

SUPPLEMENTARY INFORMATION

Malfunction of Airway Basal Stem Cells plays a crucial role in Pathophysiology of Tracheobronchopathia Osteoplastica

Yue Hong*, Shan Shan, Ye Gu, Haidong Huang, Quncheng Zhang, Yang Han, Yongpin Dong, Zeyu Liu, Moli Huang, Tao Ren*

* Corresponding authors

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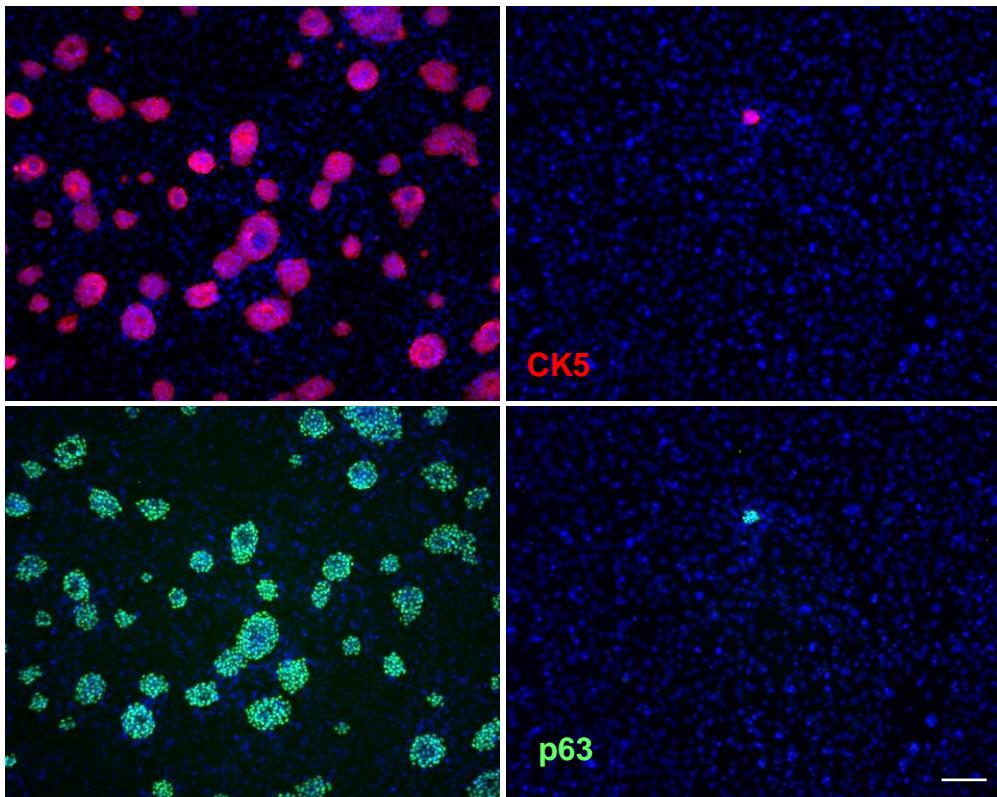
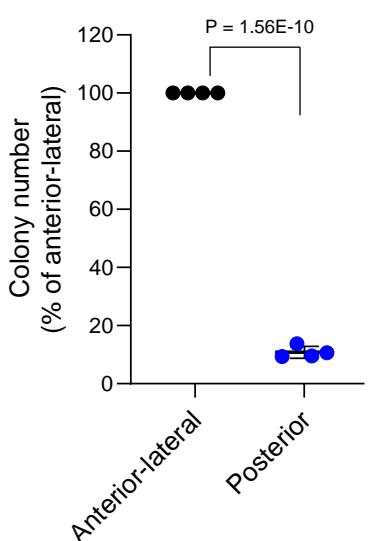
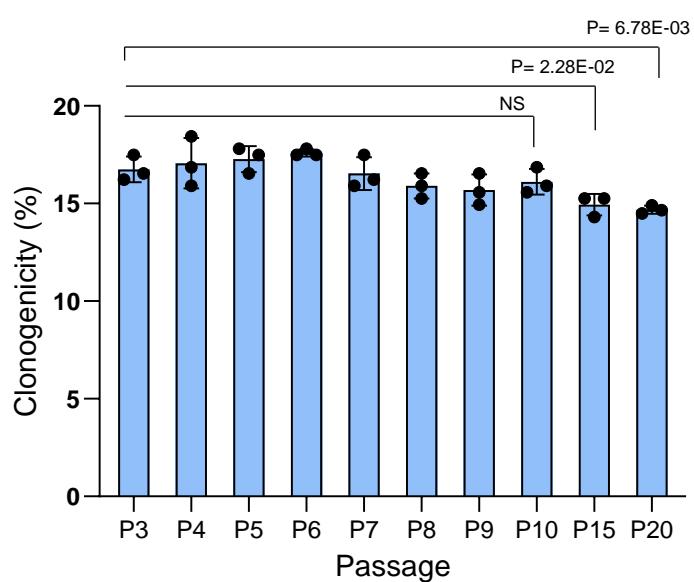
SUPPLEMENTARY FIGURES AND LEGENDS

SUPPLEMENTARY TABLES

a

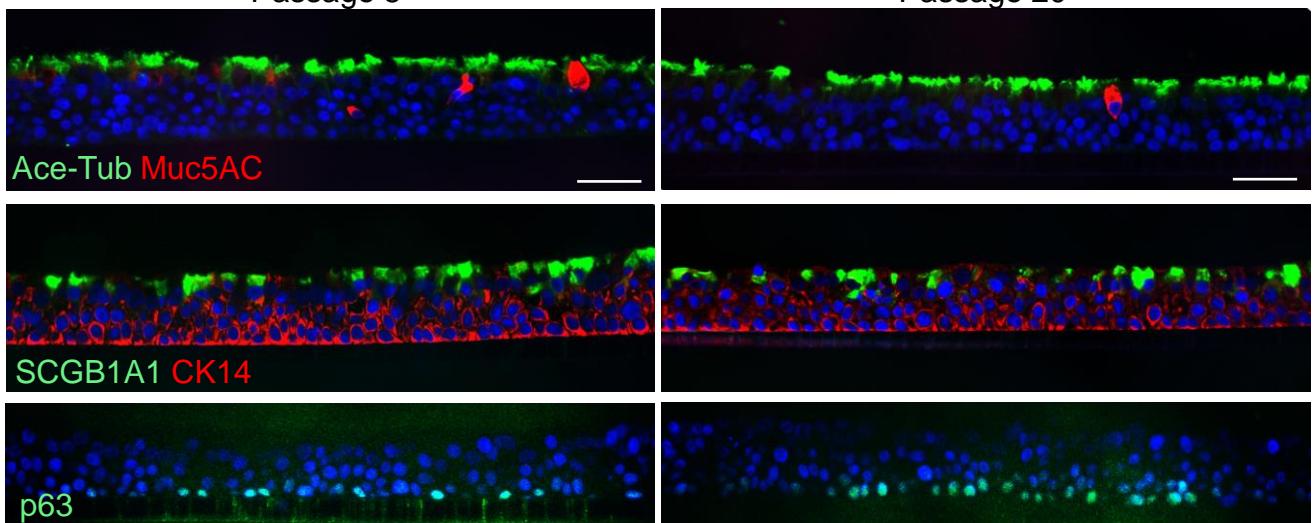
Anterior-lateral trachea

Posterior trachea

**b****c****d**

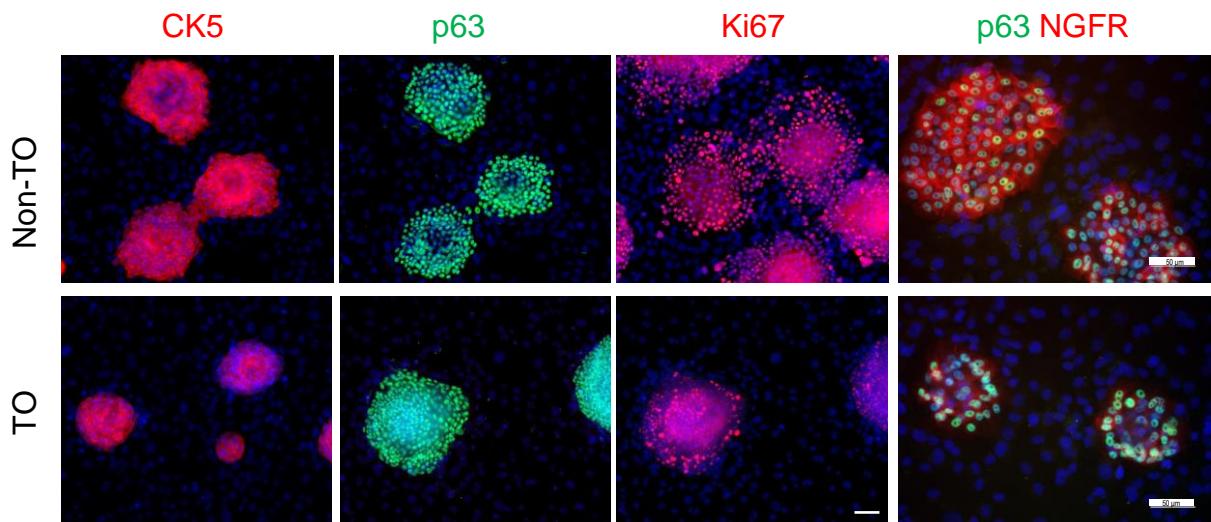
Passage 5

Passage 20

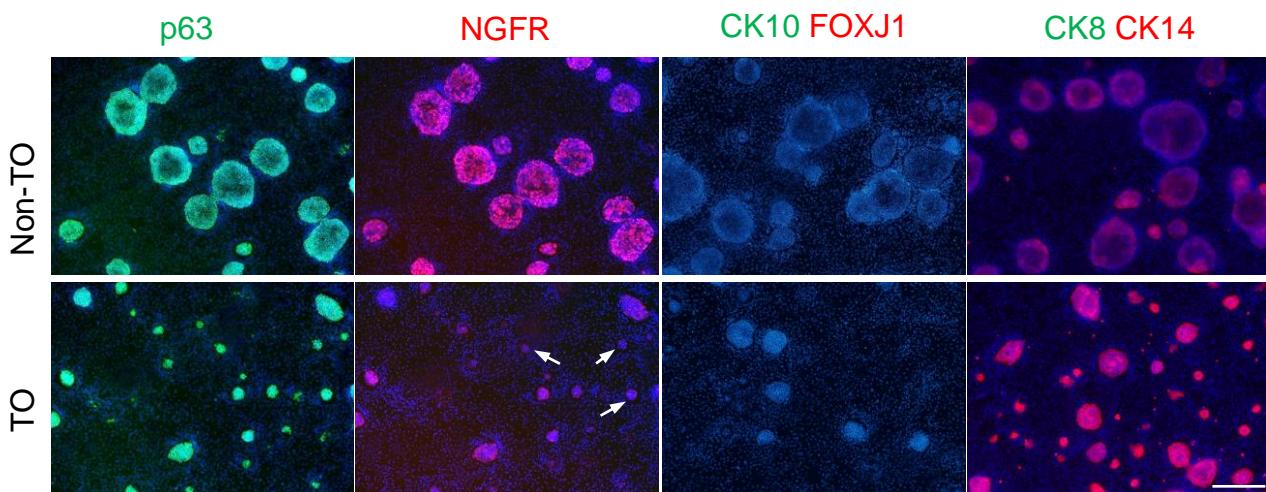
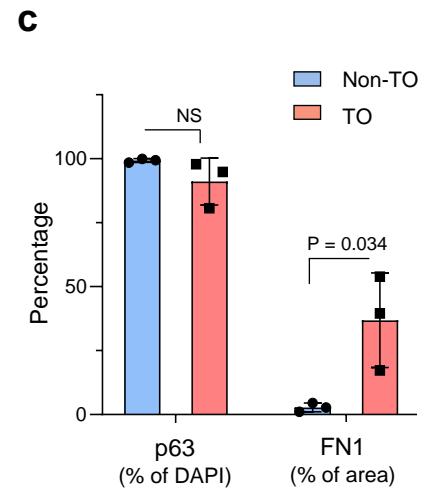
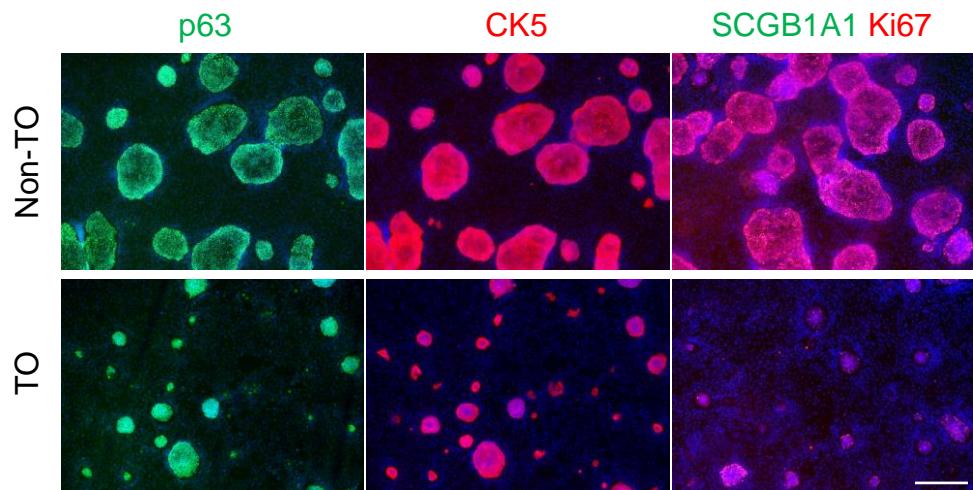


Supplementary Figure 1. Spatial distribution of proliferative basal stem cells in human tracheas, and stability of cell maintenance in vitro. (a) Representative images of primary cultures of tracheal stem cells derived from anterior-lateral and posterior portions of normal donors, respectively. Cell character was confirmed by immunofluorescent staining with basal cell markers, CK5 and p63. Scale bar, 200 μ m. (b) Scatter plot depicting clone numbers counted from sub-regional cultures of 4 independent biological samples, as percentage values of anterior-lateral counterparts. Bars represent mean \pm SD, and p value is indicated to show statistical significance. (c) Self-renewal ability of isolated normal basal stem cells was assessed by clonogenic assay, shown as percentage of plated cells that formed typical clones on Day 4-5 post-seeding from passage 3 to 20 (n=3 experimental repeats/passage). Results are represented as mean \pm SD, and p values are indicated to show statistical significance (^{NS} p > 0.05). (d) Representative images showing differentiation ability of passaged cells examined by immunofluorescent staining of ALI sections (n=3 experimental repeats) with functional cell markers, acetylated tubulin (ciliated), Muc5AC (goblet), SCGB1A1 (club) and CK14, p63 (basal). Scale bar, 40 μ m. (b, c) two-tailed Student's t-tests. Source data are provided as a Source Data file.

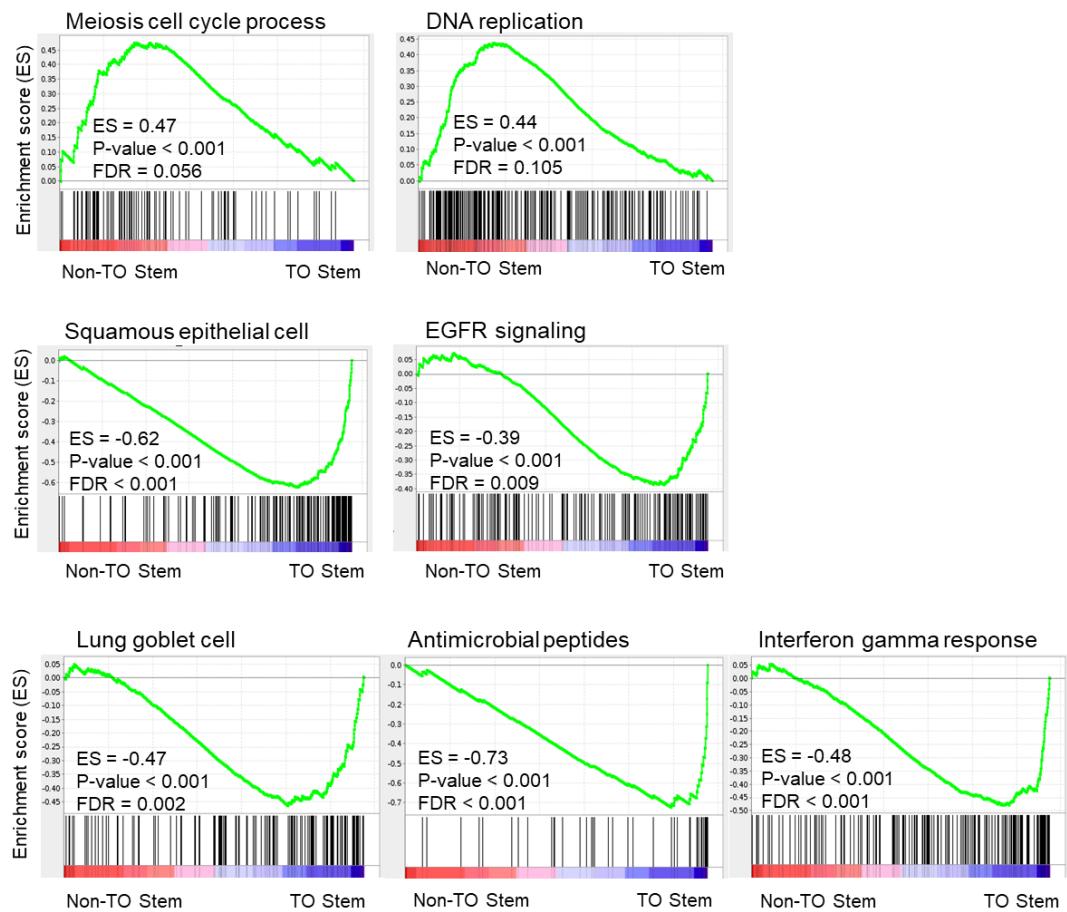
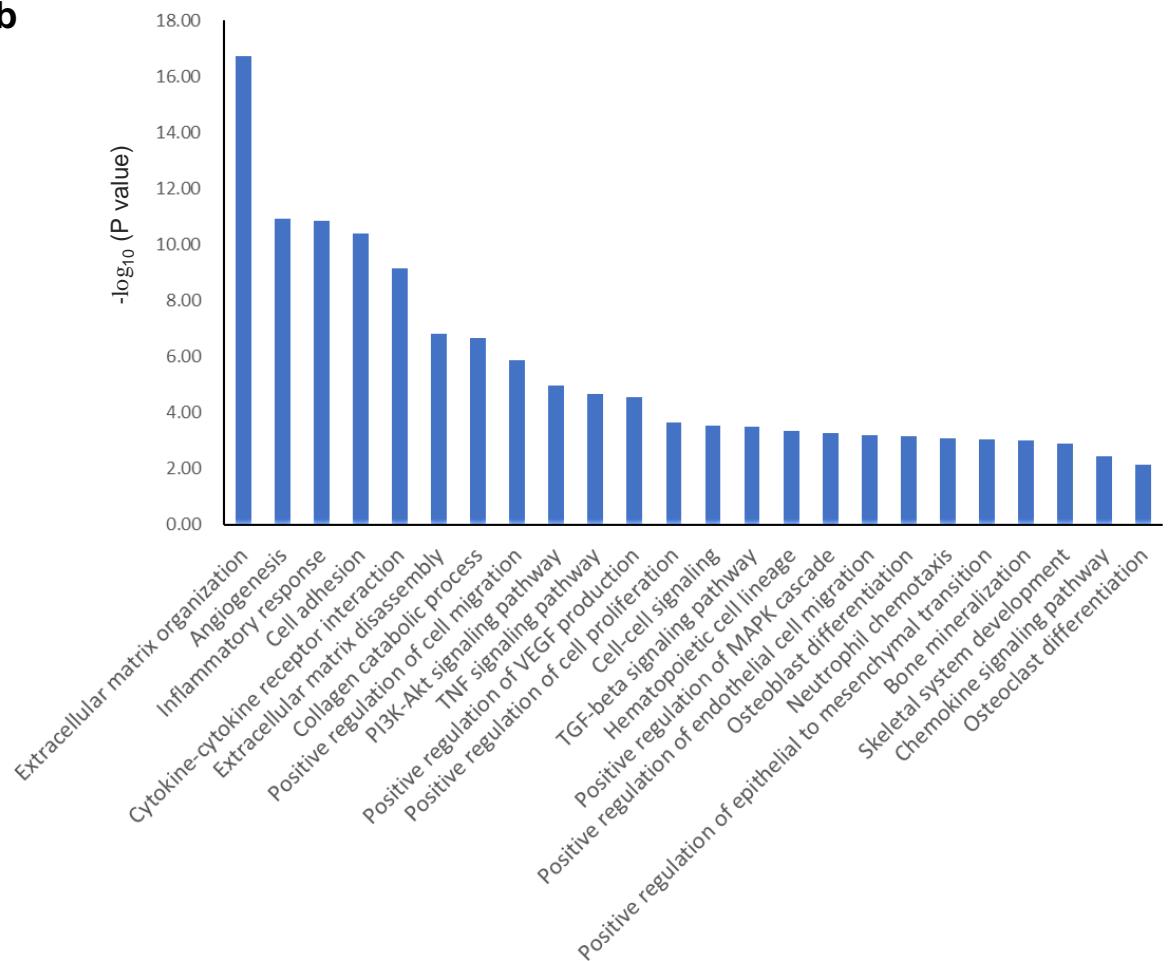
a P4 clones



