Adjusted p value | fold change * |
|------------|------------|------------------|---------------|
| Lrp5       | 0.24358948 | 1                | -0.004959042  |
| Wnt10b     | 0.24817421 | 1                | -0.009564426  |
| Ctdnep1    | 0.26188105 | 1                | 0.004854009   |
| Gata3      | 0.26193576 | 1                | 0.008821771   |
| Klh12      | 0.29226297 | 1                | -0.00096131   |
| Zbtb33     | 0.30782307 | 1                | -0.007131993  |
| Wnt16      | 0.30845578 | 1                | 0.010041711   |
| Ppp2r3a    | 0.31126921 | 1                | -0.018113983  |
| Apcdd1     | 0.32446528 | 1                | 0.003419693   |
| Foxo3      | 0.33247215 | 1                | 0.035262219   |
| Amer2      | 0.35336161 | 1                | -0.001736721  |
| Lrp4       | 0.36546713 | 1                | -0.0070059    |
| Folr1      | 0.37635542 | 1                | 0.001534577   |
| Rnf213     | 0.37677129 | 1                | -0.012488378  |
| Nphp3      | 0.38921731 | 1                | -0.010558659  |
| Dvl3       | 0.4564861  | 1                | 0.016164044   |
| Vangl2     | 0.46983741 | 1                | -0.012467268  |
| Dab2ip     | 0.48847989 | 1                | 0.007697242   |
| Nphp4      | 0.52024552 | 1                | -0.000850854  |
| Btrc       | 0.53256957 | 1                | -0.002069145  |
| Cdk14      | 0.54543235 | 1                | 0.036215784   |
| Egf        | 0.54703377 | 1                | 0.005316349   |
| D930015E06 | 0.56328183 | 1                | 0.020755905   |
| Mks1       | 0.59298446 | 1                | 0.017604022   |
| Src        | 0.60756981 | 1                | 0.022417092   |
| Grhl3      | 0.63138451 | 1                | 0.010568625   |
| Tle2       | 0.64850777 | 1                | 0.010373784   |
| Fzd4       | 0.66754654 | 1                | -0.002661444  |
| Ift80      | 0.67951483 | 1                | 0.022842719   |
| Notum      | 0.69389951 | 1                | -0.014549358  |
| Kremen1    | 0.76517881 | 1                | 0.009048712   |
| Gata4      | 0.78845555 | 1                | -0.011848359  |
| Mcc        | 0.8468829  | 1                | -0.000509576  |
| Tnik       | 0.8504737  | 1                | -0.004556618  |
| Atp6v1c2   | 0.86500392 | 1                | 0.004461883   |
| Atp6v0c    | 0.88047077 | 1                | 0.004966438   |
| Wnt11      | 0.94485515 | 1                | -0.001010819  |
| Strn       | 0.95476963 | 1                | 0.006138881   |
| Gprc5b     | 0.97324366 | 1                | -0.006814223  |
| Tle3       | 0.9774557  | 1                | 0.006577062   |
| Wnt1       | 1          | 1                | -0.005880309  |

Table S4. The differentially expression of Wnt related genes between epithelial and fibroblas

| <b>gene</b> | <b>p value</b> | <b>Adjusted p value</b> | <b>fold change *</b> |
|-------------|----------------|-------------------------|----------------------|
| Depdc1b     | 1              | 1                       | 0.000884305          |
| Naip5       | 1              | 1                       | 0.011140092          |

\* fold change for differentially expressed genes between epithelial cluster and fibroblast clus