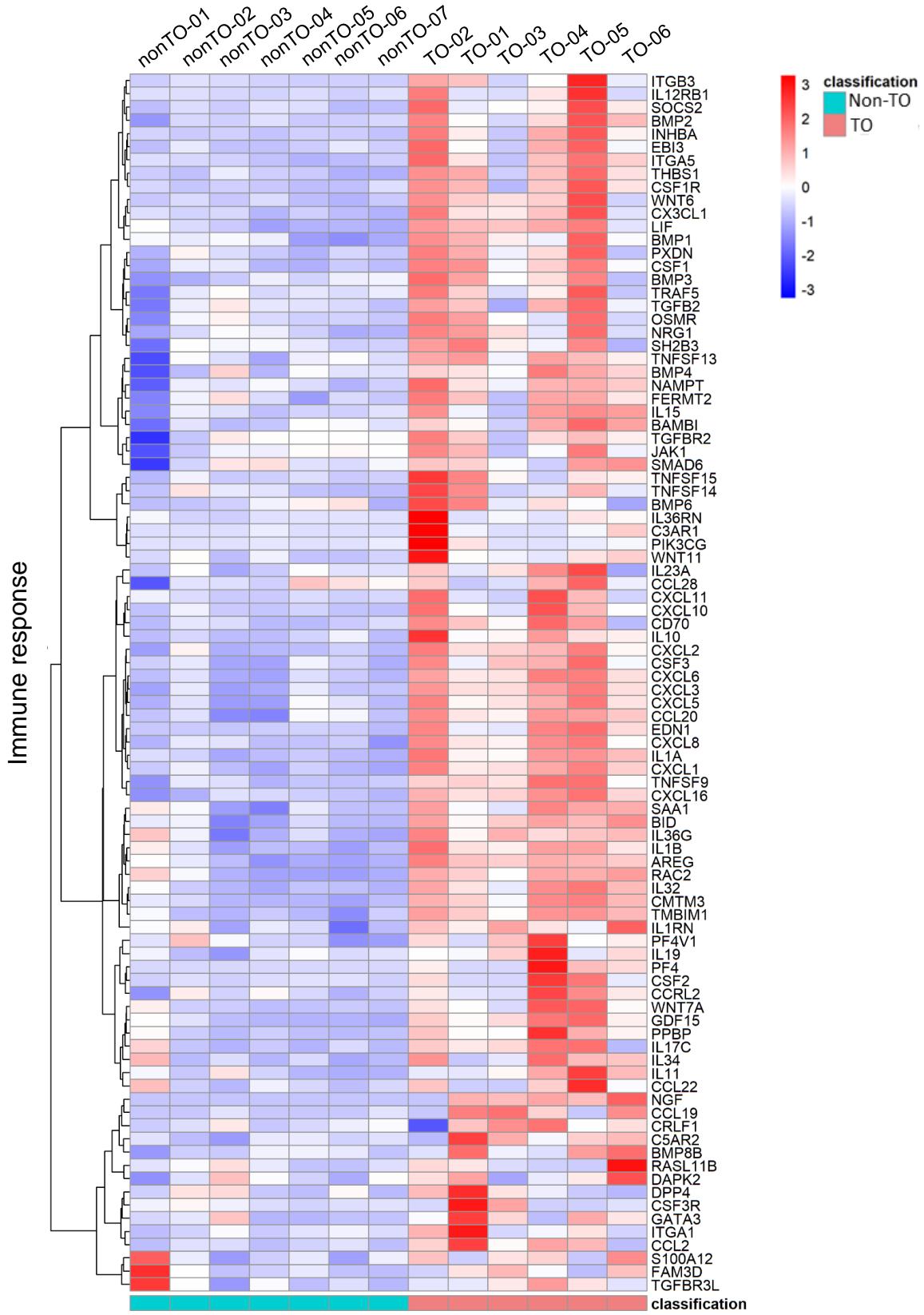
b P7 clones



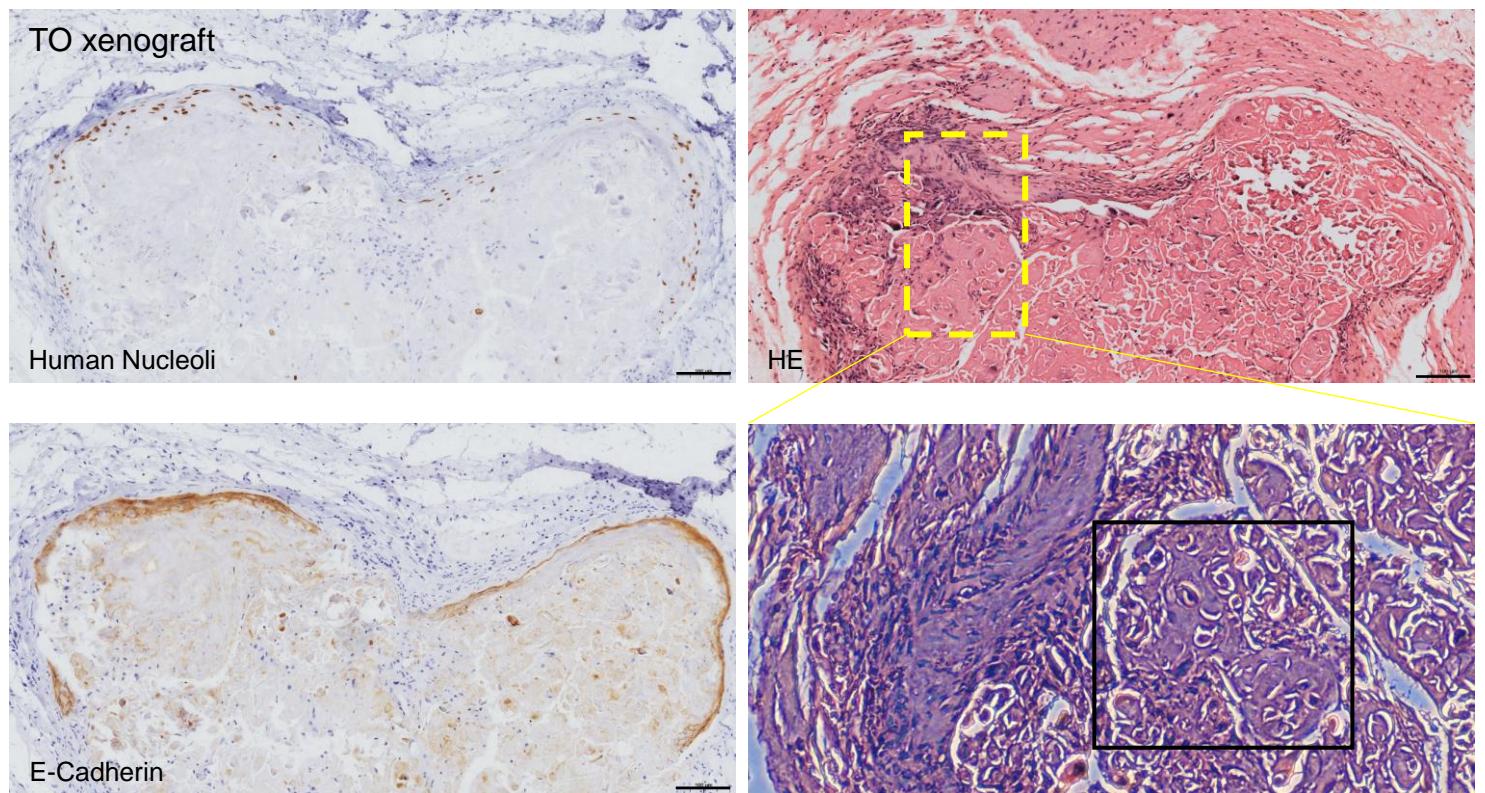
Supplementary Figure 2. Characterization of isolated TBBCs derived from non-TO controls and TO patients. (a) Representative immunofluorescent images showing the expression of key basal cell markers CK5, p63, NGFR and Ki67 on clones from P4 culture. Scale bar, 50 μ m. (b) Representative immunofluorescent images of clones from P7 culture stained with a panel of antibodies against basal cell markers (p63, CK5, NGFR and CK14), proliferation indicator (Ki67), differentiating marker (CK8) and cell-type specific markers (SCGB1A1, CK10, FOXJ1). Scale bar, 500 μ m. Cells with strong p63 immunoreactivity but almost no NGFR labeling are highlighted by white arrows as examples. (c) Quantification of immunofluorescence results from p63 and FN1 labelled TBBC monolayers using Fiji. For p63, results are presented as mean of percentage of positive cells in total DAPI nuclei via particle analysis; whilst for FN1, due to its diffuse pattern and deposition in extracellular space, results are presented as mean of area fraction. Error bars of \pm SD and p-values are indicated in the graph (^{NS} p > 0.05). (a, b, c) n=3 biologically independent experiments. (c) two-tailed Student's t-tests. Source data are provided as a Source Data file.

a**b**

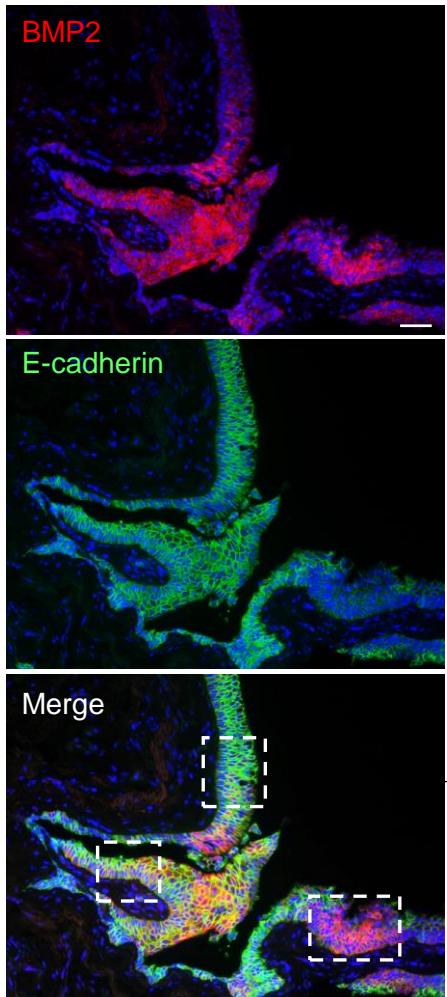
Supplementary Figure 3. Enrichment analyses of RNA-Seq datasets generated from TBBC clones and corresponding ALI differentiated cells. (a) Gene set enrichment analysis (GSEA) of basal cell RNA-Seq data. (b) GO and KEGG enrichment analysis of differentially expressing genes with further increment in severe TO cases (TO-02, 05, 06) compared to moderate cases (TO-01, -03, 04) according to ALI RNA-Seq data.



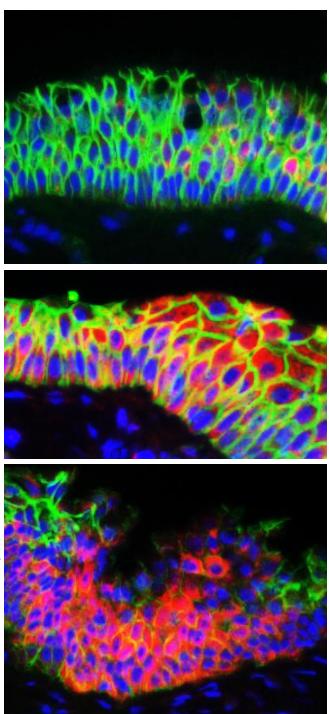
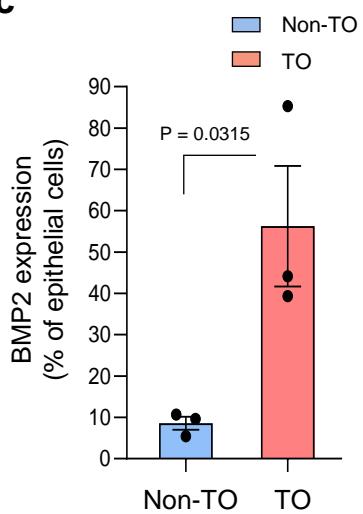
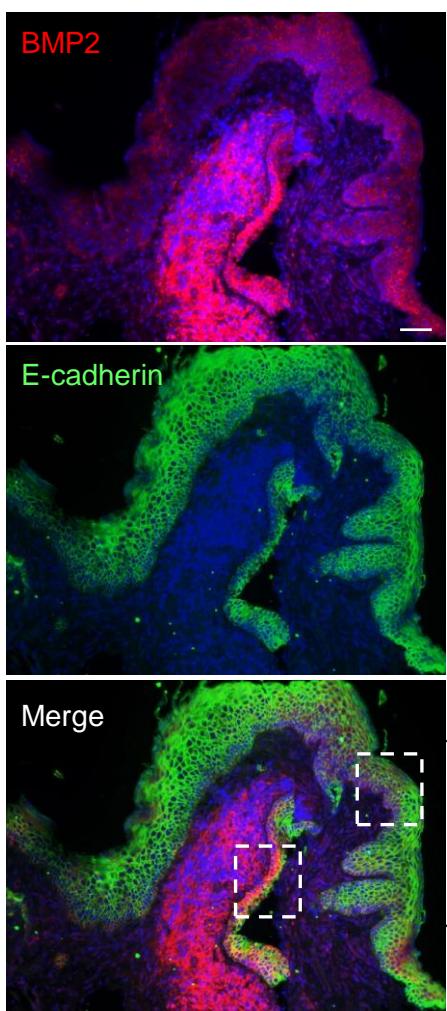
Supplementary Figure 4. Comparative heatmap showing distinct expression profiles between non-TO and TO groups. Differentially expressing genes involved in cytokine-cytokine receptor binding and chemotaxis events were selected to show in this heatmap across all non-TO controls and TO cases.



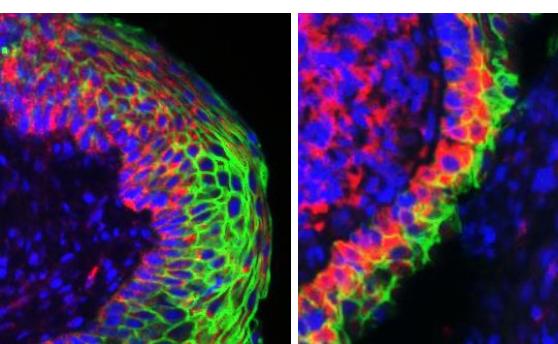
Supplementary Figure 5. Histological sections showing a representative xenograft sample derived from TO-TBCCs transplantation, which contains a suspectable cartilaginous islet. HE, immunohistochemical staining against anti-human nucleoli and E-Cadherin were performed on serial sections, to identify the transplanted epithelial portion. Yellow dotted box indicates a field that has been magnified into a separate image, and the black box is highlighting a cartilaginous-like islet. n=1 biological sample. Scale bar, 100 μ m.

a

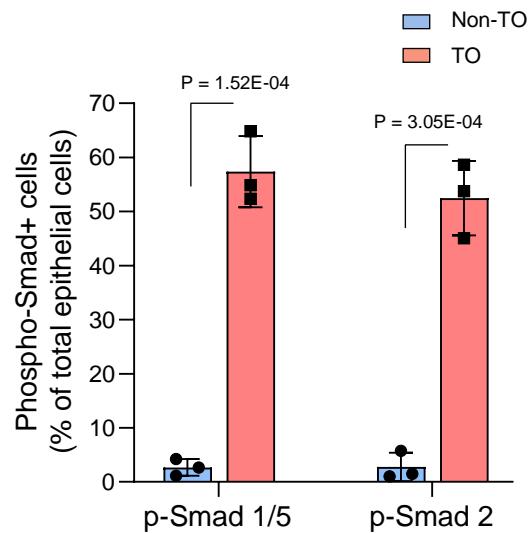
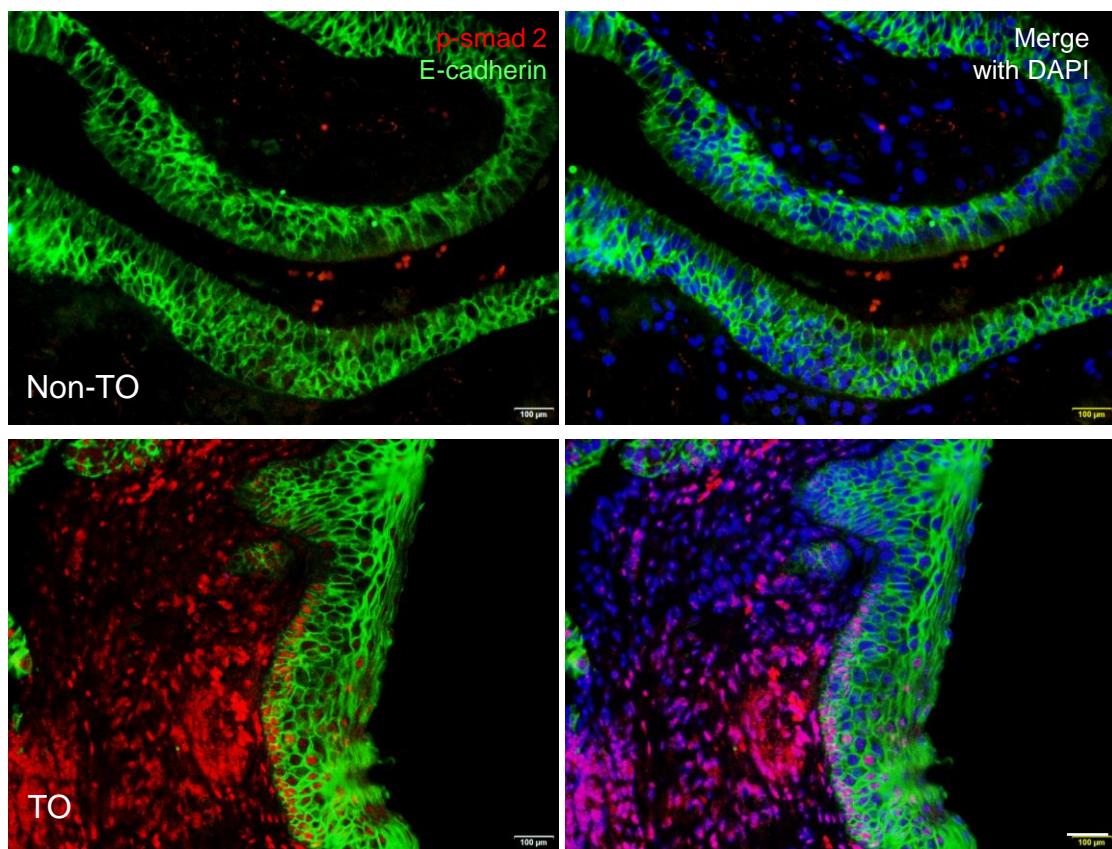
Magnified merge

**c****b**

Magnified merge



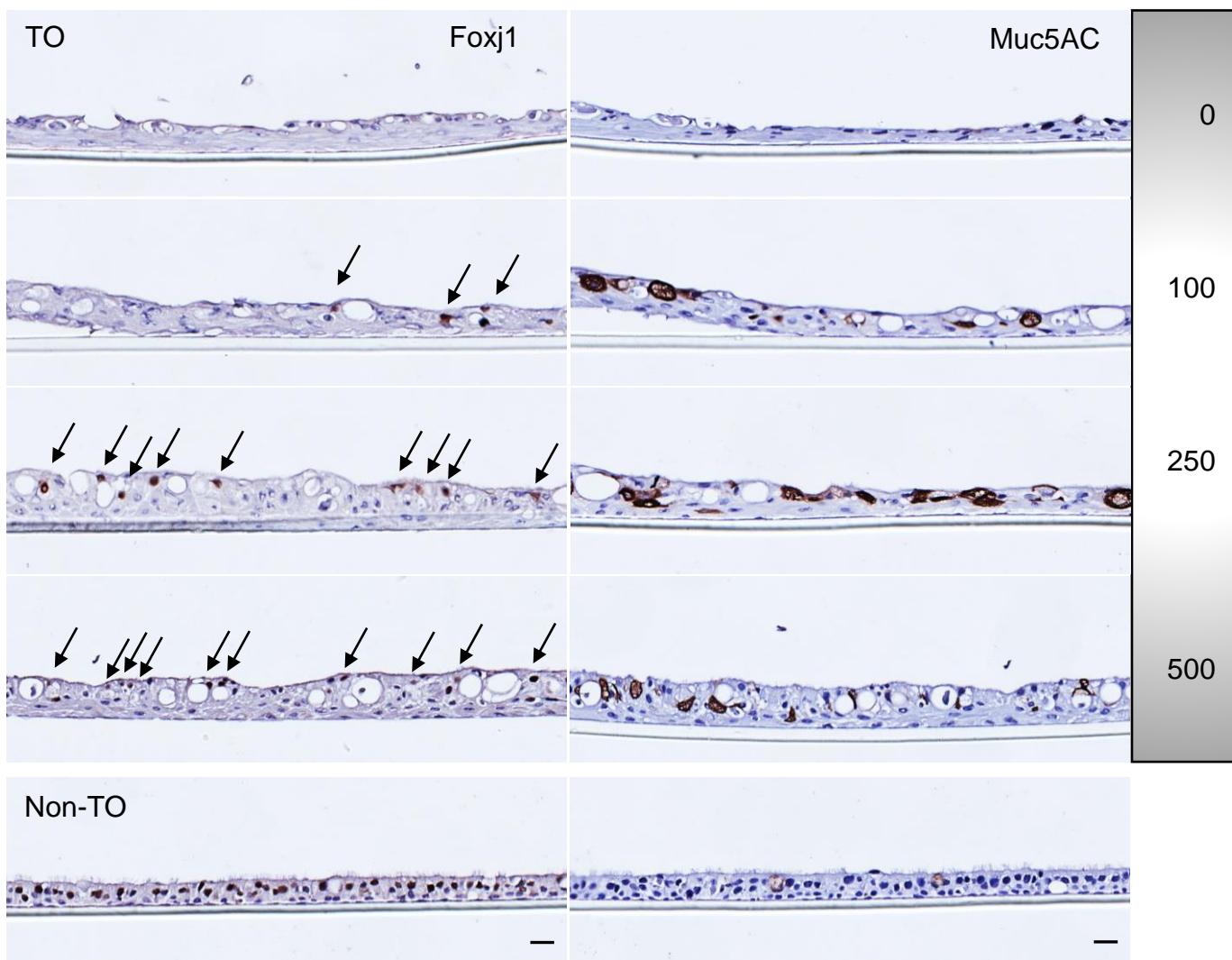
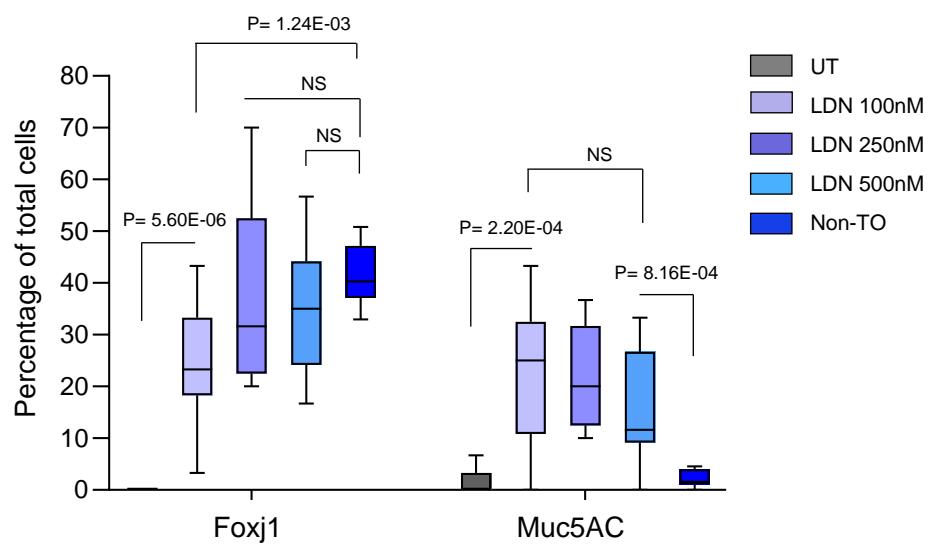
Supplementary Figure 6. Detection of BMP2 on patient-derived biopsies. (a-b) Immunofluorescent images showing BMP2 tissue expression and distribution on paraffin sections from two TO cases. E-Cadherin was stained to locate epithelial compartment in biopsies. Magnified areas were highlighted in white dotted boxes and displayed in separate images. Scale bar, 100 μ m. (c) Quantification of BMP2 expression on tracheobronchial biopsy sections based on immunofluorescence results (non-TO n=3, TO n=3 biologically independent experiments). Results were shown as mean \pm SD and statistical analysis was performed using two-tailed Student's t-test. P value is indicated to show statistical significance. Source data are provided as a Source Data file.

a**b**

Supplementary Figure 7. Detection of phosphorylated SMAD on patient-derived biopsies. (a) Quantification of p-Smad2 and p-Smad1/5 in tissue epithelia based on immunofluorescence results (non-TO n=3, TO n=3 biologically independent experiments). Results were expressed as mean \pm SD, and p values are indicated to show statistical significance based on two-tailed Student's t-tests. (b) Representative co-staining images showing p-Smad2 and E-Cadherin expression on patient biopsies that were proceeded with quantification analysis in (a). Scale bar, 50 μ m. Source data are provided as a Source Data file.

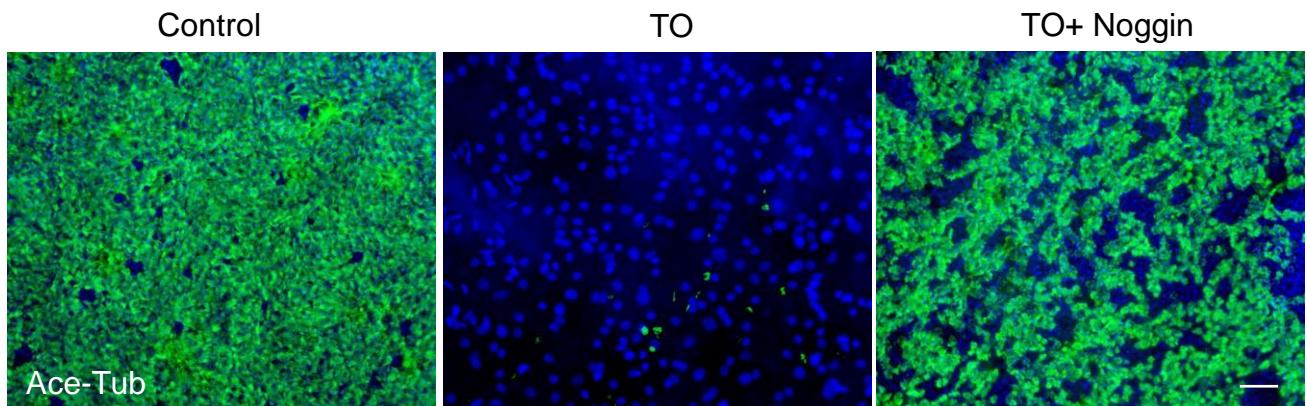
a

+ LDN-193189 (nM)

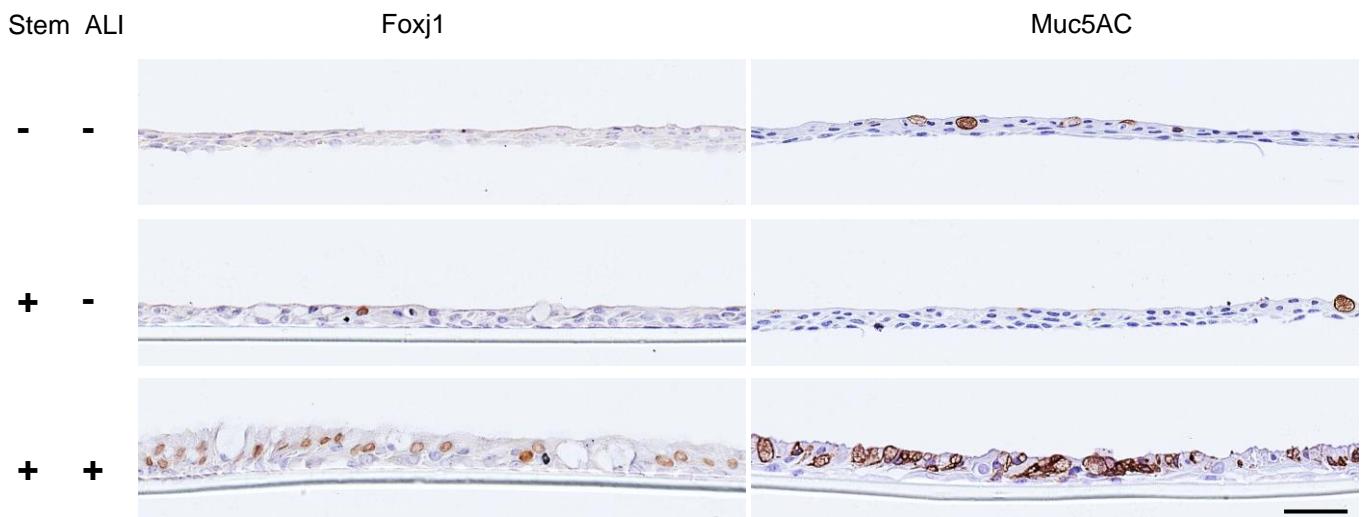
**b**

Supplementary Figure 8. Effect of BMP inhibitor LDN-193189 on TO-basal cell differentiation.

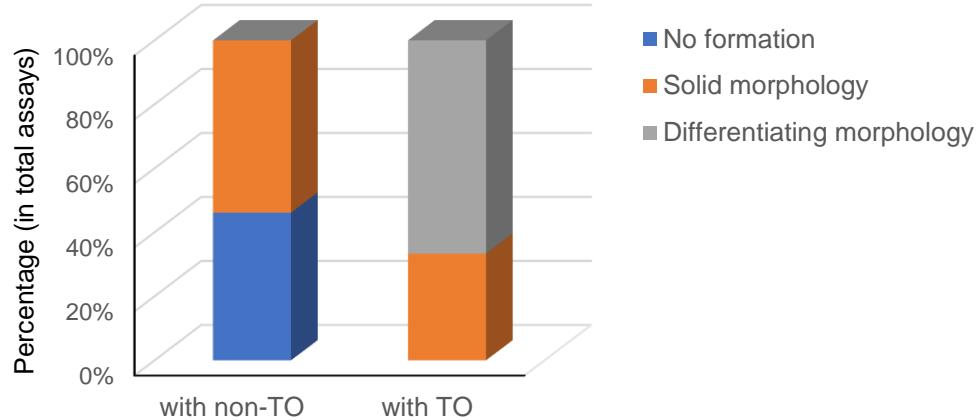
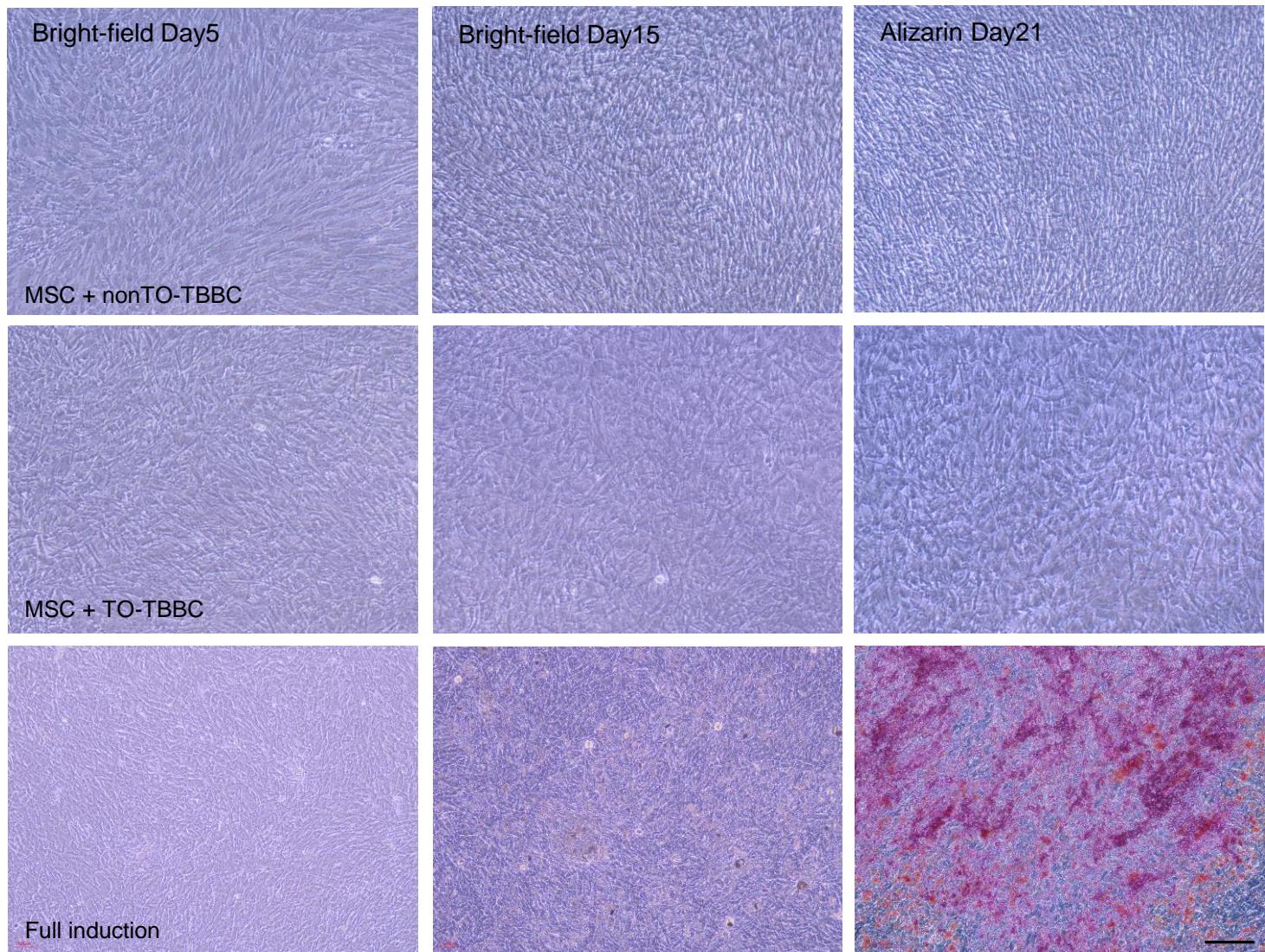
(a) TO-derived basal cells were treated with LDN-193189 at concentrations ranging between 100-500nM since Day 0 of ALI differentiation. Day20 structures were fixed to proceed with paraffin sectioning and immunohistochemical staining for mucociliary markers Foxj1 and Muc5AC. ALIs of TO-derived and non-TO basal cells without inhibitor treatment were examined as controls. Foxj1+ cells were highlighted by black arrows on TO-ALI sections. Scale bar, 20 μ m. **(b)** Quantification of ciliated (Foxj1+) and goblet (Muc5AC+) cell frequencies on TO basal cell-derived ALIs. UT (untreated TO-ALI) and non-TO basal cell-derived ALI were examined as controls. Ten sections from 3 independent experiments were counted per group. Boxes denote 25th and 75th percentile, lines denote median and whiskers min-max. P values are indicated to show statistical significance (^{NS} p > 0.05) based on two-tailed Student's t-tests. Source data are provided as a Source Data file.

a**b**

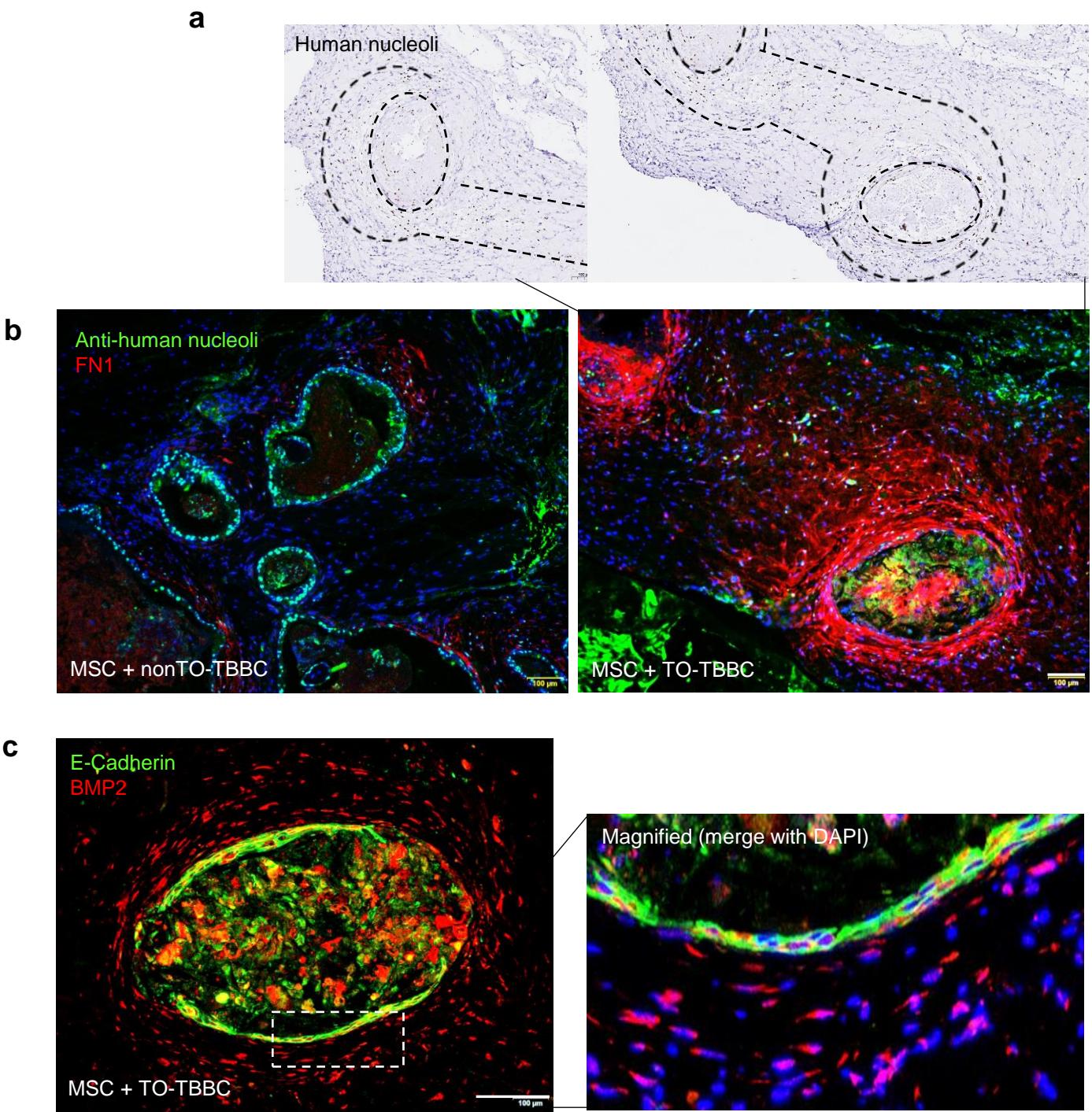
Noggin addition on TO-derived cells



Supplementary Figure 9. Effect of BMP antagonist Noggin on TO-basal cell differentiation. (a) Representative ALI top-view images showing mucociliary differentiation of TO-derived basal cells under Noggin (200ng/ml) treatment since Day 0. TO-ALI without Noggin treatment and non-TO control ALI were examined in parallel. Day 20 structures were fixed to proceed with immunofluorescent staining ($n=3$ biologically independent experiments). Scale bar, 50 μ m. **(b)** An immunohistochemical comparison of Noggin on TO-TBBCs throughout ALI differentiation and Noggin withdrawal ($n=2$ biologically independent experiments). Differentiation efficiency was examined by Foxj1 and Muc5AC staining. Scale bar, 50 μ m.

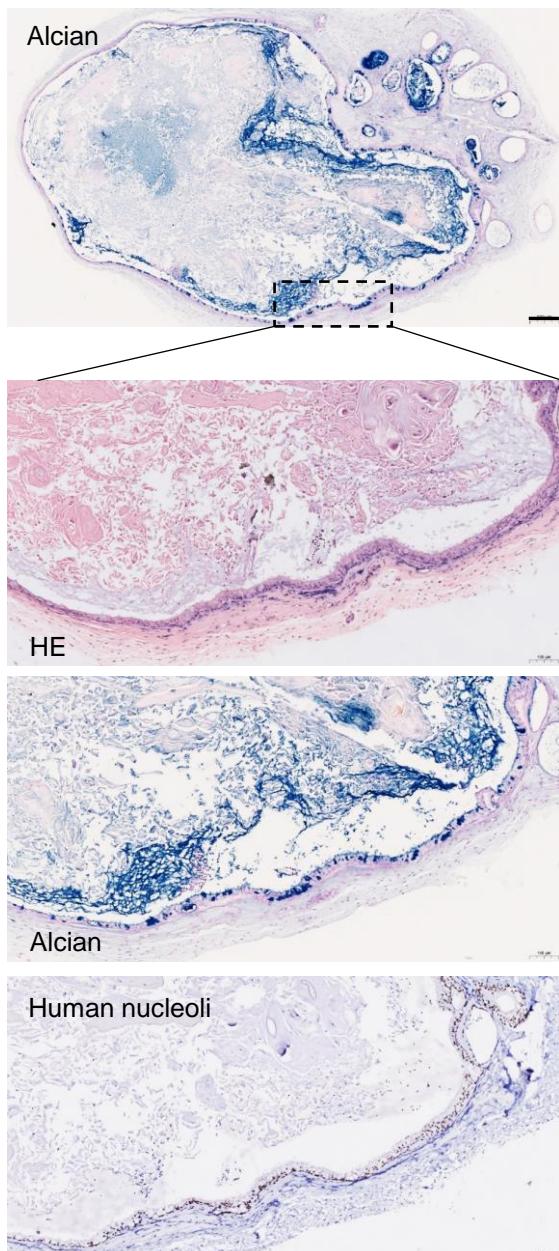
a**b**

Supplementary Figure 10. TBBC-MSC in vitro co-culture assays. **(a)** A quantitative summary of MSC spheroid formation and differentiation based on observations from chondrogenic-lineage co-culture assays. Y-axis, percentage of total MSC pellets set for co-culture (non-TO n=13, TO n=7). Results were reached from two independent experiments involving a use of 3 non-TO cases and 2 TO-severe cases in examination. **(b)** A comparison of MSC osteogenic differentiation under co-culture conditions with non-TO controls and with TO-TBBCs derived ALI epithelia. MSCs undergone standard differentiation via full induction was examined in parallel. Calcium deposit was examined by Alizarin Red S Staining. Scale bar, 200 μ m. Independent experiments n=2 were performed for examination. Source data are provided as a Source Data file.

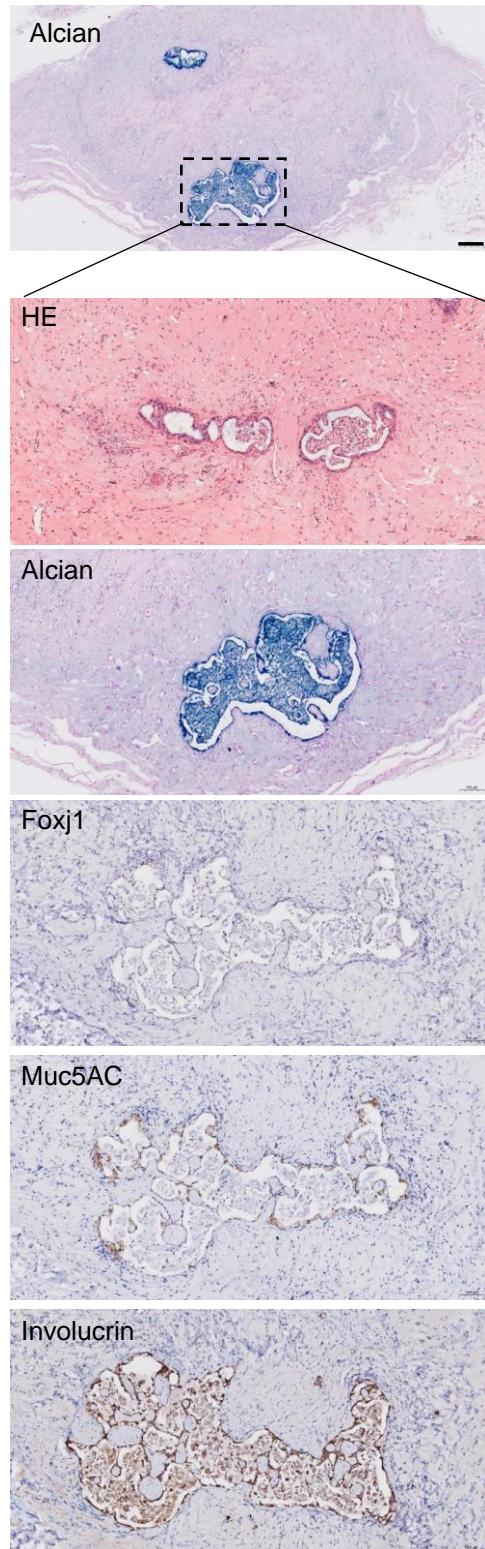


Supplementary Figure 11. TBBC-MSC *in vivo* co-culture assays. (a) Distribution of transplanted cells in xenografts was illustrated by human nucleoli staining, and circled in the pictures. (b) Immunofluorescent images showing FN1 expression in xenografts resulted from MSC growths when co-cultured with non-TO control cells or with TO-TBBCs. Scale bar, 100 μ m. (c) The serial sections of the same sets of xenografts were proceeded with BMP2 and E-Cadherin co-staining. Representative magnified image showing the area highlighted in white box. Scale bar, 100 μ m. Independent experiments n=2 were performed for examination. Source data are provided as a Source Data file.

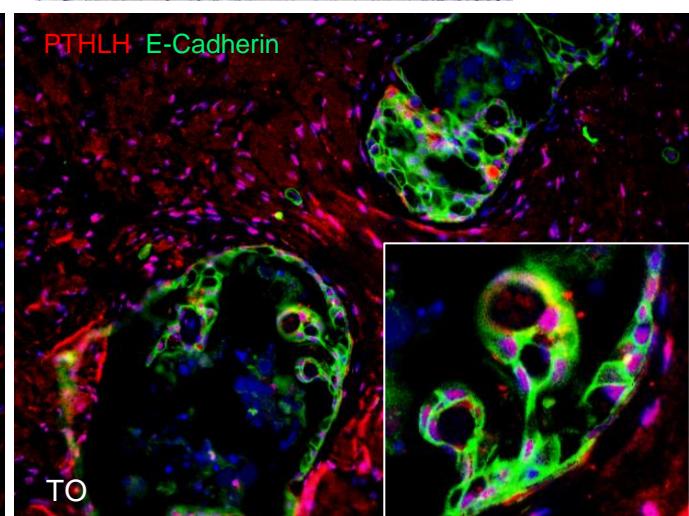
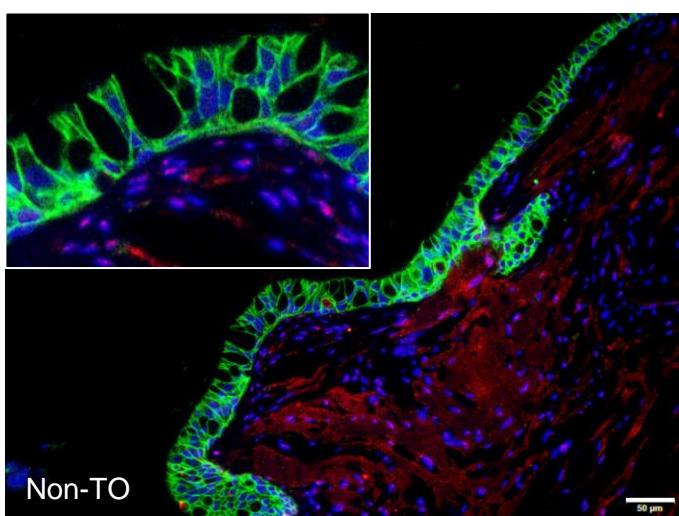
a Aggregated MSC + nonTO-TBBC



b TO-TBBC transplanted w/o MSC



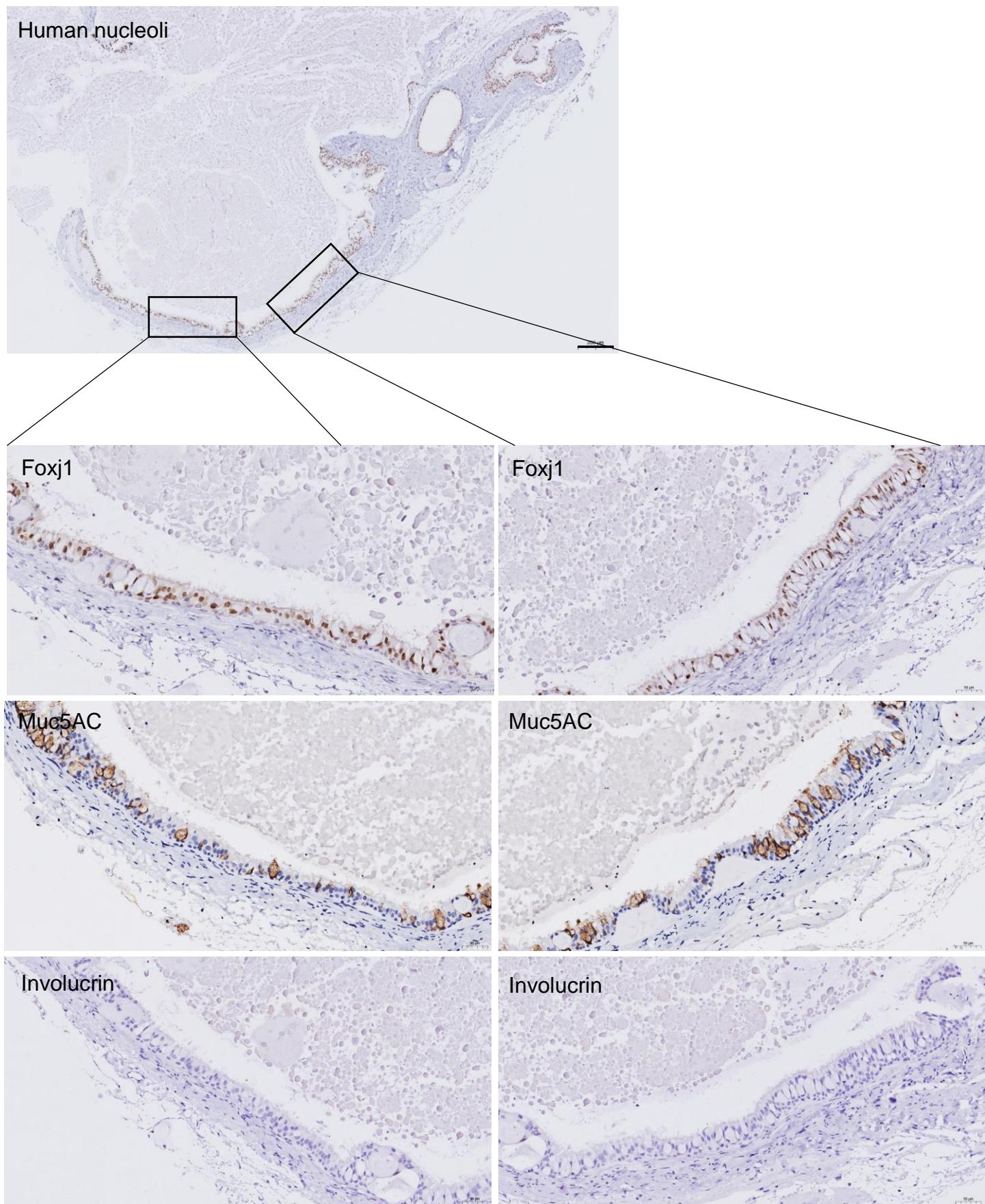
c



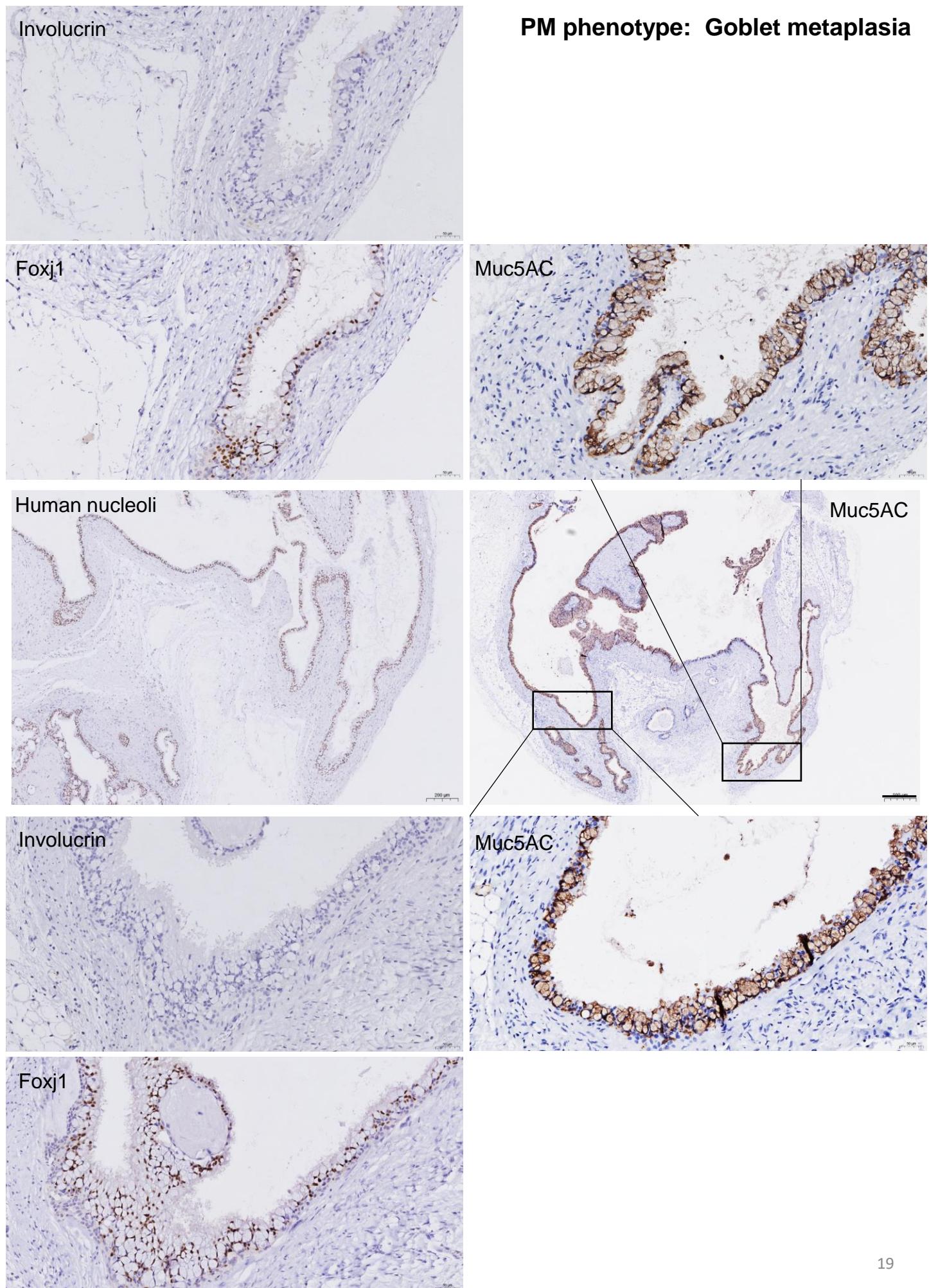
Supplementary Figure 12. Controls for co-culture assay *in vivo* and PTHLH expression in non-TO and TO xenografts. (a) Paraffin sections of 4-week xenografts formed by aggregated MSC spheroid + non-TO TBBC co-transplantation assay were examined by HE and Alcian blue staining. Human nucleoli distribution was confirmed by immunohistochemistry. Scale bar, 200 μ m. (b) Four-week xenografts formed by TO-TBBCs in the absence of co-transplanted MSC were examined by HE, Alcian blue and immunohistochemical staining for cell-type specific markers. Scale bar, 200 μ m. (c) Representative immunofluorescent images showing E-Cadherin and PTHLH co-staining on xeno-sections acquired from nonTO-TBBC and TO-TBBC transplantations. Independent experiments n= 2 were performed for examination. Scale bar, 50 μ m.

Supplementary Figure 13.

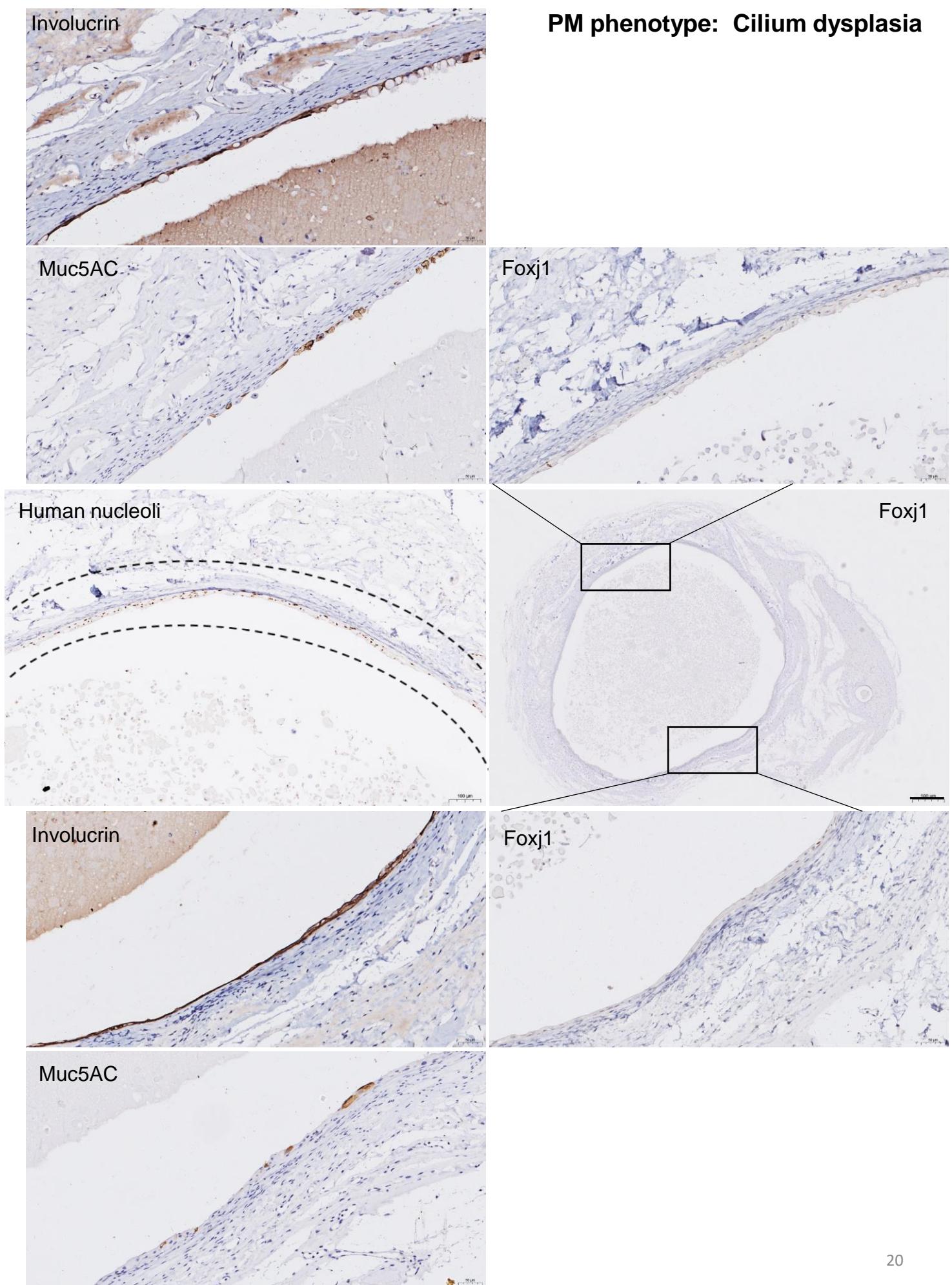
PM phenotype: Normal-like



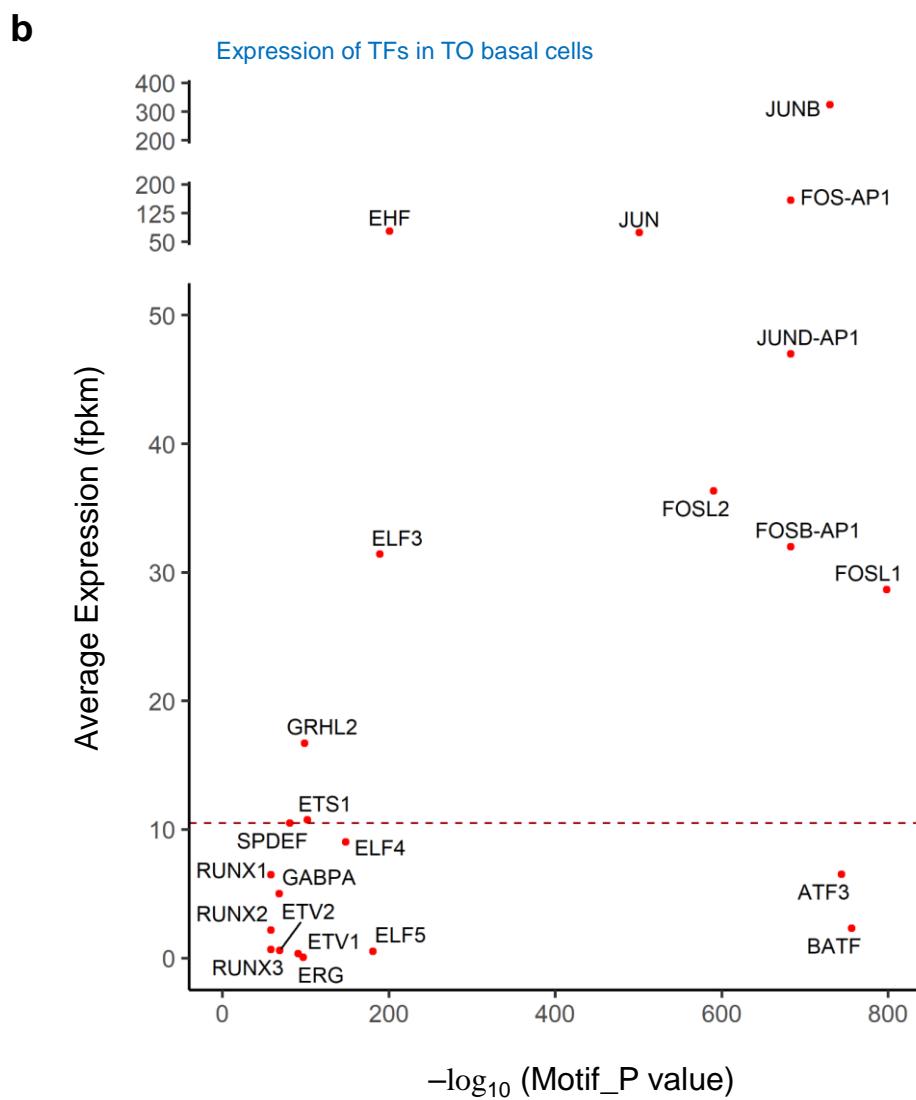
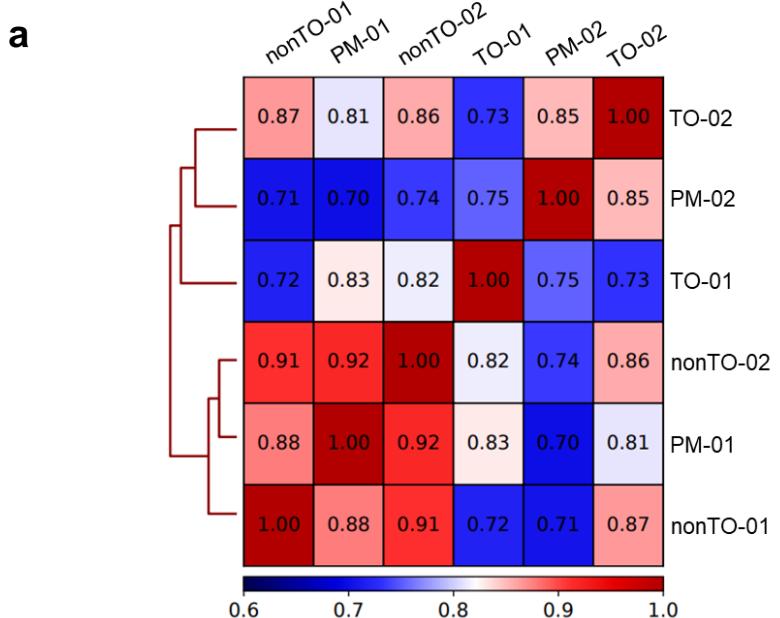
Supplementary Figure 14.



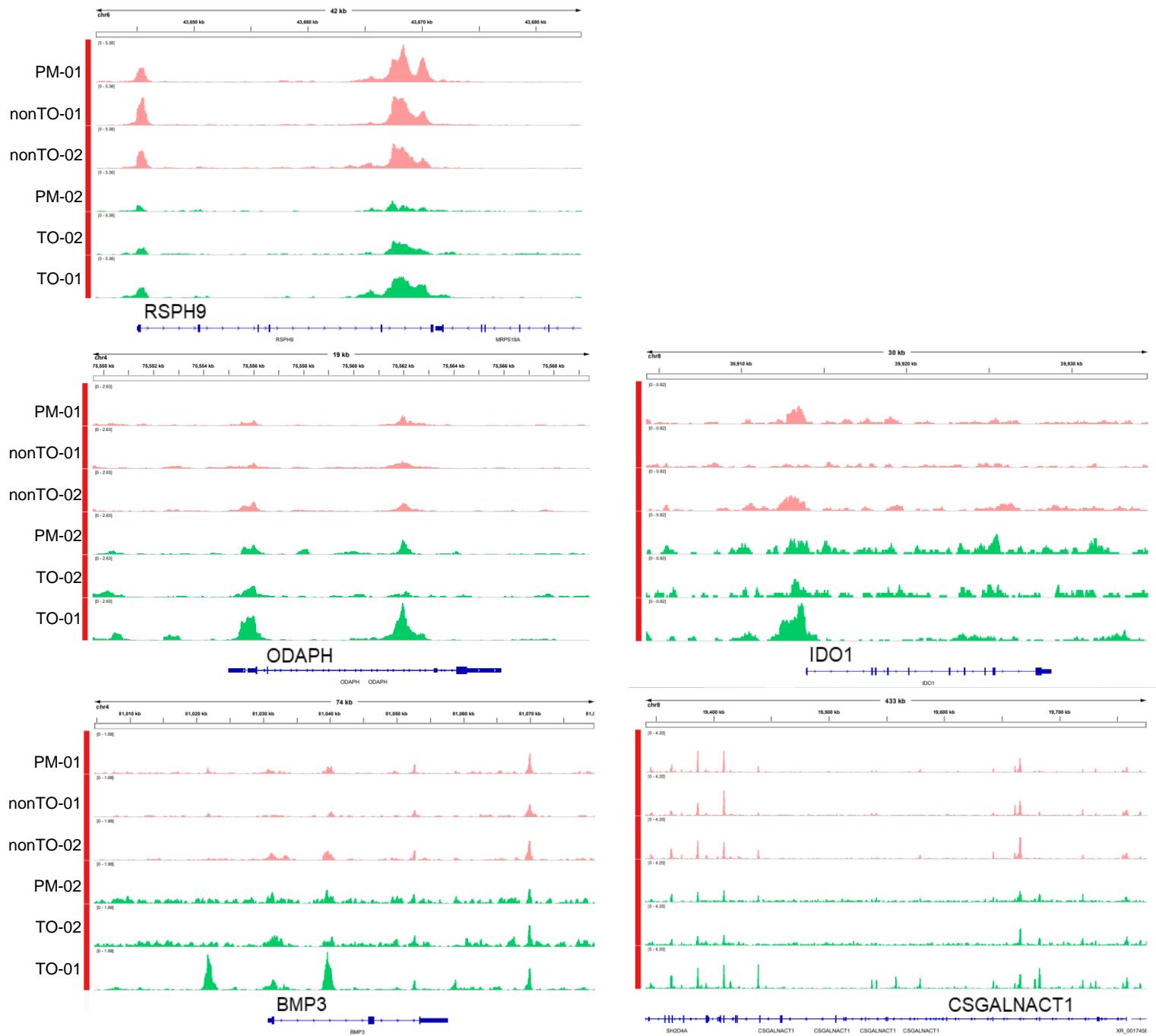
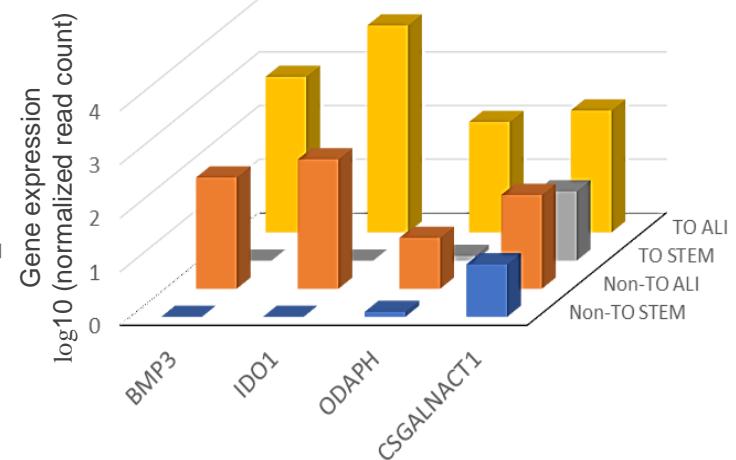
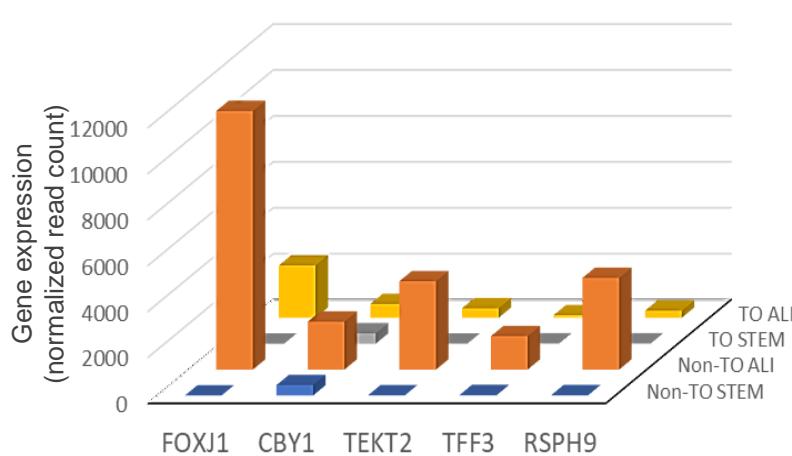
Supplementary Figure 15.



Supplementary Figure 13-15. In vivo differentiation of patient-matched TBBCs isolated from the normal-looking regions of patients' trachea-bronchi. Patient-matched (PM) TBBCs showed distinct differentiation potentials, referring to normal-like, goblet metaplasia and cilia dysplasia phenotypes observed on xenografts, which were collected at Week 4 post subcutaneous transplantation. Representative full-scale immunohistochemical images showing cell type frequencies using antibodies against Foxj1, Muc5AC and Involucrin (n=2 independent experiments). Human nucleoli antibody was used to confirm the location and distribution of transplanted cells. Scale bar, 500 μ m.



Supplementary Figure 16. ATAC-Seq of patient-derived TBBCs and joint-analysis with RNA-Seq data. (a) Pearson correlation result of ATAC-Seq data. (b) Correlation of motif enrichment with expression of corresponding transcription factors in TO-TBBCs. Red dotted line indicates the median value according to RNA-Seq data.

a**b**

Supplementary Figure 17. Status of chromatin accessibility and gene expression at key loci.

(a) IGV graphs visualizing chromatin accessibility at key loci related to cartilage development, inflammation and ciliogenesis. Peak height is positively correlated to accessibility. Genome scale is included and Y-axis is consistent for all loci. **(b)** Histogram showing transcriptional levels of selected genes between control and TO groups before and after differentiation, corresponding to IGV results shown in this figure and Fig. 7e.

Supplementary Table 1 RNA-Seq data showing differentially expressing genes between non-TO and TO basal cells

gene_id	log2FoldChange	pvalue	padj	nonTO-01	nonTO-02	nonTO-03	nonTO-04	nonTO-05	nonTO-06	nonTO-07	TO-01	TO-02	TO-03	TO-04	TO-05	TO-06	
VNN1	-7.593689504	0.001346	0.160739	0	0	0	0	0	0	0	152.8883	9.497313	0	11.20352	20.37032	0	
PSG4	-5.586023021	3.14E-05	0.013477	0	2.0028201	3.8646033	3.198896	1.042755	0.981502	0	234.0302	3.453568	1.215607	124.4835	91.06732	0	
FGF10	-5.083834405	0.000425	0.072078	0	0	0	0	0	0	0	0.854125	12.08749	9.724853	7.469012	0	3.906223	
RPE65	-5.076664789	6.31E-06	0.004376	0.6660006	1.3352134	0	0	1.042755	0	0	44.41449	10.3607	19.44971	4.979341	0	18.22904	
NELL2	-4.829188511	7.87E-05	0.024935	0	0	0	0	1.042755	0	0	3.31977065	18.79075	1.726784	3.64682	3.734568	63.50747	
PRKRAB2	-4.805790662	0.000414	0.071286	0	0	0	2.1325974	0	0	0	2.562374	4.3169	31.60577	4.979341	0	6.510371	
PHGR1	-4.802798657	0.01146	0.4902	0	0	0	0	1.042755	0	0	30.74849	0	0	3.734506	0	2.604148	
ADAM23	-4.504374426	0.000416	0.071286	1.3320013	0	0.9661508	2.1325974	0	0	0	1.10659022	11.10362	87.2026	0	1.244835	4.793017	
EBF1	-4.424426264	0.000121	0.033775	0	0	3.8646033	0	1.042755	0.981502	0	2.562374	34.53568	40.11502	18.67253	0	9.11452	
HGF	-4.418325469	1.76E-05	0.000905	0.6660006	0	0	0	2.08551	0.981502	1.10659022	0	43.08125	19.85802	34.03698	18.67253	2.396508	
CRTAM	-4.414295992	0.018321	0.576919	0	1.3352134	0	0	0	0	0	20.49899	0	0	14.93802	2.396508	0	
HOXC13	-4.387624369	1.26E-10	9.18E-07	5.3280051	2.0028201	0.9661508	2.1325974	0	0.981502	0	36.72737	87.2026	10.94046	33.61055	27.55985	24.73941	
MCOLN2	-4.274412431	0.001992	0.200767	0	0	0	1.0662987	3.128265	0	1.10659022	0	39.71604	9.724853	31.12088	0	2.604148	
NPTX1	-4.256513776	0.006266	0.358004	0	0	0	0	0	0	0	5.124749	1.726784	1.215607	8.713847	2.396508	0	
MCOLN3	-4.04029849	0.00814	0.110386	0	0	0	4.2651947	0	1.963003	1.10659022	0	2.687123	68.20797	1.215607	27.38638	0	5.208297
KLHL4	-4.142050584	0.001665	0.183791	0	0.6676067	0	2.1325974	0	0	0	23.06137	4.3169	1.215607	3.734506	0	9.11452	
GNG2	-4.09622022	0.002577	0.229754	0	0	0.9661508	0	0	0	0	0.832996	6.907137	1.215607	3.734506	0	3.906223	
KRT1	-4.045199651	0.007413	0.388152	28.638027	4.6732468	0	0	0	2.944505	1.10659022	1.70825	56.98388	3.64682	13.69319	7.189525	451.1898	
S100A7	-4.03813663	7.44E-06	0.004929	1.9980019	4.0056401	0.9661508	3.198896	1.042755	0.981502	3.31977065	138.3682	1.726784	1.215607	7.469012	41.9389	28.64563	
GREM2	-4.016717832	0.005104	0.322914	0	0	0.9661508	0	0	0.981502	1.10659022	0	3.4945768	14.94971	1.244835	0	15.62489	
CAPN13	-4.006752312	0.000417	0.171316	0.6660006	0	1.9323017	4.2651947	0	5.88901	1.10659022	143.493	0	2.431213	29.87605	11.98254	0	
WT1	-3.93990994	0.014682	0.53882	0	0	0.9661508	0	0	0	0	0	11.2241	4.862426	2.489671	0	2.604148	
PYDC1	-3.759515658	0.0140403	0.534801	0.6660006	0	0	0	0	1.963003	0	4.270624	0	1.215607	0	5.991271	20.83319	
CECR2	-3.729710755	0.025751	0.665853	1.3320013	0.6676067	0	0	0	0	0	15.37425	6.043745	0	0	8.38778	0	
IL36B	-3.6947474806	0.00363	0.270811	0	0	0	1.0662987	4.042755	0.981502	0	0	1.276784	2.15607	12.44835	5.991271	10.41659	
UBEZQ1L1	-3.666566585	0.007744	0.388152	0	0.6676067	0	0	0	0.981502	0	0.854125	0.863392	6.078033	0	5.991271	9.11452	
EBI3	-3.652528592	0.014232	0.534426	0	0	0.9661508	1.0662987	0	0	1.10659022	23.06137	0	0	2.15607	2.489671	3.594763	
CXCL11	-3.594252613	0.001233	0.160118	1.3320013	4.6732468	0	0	1.042755	0	0	15.37425	1.726784	1.215607	49.79341	5.991271	5.208297	
MYL7	-3.578196769	0.033845	0.739169	0.6660006	0	0	0	0	0	0	2.562374	3.453568	1.215607	8.713847	0	0	
WDR72	-3.482062504	0.014078	0.531402	1.3320013	0	8.6953575	5.3314934	2.513776	0.981502	6.63954131	27.33194	0	4.862426	4.979341	231.2631	0	
NPY4R	-3.472453632	0.000349	0.065591	0	2.6704267	0.9661508	3.198896	0	0	0	9.395373	18.13123	4.862426	2.396508	3.906223		
SLURP2	-3.469626236	0.03742	0.765694	0	0	0	3.198896	0	0	0	0	3.453568	2.431213	0	7.189525	14.32282	
SPRR2B	-3.44266707	0.021858	0.620275	0	1.3352134	0	0	0	0	11.10362	1.726784	2.431213	0	1.198254	2.604148		
CACNG7	-3.353293139	0.027515	0.675007	0	0	0	0	0	0.981502	1.10659022	0	3.453568	6.078033	7.469012	0	1.302074	
P13	-3.249264345	2.18E-07	0.00053	779.22075	920.62629	445.39553	1891.6139	555.7885	334.6921	1498.32316	5971.180	2090.272	1845.291	1744.014	7968.391	32751.07	
RUNX1T1	-3.193022074	0.007459	0.388152	0	0.6676067	0	1.9323017	4.042755	2.944505	0	0	13.81427	20.66531	8.713847	0	7.812445	
SP140	-3.19245536	0.039586	1	0	0	0	0	0	1.10659022	0	5.124749	0.863392	3.64682	1.244835	0	1.198254	
CASP1	-3.152194279	0.039944	0.770863	9.3240089	0	0	0	0	1.10659022	31.60262	33.67229	0	2.489671	0	14.32282		
EMX2	-3.098102785	0.009002	0.431743	0	0.6676067	0	0	2.08551	0.981502	3.1977065	0	14.67677	13.37167	8.713847	0	13.02074	
STUM	-3.096278246	0.0030548	0.70536	0	1.3352134	0	0	1.042755	0	0	20.49899	0	0	7.469012	1.198254	2.604148	
ENPP2	-3.090341113	0.003168	0.256454	0.6660006	0	1.0662987	0	1.042755	0	0	2.562374	6.043745	3.64682	1.244835	9.586034	1.302074	
OR7D2	-3.055777747	0.01143	0.4902	0	0	1.9323017	2.1325974	1.042755	0	2.21318044	11.10362	15.54106	2.431213	0	20.37032	0	
CARD18	-3.042366809	0.007048	0.001161	21.31202	6.6766069	11.59381	6.3977005	46.39705	13.3977065	46.12274	49.21335	14.58728	51.03825	31.15461	22.0505		
PRRX1	-3.037801856	0.000449	0.075194	3.3300032	11.349314	59.101352	0	11.47031	23.55604	11.0659022	24.76961	79.739	258.9242	144.4009	1.198254	139.3219	
FAP	-3.035702176	0.022554	0.62835	0	0	0	1.0626987	0	0.981502	0	4.276782	2.590176	1.215607	2.489671	0	3.906223	
SORCS1	-3.022393399	0.007195	0.386028	0	0	3.8646033	0	0	0.981502	0	2.562374	5.180352	8.509246	4.979341	1.198254	10.41659	
HOXD8	-3.017281237	0.002729	0.23949	0	0.6676067	10.672659	0	0.20851	1.01659022	0	1.10659022	3.164699	18.13123	26.74334	19.91736	1.198254	
DEPP1	-3.023713238	0.004227	0.287825	3.9960038	16.690167	28.018734	31.98896	4.171021	8.833516	16.5988533	572.62636	4.31696	7.293639	41.07956	118.6722	2.604148	
CALML5	-2.959710717	3.35E-05	0.013553	45.288043	40.056401	17.3032107	0	0	0	13.861883	9.384796	8.915017	4.42636087	9.395373	73.18833	0	
ITGA7	-2.902816715	0.001944	0.172804	9.9900096	16.690167	9.3464936	0	4.2651947	3.128265	0	0	3.31977065	30.74849	86.33921	8.509246	41.07956	0
COL6A3	-2.899559707	0.017263	0.571147	0.6660006	0	0.9661508	0	0	70.66812	1.10659022	0	8.633921	6.078033	9.958682	4.793017	0	
SPRK2E	-2.889475771	1.39E-07	0.000406	46.620045	47.400075	22.214261	54.381233	14.59857	7.852014	101.8063	327.1298	23.47328	131.2855	95.85232	274.4002	817.7026	
BRINP3	-2.873497803	0.002576	0.229754	0	0.6660006	2.6704267	16.425464	0	8.833516	3.1977065	12.81187	47.48656	6.42715	39.83473	0	35.156	
SFRP2	-2.852244374	0.001538	0.176412	0	0.3380334	0	0	0	0.981502	0	4.171021	7.852014	4.42636087	9.395373	62.16423	6.42715	
NEFL	-2.845606667	0.002586	0.229754	17.316017	9.3464936	0	4.2651947	3.128265	0	0	3.31977065	30.74849	86.33921	8.509246	41.07956	0	
MAP1B	-2.806600233	0.001286	0.158848	404.92839	10.681707	3.8646033	2.1325974	1.042755	11.77802	0	16.14296	50.07674	4.862426</				

gene_id	log2FoldChange	pvalue	padj	nonTO-01	nonTO-02	nonTO-03	nonTO-04	nonTO-05	nonTO-06	nonTO-07	TO-01	TO-02	TO-03	TO-04	TO-05	TO-06	
S100A12	-2.305434901	0.000277	0.058748	3.3300032	18.025381	10.627659	23.458571	5.213776	10.79652	23.2383946	146.0553	12.08749	12.15607	44.81407	35.94763	148.4365	
ZFP42	-2.284652026	0.028078	0.679555	0.666006	2.0028201	1.9323017	0	0	0.981502	1.10659022	11.10362	6.907137	1.215607	1.244835	0	7.812445	
KRT77	-2.274731678	0.001645	0.18356	1.3320013	2.0028201	3.8646033	2.1325974	5.213776	1.963003	4.42636087	14.52012	0	13.37167	7.469012	19.17207	31.24978	
HIST2H3D	-2.261885011	0.002911	0.249163	0.666006	1.3352134	0	6.3977921	0	2.944505	1.10659022	14.52012	5.180352	6.078033	9.958682	8.38778	5.208297	
KRTDAP	-2.259921427	0.003619	0.270811	101.2321	10.681707	6.7630558	33.055259	13.55582	16.68553	30.9845261	10.2495	239.1596	48.62426	27.38638	35.94763	515.6214	
CCL20	-2.25571701	0.001425	0.16882	5.9940057	65.425455	59.901352	28.790604	19.81235	16.68553	34.3042968	627.7817	23.31159	23.09653	95.85232	43.13715	131.5095	
MMP1	-2.25379055	0.004316	0.291145	124.54212	2445.4433	24.153771	13.861883	16.685463	11.77802	78.5679055	1005.305	94.97313	19.44971	265.1499	9.586034	158.8531	
MYO7A	-2.25211353	0.00056	0.086777	7.326007	2.6704267	9.6615083	1.0662987	1.042755	2.944505	0	15.37425	9.497713	9.724853	24.89671	10.78429	33.85393	
HEPH1	-2.247701889	0.027007	0.672647	93.906095	82.783229	10.627659	9.5966881	3.128265	0	3.31977065	295.5272	257.2908	44.97744	69.71078	34.74937	128.9053	
MARCO	-2.24528001	0.003862	0.27518	0.666006	4.0056041	11.59381	23.29227	1.042755	0	11.0659022	77.72535	9.497313	13.37167	31.12088	27.55985	44.27052	
PCDH16	-2.244125012	0.017359	0.572219	1.3320013	0.6676067	9.961508	2.1325974	1.042755	0	5.124749	5.180352	7.293639	2.489671	4.793017	0		
CLDN17	-2.237393904	0.002095	0.203973	5.3280051	10.0141	6.7630558	14.928182	32.32541	5.88901	11.0659022	40.99799	7.770529	36.4682	17.42769	8.38778	236.9775	
APOL1	-2.215663376	4.25E-05	0.01167	133.20013	465.32186	710.12086	609.9284	481.7529	396.5257	4.1791332	74.2053	151.919	107.2165	1440.274	1082.024	513.0172	
TUBA1A	-2.190649677	7.17E-07	0.00161	160.56105	120.1692	51.205994	31.98986	54.22327	118.7617	55.3295109	743.0888	249.5203	249.1993	497.9314	116.2307	467.4446	
TLR2	-2.178445648	0.000356	0.065591	7.9920076	4.6732468	3.8646033	7.4640909	3.128265	117.77802	12.1724924	105.9115	31.94551	14.58728	19.91736	16.77556	6.510371	
TMPRSS11B	-2.169322634	0.000395	0.070286	64.60262	17.357774	16.425464	50.116038	39.6247	11.77802	38.7306576	399.7304	8.633921	79.01443	159.3389	61.11097	212.2381	
PDE3B	-2.167296745	0.004037	0.283086	2.6640025	12.01692	4.8307542	17.060779	11.47031	3.926007	13.2790826	18.79078	5.345368	24.31213	4.979341	167.7556	31.24978	
MAP6	-2.158214975	0.018163	0.576919	0.666006	5.3408535	4.8307542	1.0662987	1.042755	0.981502	0	20.49894	5.250917	6.078033	14.93802	0	10.41659	
NHLH2	-2.153095577	0.007529	0.390365	12.654012	14.01974	9.9661508	7.4640908	2.08551	0.981502	4.24636087	72.60061	8.53568	10.94046	22.40704	23.95608	0	
GLDN	-2.147150104	0.018013	0.576919	2.6640025	6.6676067	3.8646033	5.3134934	16.68408	0	2.21318044	28.18612	9.497313	40.11502	0	34.74937	5.208297	
HIST1H1D	-2.137072623	0.047917	0.848751	1.3320013	0.6676067	9.9661508	1.0662987	0	0.981502	3.361428	4.31696	1.215607	0	3.594763	1.302074		
FER1L6	-2.132673462	0.039567	0.773798	76.590073	53.408535	87.919726	26.657467	54.22327	40.24157	15.4922631	1032.631	1.726784	23.09653	174.2769	97.05859	3.906223	
KRT79	-2.118456656	0.00723	0.386028	0	2.0028201	3.8646033	5.3134934	2.08551	0.981502	2.21318044	23.06137	1.726784	2.431213	16.18286	9.586034	6.510371	
IL33	-2.112316324	0.038087	0.274565	18.648018	3.8540836	28.018374	4.982182	15.64133	5.1202514	58.8901	21.0522141	586.7837	115.56579	21.88092	115.7697	8.38778	42.96845
EEF1A2	-2.110523784	0.008975	0.431743	23.976023	2.0028201	28.98452	102.36467	18.76959	20.61154	8.85272174	398.8763	1.726784	131.2855	49.79341	135.4027	41.66637	
HIST1H2BG	-2.103579813	1.8E-05	0.008871	15.984015	18.025381	19.32031	26.657467	15.64133	12.75952	28.7713457	198.1569	24.17498	19.44971	126.9732	57.15162	76.82238	
WDFC12	-2.092273832	7.12E-05	0.023064	12.654012	6.0084602	4.8307542	5.830395	3.1286075	7.74613153	42.70624	9.7497313	41.33062	6.224176	39.54239	33.85393		
PLGVRP4	-2.086664476	4.11E-06	0.003326	18.798217	18.025381	83.08978	56.513886	33.36816	51.021959	21.0252141	24.3853	92.62395	62.66125	136.9319	117.4289	380.2057	
SLC24A3	-2.084743317	0.014012	0.530288	13.986013	5.3352134	9.9661508	11.729285	2.08551	0.981502	15.069022	15.3743	8.623921	6.078033	4.979341	74.29176	9.11452	
FPR1	-2.073123893	0.049544	0.855164	1.998019	0	3.8646033	5.3134934	0	0	3.31977065	30.74849	1.726784	1.215607	11.20352	4.793017	1.302074	
TRABD2A	-2.072953979	0.02671	0.676247	1.3320014	5.3408535	19.32031	1.0662987	0	0	3.31977065	21.35312	7.770529	2.431213	9.595682	5.991271	0	
CSAR2	-2.06782489	0.005635	0.336498	1.9980019	3.3380334	15.485413	9.5966881	9.384796	6.870512	3.137167	6.931513	41.33062	8.28303	2.604148			
DAPK1	-2.06170582	0.007099	0.385943	19.82017	14.01974	102.41199	29.856836	22.94063	106.00201	7.74613152	49.40267	14.58728	117.0145	391.8291	37.76015		
OASL	-2.05378481	0.00536	0.328129	8.6580083	23.71874	67.630558	49.047939	55.26602	24.53754	109.552432	49.24548	19.85802	14.58728	724.4941	301.9601	62.49956	
PLDGHG1	-2.032580156	0.008704	0.424122	3.3300032	1.3352134	2.8984525	1.0662987	4.171021	0	0	7.86123	9.601377	3.364682	18.67253	2.396508	6.510371	
DHR52	-2.03091794	0.013081	0.51512	2.6640025	3.5408535	3.8646033	2.6521947	1.042755	0	4.42636087	9.395373	11.2241	0	38.58989	13.1808	3.906223	
GABRO	-2.017745796	0.032601	0.370377	9.180019	6.6676067	0.9661508	12.352974	1.042755	0.981502	1.215607	2.416499	11.2241	1.215607	7.469012	0	3.906223	
ATP6V0A4	-2.012375845	0.003009	0.249163	2.6640025	4.6732468	23.18762	36.254155	17.72684	16.68553	12.1724924	174.42415	2.590176	21.76456	56.01759	52.72319	74.21823	
CSNK1A1L	-2.012340479	0.044981	0.836779	0	0.6676067	15.458413	1.0662987	2.08551	6.870512	0	0.854125	32.8089	23.09653	16.18286	14.32282		
SLC10A6	-2.006230183	0.002556	0.572647	1.998019	28.039481	18.356886	3.198896	7.292898	0.981502	4.24636087	138.9058	5.209015	12.15607	11.20352	63.50743	1.302074	
CEACAM7	-1.993375465	0.010366	0.464721	14.652014	6.4732468	18.356886	7.9896102	49.09949	37.29707	28.7713457	45.71409	13.7187	9.93247	14.33062	14.32282		
AKNA1D	-1.986382893	0.023928	0.5724806	7.3436735	0	1.2325974	0.981502	3.31977065	14.0659022	21.2318044	4.2167064	1.9705179	6.91516	23.52739	28.7581	63.80164	
MDGA1	-1.976114549	0.012974	0.514478	88.578085	94.801049	15.9381	27.73766	19.81235	46.13058	15.4922631	13.666	15.54106	55.60698	32.36572	67.384	31.70120	
CDYL2	-1.973422204	0.0044779	0.312217	4.6620025	3.74346735	2.8984525	0	1.062779	0.981502	1.215607	25.62374	50.526692	35.87232	52.66692	7.293639	31.12088	
GATA2	-1.972823002	0.014329	0.739169	117.21611	111.49032	67.630558	56.51388	45.88123	35.33406	30.564419	137.2793	6.90173	15.726784	25.52774	11.20352	1.198254	
CIDEA	-1.972394575	0.023874	0.642071	0.6660004	16.205226	10.16247	107.69617	138.6864	18.54223	157.135811	133.1581	718.3422	67.95241	312.4537	58.84328	298.175	
ESR1	-1.968571059	0.009099	0.433243	6.676006	2.6704267	6.062987	1.042755	0.981502	0	2.1312047	99.9236	10.74237	104.5422	52.28308	32.35286	59.34758	
CD1D	-1.957041787	2.16E-05	0.010842	16.650016	13.757774	22.21469	10.760779	22.94061	6.870512	13.2709826	89.6831	69.93476	24.31213	21.1622	115.0324	39.06223	
HIST1H2BC	-1.950134859																

gene_id	log2FoldChange	pvalue	padj	nonTO-01	nonTO-02	nonTO-03	nonTO-04	nonTO-05	nonTO-06	nonTO-07	TO-01	TO-02	TO-03	TO-04	TO-05	TO-06	
TMC1	-1.602100293	0.024949	0.654975	4.6620045	2.0028201	2.9894525	2.1325974	2.08551	0	2.21318044	7.687123	0.863392	8.509246	4.979341	14.37905	6.510371	
HSD17B2	-1.601790344	0.030407	0.704335	0.666006	2.0028201	12.559961	3.198896	6.256551	4.907509	0	30.74849	10.3607	8.509246	11.20352	11.98254	2.604148	
SLC6A11	-1.600223799	9.98e-05	0.029663	107.8921	237.00037	259.89457	148.21552	143.9002	55.9456	138.323777	352.7535	873.7528	587.138	562.6656	121.0237	338.5393	
CNFN	-1.597930355	0.00332	0.265978	45.954044	22.698627	55.070597	151.41441	66.73633	112.8772	54.229207	210.9686	57.84727	128.8543	68.46594	176.1434	67.0786	
KNDC1	-1.596884712	0.000986	0.128297	4.6620045	4.6732468	7.7292067	3.6977921	17.72684	2.944505	9.95931196	9.395373	34.53568	13.37167	33.61055	27.55985	19.53111	
IGFBP3	-1.593133694	0.04464	0.833845	13.320013	20.695807	1.9323017	1.0626987	10.42755	15.70403	4.42636087	20.49899	39.71604	14.58728	85.89364	0	15.62489	
APOL2	-1.590138465	0.00015	0.038454	111.88811	277.05677	197.09477	282.56915	163.7126	242.4309	147.176499	1726.186	375.5756	309.9797	612.459	361.8728	281.248	
C1QL1	-1.5821913	0.01947	0.583617	7.326007	7.3436735	7.7292067	8.5303895	9.384796	12.759552	4.42636087	1.70825	5.180352	23.09653	11.20352	86.2743	20.83319	
DGAT2	-1.577123101	1.15e-05	0.006719	93.240089	148.20868	145.88878	250.58019	204.38	138.3917	235.703716	653.4055	265.0614	246.7681	367.2264	479.3017	1096.346	
HIST2H2Bf	-1.576705971	0.006205	0.355949	7.326007	10.681707	6.7630558	12.795754	6.256531	15.70403	3.1977065	68.32998	4.31696	15.80289	38.58989	21.56858	11.71867	
ICOSLG	-1.576069666	4.59e-06	0.003347	18.648018	17.357774	25.11992	23.458571	19.81235	58.8901	15.4922631	93.95373	87.2026	98.46413	70.95561	50.32668	53.38504	
ESPNL	-1.570512545	0.014663	0.53882	2.6640025	2.0028201	0	2.1325974	6.256531	3.926007	2.21318044	9.395373	14.67676	6.078033	2.489671	7.189525	7.812445	
XG	-1.553045757	3.44e-06	0.002946	122.54412	95.467756	56.036748	81.46464	79.51837	213.5312	120.0115	393.8565	199.1736	210.8927	52.21318			
GNAO1	-1.544776244	0.00792	0.403454	29.97029	10.0141	9.6615083	9.5966881	7.299286	5.88901	8.85272174	5.978873	83.74903	36.4682	44.81407	10.78429	23.43734	
IL1A	-1.533389512	0.003587	0.270811	98.568094	498.03459	127.53191	172.74039	237.7482	48.09358	126.151285	792.6278	1263.143	153.1664	387.1438	215.6858	437.4969	
CDRT1	-1.524927397	0.018492	0.576916	3.9960038	12.684527	24.153771	14.928182	6.256531	16.68533	2.21318044	91.16298	6.047345	8.509246	65.97672	25.16334	18.22904	
TLR1	-1.524877738	0.002238	0.213166	5.3280051	9.3464936	15.458413	19.193376	8.342041	9.815017	13.790826	82.8501	13.81427	29.17456	31.12088	9.586034	29.94771	
GYGV	-1.517728141	0.022567	0.62835	1.998019	2.0028201	4.8307542	5.3134934	4.171021	4.907509	1.10659022	17.93662	8.633921	9.724853	0	15.7731	6.510371	
TMEM45A	-1.516665859	0.002989	0.249163	398.26838	15.88757	91.784329	9.7972401	47.96674	88.33516	6.86085935	497.9547	233.1159	184.7722	145.3596	327.1234	893.2229	
PCDHAC1	-1.515385347	0.039319	0.777398	0.6660000	3.3380334	8.6953575	5.3134934	2.08551	3.926007	2.21318044	26.4778	4.3169	3.64682	21.1622	2.396508	5.208297	
TUBB2A	-1.511192853	3.33e-05	0.013553	218.44821	180.25381	88.885877	205.79565	134.5154	148.2088	147.176499	699.5282	370.3952	193.2814	414.5302	189.3242	87.9003	
SAMD9L	-1.510704562	0.023664	0.640303	4.6620045	4.67058962	42.510637	92.769785	58.39429	64.77911	43.1570185	512.8070	23.31159	31.60577	153.1147	112.6359	40.3643	
CA2	-1.509123941	2.27e-06	0.02359	455.5444	407.70976	187.43326	42.615759	393.1174	147.2253	107.013	1480.717	485.027	812.8774	899.8889	739.5782		
FN1	-1.501446105	0.017803	0.575152	137.19613	30.70908	83.08972	24.52487	6.962938	20.05999	38.7306576	398.0221	22.7552	289.3144	399.5921	13.1808	61.19749	
INA	-1.499319797	0.007397	0.388152	5.2597025	35.383154	22.21469	30.926266	33.36816	23.55604	52.0097402	76.87123	9.497313	32.82138	105.811	37.14588	279.946	
GRB14	-1.493868871	0.038945	0.774984	13.986013	2.6704267	4.6953575	3.5134934	2.08551	3.926007	3.1977065	47.83099	4.31696	6.078033	27.38638	4.296508	9.11452	
PGPDS	-1.480293423	0.004189	0.287282	119.98801	58.018782	19.16247	60.77925	128.2589	103.0577	170.414984	77.4916	174.4052	49.5196	47.2822	98.25685	361.9766	
POU3F1	-1.47872116	0.001996	0.200767	109.2241	42.052921	20.89167	61.84532	65.693597	32.389576	17.7045435	206.3507	162.8913	148.1354	179.7381	115.8846		
PTHLH	-1.476097959	0.00151	0.457157	2909.9085	3085.0105	1208.6547	908.99479	1007.301	497.6214	81.08942	126.2997	462.057	2352.199	6765.68	2316.225	2812.48	
KRT14	-1.473398849	0.003575	0.270811	2314.085	89955.328	49090.124	4516.8412	64183.66	1581.97	86190.0898	90409.11	305917.7	215824.9	186073	104426.7	481465.4	
LTBP1	-1.467160907	0.003469	0.270811	1768.8977	284.00217	656.01641	89.2931	723.6721	207.0957	650.675048	286.3367	720.597	2201.464	2423.694	130.502	2308.578	
CYVR1	-1.464944341	0.005144	0.329214	107.8921	66.93062	15.458413	55.915168	20.8551	54.9641	12.174294	84.5124	261.6078	168.9693	57.26242	74.29176	9.21616	
AFAPII2	-1.455699045	4.98e-05	0.015828	73.0626	84.786049	137.19342	115.16025	56.30878	137.4120	73.034944	81.476054	481.7264	439.4666	203.0063	211.622	387.0361	341.1434
ATG9B	-1.452233317	0.027194	0.672683	149.18414	30.624301	9.615083	15.16026	46.92398	81.46464	18.812037	34.526057	25.03837	326.9982	90.87298	424.182	15.62489	
ITGBL1	-1.444690446	0.044406	0.813162	9.3240089	32.045121	38.646033	13.861883	7.299286	1.963003	37.6240674	67.47586	44.89639	32.82138	1.244835	32.35286	149.7385	
HIST1H2BD	-1.419036508	0.02321	0.215395	61.272059	47.852385	134.29497	99.165779	86.548668	110.9097	128.364655	730.2767	67.34458	93.60171	192.9495	210.8927	235.6754	
SLT3	-1.418973022	0.047755	0.4884751	632.0346	16.022556	6.763058	1.062987	6.256531	47.11208	1.10659022	22.20724	33.67229	109.4046	24.89671	21.56858	19.53111	
KLF13	-1.413182454	0.045428	0.367879	86.58003	48.067681	9.9661508	21.524957	176.22524	44.17675	113.978792	57.22638	404.9309	56.04195	296.27708	46.73192	199.2174	
SERPING1	-1.403831881	0.032411	0.739169	17.316017	10.258381	3.861998	4.9374939	5.180518	7.4051508	9.075099	14.3856728	25.1127	25.90176	48.62426	36.575728		
VGLL3	-1.401942093	0.02342	0.635429	1.6352983	149.18414	13.85612	4.6732468	18.356866	14.928182	9.3987478	247.2354	73.16119	114.9964	590.0519	283.9863	207.0298	
S100A9	-1.40022075	0.018319	0.576919	4274.5901	211.650404	202.48134	317.394314	190365.54	15356.58	34492.4171	522.708	1367.32	21728.6	50259.58	144130.5		
BSRK2	-1.398521308	0.019043	0.582902	5.3280021	2.0028201	37.69882	23.392272	39.6247	3.926007	0	9.39537	4.31696	7.293639	17.42769	11.98254	7.812445	
WNT6	-1.369294516	0.017157	0.571147	3.9960038	12.684527	7.292067	5.303895	6.256531	3.926007	2.21318044	17.0825	11.2241	12.15607	4.979341	9.586034	46.87467	
BMP6	-1.369294516	0.017157	0.571147	3.9960038	12.684527	7.292067	5.303895	6.256531	3.926007	2.21318044	17.0825	11.2241	12.15607	4.979341	9.586034	46.87467	
LHXS	-1.365800918	0.001786	0.192717	11.322011	16.022556	9.6615083	9.5966881	15.625631	9.782014	4.42636087	6.261507	17.01849	26.65077	17.01849	2.18294		
RHBG	-1.344422298	0.0229346	0.659232	3.3300032	8.0012802	22.21469	47.934834	15.61433	16.68533	16.5988533	12.364955	10.4386	5.018352	25.52774	92.11781	92.26558	
WDFC5	-1.334024527	0.0030193	0.4816047	48.618047	18.265381	28.8649525	24.52487	32.32541	20.611584	14.3857628	72.60036	63.59405	63.21154	23.65187	69.00993	20.1085	
COL1A1	-1.332052749	0.010545	0.471311	468.19845	114.160												

gene_id	log2FoldChange	pvalue	padj	nonTO-01	nonTO-02	nonTO-03	nonTO-04	nonTO-05	nonTO-06	nonTO-07	TO-01	TO-02	TO-03	TO-04	TO-05	TO-06	
IQCA1	-1.125073355	3.45E-05	0.013595	33.300032	50.070501	28.06072	44.784545	44.83847	55.9456	50.90315	132.3893	93.24634	53.48669	125.7284	97.05859	67.70786	
SLC39A2	-1.12394343	0.027805	0.67859	40.626039	25.369054	48.307542	69.309414	81.3349	67.72362	136.110597	245.1338	29.35533	52.53267	56.01759	118.6272	337.2372	
MARCKSL1	-1.114131756	0.018945	0.58233	304.36229	388.54709	636.6934	213.25974	134.5154	215.9304	252.30257	1883.345	204.6239	260.1398	520.3412	567.9725	544.267	
BCAT1	-1.112018569	0.012312	0.502493	191.80818	552.11073	351.6789	942.60803	507.8128	226.7269	193.653288	149.5572	1625.767	407.2282	368.4712	721.349	874.9933	
TMPRSS13	-1.109635056	0.027961	0.678993	49.284047	88.124083	79.224368	103.43097	462.9833	267.95	217.998273	524.4326	126.0552	265.0022	323.8572	321.1321	785.1508	
CTSV	-1.104062602	0.000186	0.044509	768.56474	459.3134	256.99612	380.66863	314.9121	270.8945	712.6441	92.4545	910.8786	971.2697	1004.582	644.6608	1378.897	
CTXN1	-1.1031344405	0.011341	0.4902	25.308024	30.709908	25.119922	24.52487	9.384796	8.833916	28.7713457	78.5794	22.44819	34.03698	89.62814	31.15461	26.04148	
RIM53	-1.103134672	0.004882	0.31472	169.16416	73.436735	70.529011	44.784545	92.80521	49.07509	28.7713457	183.6368	265.9248	178.6942	149.3802	73.09351	124.9991	
ADTRP	-1.100465624	0.01303	0.514478	91.908088	62.087422	24.153771	37.320454	67.77908	22.57454	32.091163	43.56036	155.6945	55.9179	77.17979	89.86907	242.1858	
HIST1H4I	-1.099908822	0.009624	0.446564	32.634031	19.360594	48.307542	47.983441	47.75296	31.40806	45.3701989	180.2203	21.5848	35.25259	92.11781	69.49875	91.1452	
CNNM1	-1.095924162	0.011594	0.4902	49.15804	52.740928	28.018374	44.784545	42.7529	41.223307	24.4499484	27.33194	50.07674	65.64276	62.24176	239.6508	62.49956	
TLR6	-1.094901725	0.01993	0.595967	38.628037	19.360594	33.815279	58.958636	5.213776	11.77802	13.2790826	51.24749	43.1696	59.56472	75.93495	37.76015		
ANGPTL4	-1.094210936	0.013508	0.524838	713.95268	668.9419	311.10057	366.80675	235.6627	237.5234	317.591393	2460.733	383.3461	410.875	754.3702	653.0486	557.2878	
TMEM204	-1.093519331	0.046672	0.840239	15.18015	46.687347	38.646033	6.397792	12.51306	14.722353	3.3197705	26.47787	40.57943	9.724853	28.63121	14.37905	74.21823	
EHD3	-1.093094937	0.018462	0.576919	100.5661	140.1974	349.7466	412.65759	300.5534	199.2449	327.550705	128.598	88.06599	390.2097	40.4651	680.6084	490.882	
ADAMTS17	-1.092506739	0.026592	0.672647	689.3106	9.3464936	6.7630536	36.254514	9.384798	33.37106	6.63954131	35.01912	52.66692	40.11502	13.69319	39.54239	58.59334	
ZNF883	-1.092071000	0.000536	0.085199	33.300032	24.701447	39.612184	63.97972	37.53919	17.66703	47.5833794	115.3068	70.97815	49.83987	59.75209	103.0499	80.7286	
HIST1H1C	-1.081732191	0.017566	0.573917	121.21212	127.51288	365.20501	317.75701	214.8076	281.691	374.02794	1211.149	91.51956	294.1768	438.182	674.6171	557.2878	
DACT2	-1.076595897	0.036505	0.757515	58.60805	22.698627	3.8646033	19.81235	50.05674	21.0252141	13.666	44.89639	96.03292	53.52792	77.88653	76.82238		
BIRC3	-1.066378479	0.011638	0.4902	70.596086	59.54966	54.104447	123.69065	44.83847	40.24157	89.638077	399.7309	119.1481	151.9508	210.3772	107.8429	104.1659	
MICAL1	-1.065581718	0.011771	0.4914176	339.66033	405.23726	107.24274	97.03188	165.7981	135.1744	203.6126	537.2445	717.4778	226.1028	539.0137	129.4115	462.2363	
SPRR1B	-1.065510176	0.002039	0.200767	391.20877	465.12158	333.1865	744.8331	610.3246	635.7187	75.7134758	185.787	435.813	6226.337	9908.889	11398.99	20054.55	
CCDC71L	-1.064633141	0.002197	0.210629	282.38427	232.99473	116.90425	129.02214	112.6176	258.135	147.176499	569.7012	539.6201	238.2589	245.2326	176.1434	526.038	
TMMEM86A	-1.053906024	0.039396	0.777398	9.990096	71.433915	107.24274	37.320458	68.821408	30.426655	46.4767892	23.3219	34.53568	41.30062	113.28	80.28303	161.4572	
CD4	-1.058581464	0.021898	0.620275	63.938061	63.422635	79.24368	60.779025	86.54868	53.0019	252.30257	47.74558	76.8419	165.3225	118.6272	217.4464		
CS7A	-1.051092981	0.037418	0.765569	33.00032	327.32756	47.11176	93.10157	85.73253	465.7226	107.20414	1048.069	4868.668	5814.246	5543.252	8469.261	44112.97	
GPRC5D	-1.045458458	0.019305	0.585598	5.328005	15.354954	27.02223	19.193376	18.76959	12.75952	6.63954131	33.31087	19.8502	9.724853	44.81407	33.55112	44.27052	
SLC31A2	-1.044724914	2.92E-06	0.002659	398.26838	472.66555	282.11604	358.27636	333.6816	188.4483	382.880215	855.334	768.419	536.0825	687.1491	536.8179	911.452	
HERC6	-1.042137962	0.043366	0.820575	52.82049	62.08742	108.20889	133.2873	83.42403	106.02202	172.62089	520.162	74.25172	59.84912	395.8576	155.7731	58.59334	
EPGN	-1.029536982	0.020286	0.59784	76.590073	38.721188	112.0735	27.73736	94.89072	61.83461	52.0097402	140.0765	144.1865	55.9179	73.44528	63.50747	334.6331	
TH	-1.018814744	0.03407	0.739169	27.306026	15.354954	4.837054	11.729376	10.42755	5.88991	19.198239	16.22837	51.80352	37.6883	32.36572	14.37905	14.32282	
BBS12	-1.018369786	0.005879	0.346763	31.968013	40.456401	38.18977	65.67467	23.98337	15.70403	40.943881	107.1697	101.8803	38.89941	43.56924	29.95636	42.96845	
CCND2	-1.013956743	0.014365	0.534801	650.68626	394.55555	1027.0183	371.07194	76.43646	332.7291	286.60866	1751.81	74.7697	391.4253	520.0423	523.4338		
JAZF1	-1.011731762	0.008104	0.407972	27.306026	28.707087	35.745871	20.259576	31.282365	79.99286	96.18717	38.7305676	51.24749	39.71604	53.48669	14.93802	55.11969	24.73941
ELOVL7	-1.011308917	0.008052	0.419397	53.280051	15.55236	76.325916	45.850843	71.95011	44.16758	85.2074468	327.9832	116.55759	110.6202	179.2563	80.28303	105.468	
IFIT2	-1.012044984	0.018921	0.58233	4.956042	72.101522	47.341391	81.0387	53.18051	73.61263	76.579055	82.8501	53.53031	74.152	375.9403	128.2132	62.49956	
HIST2H2BE	-1.007712001	0.018343	0.576919	71.928069	76.774769	115.9381	149.28182	130.5397	57.5426913	476.6016	48.34996	134.9323	275.1086	190.5224	113.2805		
P3H3	-1.004905252	0.030907	0.710858	388.27837	64.757849	113.03965	340.14928	178.3111	318.9881	326.444114	93.9537	23.1159	212.7312	102.0765	159.3678	148.4365	
RHOBTB3	-1.016355574	0.007031	0.38366	801.86477	1008.7537	216.31033	107.22322	22.39227	19.81239	117.20213	23.0223	72.71003	104.0811	29.9613	82.29657	25.2065	20.83319
CNTNAP3B	-1.029926864	0.016788	0.569971	109.1901	190.26791	17.390715	6.325916	15.7122	158.4988	358.2481	49.765598	71.74649	57.84727	14.74197	20.94928	50.78089	
RBMS3	-1.025255026	0.012944	0.514478	175.15817	92.797329	33.815279	60.779025	72.99286	96.18717	38.7305676	51.24749	39.71604	53.48669	14.93802	55.11969	140.1957	
SLC16A14	-1.024596248	0.008472	0.567554	16.741616	56.078962	427.03867	154.61331	124.0879	111.76512	55.5181	74.8472	138.5792	39.84373	124.6184	87.23897		
SPRY2	-1.0153680502	0.006541	0.36065	1680.9856	353.16394	268.58993	340.14928	311.7838	490.7509	30.7632081	194.7404	240.023	362.2508	150.6251	246.8404	252.6024	
STON1	-1.015619124	0.034543	0.739169	13.986013	33.380334	111.59381	7.4640904	19.81235	8.351066	38.95783	4.213305	44.8173	12.44835	10.78429	9.11452		
SEMA3B	-1.022564964	0.007139	0.672683	119.88011	174.245343	111.00538	146.08299	18.021874	38.13681	24.049484	35.87324	10.3607	2.431213	17.42769	4.793017	1.302074	
FARP1	-1.00595718	0.008898	0.430707	461.53844	336.47377	639.59185	480.90071	57.64634	877.4625	453.701983	36.12914	21.81335	24.91235	27.9837	134.5132	130.2074	
USP2	-1.045050755	0.027937	0.678993	16.650016	18.692987	89.85207	79.97401	44.83847	84.40915	26.5581652	24.76962	10.3607	30.39016	19.91736	47.93017	10.41659	
DNAJC22	-																

gene_id	log2FoldChange	pvalue	padj	nonTO-01	nonTO-02	nonTO-03	nonTO-04	nonTO-05	nonTO-06	nonTO-07	TO-01	TO-02	TO-03	TO-04	TO-05	TO-06		
ATAD3C	1.595897871	0.006424	0.365317	31.30203	28.039481	98.547385	21.325974	52.13776	66.74212	28.7713457	40.14386	0.863392	10.94046	19.91736	5.991271	14.32282		
ZBTB10	1.621188717	0.005241	0.324151	56.610054	98.805789	74.393614	27.723766	19.81235	137.4102	32.0911163	50.39336	2.590176	29.17456	17.42769	16.77556	7.812445		
LOX	1.639605684	0.008499	0.419397	861.80482	107.48468	57.002899	105.56357	106.361	281.691	44.2636087	53.80984	42.30621	177.4786	34.85539	57.5162	65.10371		
KISS1R	1.653945403	0.039755	0.777398	106.5601	19.360594	1.9323017	11.729285	4.171021	7.852014	17.7054435	17.93662	3.453568	12.15607	2.489671	3.594763	6.510371		
EYA1	1.666899613	2.24E-05	0.010842	46.620045	38.721188	30.916827	39.453051	35.45367	76.55713	32.0911163	5.124749	20.72141	20.66531	8.713847	19.17207	6.510371		
DOC2B	1.670587536	0.032902	0.732997	1.9980019	2.0028201	19.323017	40.51935	25.02612	44.16758	17.7054435	7.687123	0	7.293639	7.469012	15.57731	2.604148		
CHDH	1.679584463	0.001449	0.170308	54.612052	8.6788869	57.002899	18.127078	35.45367	93.24276	46.4767892	9.395373	5.180352	12.15607	19.91736	28.7581	9.11452		
DGC6	1.72988444	0.010296	0.464721	39.294038	14.01974	19.323017	20.259675	70.90735	91.27966	5.53295109	0.854125	7.770529	14.58728	28.63121	9.586034	6.510371		
HHEX	1.735527674	0.004936	0.31682	3.3300032	12.01692	19.323017	12.795584	5.213776	17.66703	9.05931196	4.270624	2.590176	0	2.489671	4.793017	6.510371		
VMO1	1.75344315	0.011489	0.4902	5.3280051	7.3436735	112.0735	29.856363	35.45367	60.85311	57.5426913	16.22837	7.770529	14.58728	0	22.76683	16.92696		
EPX	1.768577629	0.004493	0.300276	14.652014	9.3464936	5.796905	11.729285	15.64133	24.53754	2.21318044	2.562374	6.043745	4.862426	1.244835	4.793017	1.302074		
TENM3	1.77532556	0.015221	0.548937	225.77422	13.352134	13.526112	18.127078	34.41094	34.35254	4.2636087	22.17695	8.633921	21.88092	27.38638	10.78429	7.812445		
CACNB4	1.823416928	0.000105	0.030551	20.64602	24.701447	14.492262	7.4649008	10.42755	19.63030	15.4922631	6.832998	4.3169	3.64682	2.489671	5.991271	3.906223		
CHL1	1.82395616	0.034943	0.447436	2.6640025	19.360594	9.615083	5.3134934	26.653541	49.07509	6.63954131	10.2495	0	7.293639	0	3.594763	2.604148		
PLCH1	1.824775843	0.012851	0.514478	27.97207	0.0084602	5.796905	5.3134934	4.171021	8.678052	22.1318044	6.832998	5.180352	0	2.489671	1.198254	2.604148		
C9orf131	1.834517167	0.017029	0.569971	16.650016	14.687347	18.356866	15.99448	5.213776	14.72253	0	5.124749	0.863392	2.431213	8.713847	3.594763	0		
IFTIM7	1.835437593	1.8E-06	0.02016	327.67231	250.35251	472.44776	32.0222	271.1163	598.7161	735.862495	19.59446	31.94515	130.0699	67.22111	150.9	139.3219		
DMRT2	1.835904579	8.18E-05	0.025358	40.626039	117.49878	74.61312	10.42755	19.63030	15.4922631	6.832998	0	0	0.78033	2.489671	4.793017	2.604148		
B3GAT1	1.851515049	0.05442	0.330354	5.9940057	10.0141	6.985375	14.928183	8.324018	8.833574	6.63954131	0	0	0	2.489671	4.793017	2.604148		
MRAF	1.863841417	0.038751	0.774984	3.3300032	0.0028201	7.7292067	3.198896	6.256531	4.907509	1.10659022	0	0.863392	2.431213	1.244835	2.396508	0		
CDH4	1.864747252	0.001188	0.149247	22.640022	4.0056401	17.390715	28.956363	18.76599	9.815017	37.6240674	5.124749	0.863392	6.078033	6.224176	4.793017	10.41659		
SOBP	1.871690334	0.039467	0.777398	1.998019	35.381534	45.409809	18.127078	11.47031	173.7258	13.2790826	4.614699	0	26.74334	18.67253	20.37032	1.302074		
CCDC8	1.889763796	0.007445	0.388152	482.18446	27.724376	27.02223	140.75143	61.52552	29.42875	15.049627	9.395373	17.770529	79.01442	38.58989	3.594763	136.7178		
SYCP2	1.901665657	0.006138	0.353503	30.513634	41.391615	28.94852	15.99448	23.98337	29.98216	14.3856728	9.395373	31.08211	37.6883	11.20352	26.36159	14.32282		
ZNF423	1.96232323	0.014549	0.534801	10.65601	0.0028201	2.984952	4.2651947	5.213776	14.72253	5.53295109	8.854125	0.863392	3.64682	1.244835	3.594763	0		
NUP210	1.968577312	0.001838	0.19368	43.290041	65.425455	259.89457	37.320454	27.11163	112.8727	100.66971	46.97686	2.590176	17.01849	37.34506	33.55112	3.906223		
CKM	1.979495002	0.043996	0.827123	7.316017	3.3300032	4.830754	2.1325974	6.256531	11.77802	0	0.854125	0.863392	3.64682	0	4.793017	0		
LDOC1	1.985807173	0.009479	0.442666	129.20412	15.354954	84.051122	9.7627985	44.83847	6.477991	139.430367	4.270624	0.863392	6.224176	4.793017	32.36572	35.94763	50.78089	
SDK1	1.986272794	0.017216	0.571147	10.65601	5.3408535	5.796905	3.198896	42.75296	70.66812	7.74613153	8.514248	4.31696	2.431213	13.69319	2.396508	0		
HAPLN2	1.99047851	0.041837	0.803122	3.9240089	2.0028201	4.8307542	7.4640908	1.593001	1.10659022	0	0	2.431213	0	5.991271	2.604148	0		
KCNE3	2.032847542	0.004214	0.287825	14.70153	1.390175	14.71826	1.329837	1.383374	7.852014	15.4922631	8.514248	0	13.37167	6.224176	8.38778	3.906223		
AMOT	2.078631411	0.003749	0.274565	47.248047	14.39074	14.672468	52.180715	17.067708	17.22684	10.92826	26.5816562	0.498959	0	15.80289	6.224176	8.38778	5.208297	
TSPO2	2.085380983	0.004826	0.312497	33.966003	7.3436735	7.7292067	3.198896	5.3134934	10.42755	16.68535	3.31977065	4.270624	0.863392	4.862426	0	5.991271	1.302074	
SGCE	2.096894368	0.013797	0.529405	181.15217	70.766309	56.036748	70.375173	14.59857	64.77991	18.8120337	7.687123	0.863392	38.89941	47.30374	0	1.302074		
ARL13A	2.108786967	0.019512	0.5589807	11.988011	4.0056401	0	5.3314934	6.256531	14.72253	2.21318044	1.70825	0	1.215607	2.489671	11.64154	55.11969	26.04148	
ZDHHC2	2.130487723	0.003054	0.065591	47.952046	18.474367	27.02223	140.75143	61.52552	29.42875	15.049627	3.5641371	35.472864	52.95574	7.770529	93.60171	94.60748	16.92696	
JAM3	2.139494050	0.001118	0.442926	259.07425	26.036661	23.18762	14.928183	52.187145	10.760977	17.22684	10.24989	19.85802	10.494046	19.91736	14.37905	10.41659	0	
HCL51	2.142986884	0.000333	0.065231	15.318105	14.104664	5.670426	14.685655	6.760358	5.986363	54.22327	11.48357	5.53295109	1.70825	0.863392	21.88092	3.734505	3.594763	5.208297
ITGB2	2.198107077	0.000776	0.110386	9.3240089	130.85091	26.086072	18.361888	17.86959	16.848583	18.8120337	4.316499	4.31696	3.64682	13.69319	11.98254	7.812445	0	
SUPT4H1	2.219797358	0.021279	0.615155	7.326007	4.0056401	5.796905	3.198896	2.085511	3.926007	1.10659022	1.70825	0.863392	1.215607	0	0	0	0	
GPR18	2.229764533	0.040827	0.849211	1.9980019	4.0056401	11.5938	9.5966881	5.213776	11.292037	0	0	1.215607	0	4.979341	0	0		
NDN	2.231104081	0.009089	0.433244	2.6704026	22.214269	66.110518	96.97623	305.207	26.932706	30.207	0.53295109	15.37425	0	3.64682	1.244835	2.396508	0	
RUNX3	2.266360766	0.000881	0.110386	418.2484	24.033841	39.18594	116.22655	150.1567	32.72291	130.577646	34.16499	0.863392	34.03698	104.5662	83.8778	22.13526	0	
SFMBT2	2.311823522	0.0033551	0.736561	40.626039	26.074267	7.7292067	2.125974	0.1024755	2.944505	0	2.562374	52.95574	7.770529	93.60171	94.60748	16.92696	0	
RNF144A	2.319493488	0.000339	0.0270811	36.630035	20.039481	18.019519	15.71821	30.474486	15.684004	21.59304	15.4922631	4.16499	0	3.64682	1.244835	2.396508	0	
FAIM2	2.317625155	4.43E-06	0.003347	16.65061	4.6730243	20.384476	1.325974	1.319896	2.1325974	10.760977	0	0	10.67934	3.734505	3.594763	9.11452	0	
PKS1	2.355814074	0.000551	0.022911	16.17215	66.676067	0	0.9661508	3.198896	2.08551	12.75952	0	0	1.215607	0	0	0	0	
BGN	2.313045104	0.00514	0.022914	161.22914	1.325974	5.796905	0	0	0	10.215607	0	0	0	0	1.215607	0	0	
CHST9</td																		

Supplementary Table 2. List of genes with increased chromatin accessibility at promoter region and their expressions at stem state and differentiated state

Gene expression linked to peaks up in TO	Gene ID	Peak Annotation	Distance to TSS	p-value	Fold Change (log2)	TO vs. Non-TO
Stem state	FGF10	promoter-TSS (ENST00000264664.4)	-279	0.006825	6.49	up
	ITGAX	promoter-TSS (ENST00000562522.2)	-291	0.011157	4.35	up
	KLK12	promoter-TSS (ENST00000250351.4)	-53	0.001547	2.26	up
	RUNX1T1	promoter-TSS (ENST00000614812.4)	-12	0.019282	5.10	up
	ARHGAP24	promoter-TSS (ENST00000264343.4)	-906	0.005496	-1.52	down
	GRAMD1B	promoter-TSS (ENST00000646146.1)	-346	0.009418	-3.50	down
	IPCEF1	promoter-TSS (ENST00000367220.8)	-25	0.027998	-1.88	down
	RARB	promoter-TSS (ENST00000458646.1)	-76	0.020646	-3.20	down
	SEC16B	promoter-TSS (ENST00000308284.10)	-60	0.03691	-1.12	down
Differentiated state	ADAMTS5	promoter-TSS (ENST00000284987.5)	-899	0.000927	6.34	up
	AGMO	promoter-TSS (ENST00000342526.7)	11	0.015141	3.33	up
	ATP6V0D2	promoter-TSS (ENST00000285393.3)	49	0.000745	5.49	up
	C4orf19	promoter-TSS (ENST00000284437.6)	59	0.023027	1.28	up
	CD69	promoter-TSS (ENST00000228434.7)	-302	0.006832	5.20	up
	COL5A2	promoter-TSS (ENST00000374866.8)	-612	5.35E-07	3.35	up
	CSGALNACT1	promoter-TSS (ENST00000332246.10)	66	0.006357	1.75	up
	GABRP	promoter-TSS (ENST00000518525.5)	-55	1.28E-11	1.41	up
	GNG4	promoter-TSS (ENST00000484517.2)	-505	0.02777	2.29	up
	IDO1	promoter-TSS (ENST00000518237.5)	-201	1.34E-05	4.80	up
	MICAL2	promoter-TSS (ENST00000527546.5)	-478	6.05E-05	1.65	up
	ODAPH	promoter-TSS (ENST00000616557.1)	-209	0.000544	3.74	up
	PITPNM2	promoter-TSS (ENST00000542749.5)	-284	0.000982	1.18	up
	PTPN22	promoter-TSS (ENST00000525799.1)	-159	0.03057	2.51	up
	SATB2	promoter-TSS (ENST00000457245.5)	-242	0.026141	1.53	up
	SH2D1B	promoter-TSS (ENST00000367929.2)	23	0.007382	3.07	up
	TENM2	promoter-TSS (ENST00000518659.5)	-385	1.3E-07	1.99	up
	TNFSF11	promoter-TSS (ENST00000358545.6)	-383	0.006503	2.01	up
	BTNL8	promoter-TSS (ENST00000410920.1)	112	0.026586	-3.69	down
	CFAP58	promoter-TSS (ENST00000369703.1)	50	0.002	-2.39	down
	FABP6	promoter-TSS (ENST00000402432.3)	-590	2.12E-06	-4.35	down
	KLK14	promoter-TSS (ENST00000650543.1)	-348	0.016259	-2.31	down
	LYZ	promoter-TSS (ENST00000549690.1)	56	0.005913	-1.48	down
	MS4A8	promoter-TSS (ENST00000300226.6)	100	0.00853	-2.70	down
	NEK10	promoter-TSS (ENST00000383770.4)	-458, -640	0.041795	-1.76	down
	PACRG	promoter-TSS (ENST00000611387.1)	-900	0.003251	-2.72	down
	PPCDC	promoter-TSS (ENST00000563393.1)	98	0.039533	-1.66	down
	RP1	promoter-TSS (ENST00000637698.1)	94	0.036107	-1.83	down
	SMIM6	promoter-TSS (ENST00000579469.1)	-232	3.73E-06	-4.29	down
	TEKT4	promoter-TSS (ENST00000295201.4)	-443	0.001103	-3.05	down

Supplementary Table 3. List of genes with decreased chromatin accessibility at promoter region and their expressions at stem state and differentiation state

Gene expression linked to peaks down in TO	Gene ID	Peak Annotation	Distance to TSS	p-value	Fold Change (log2)	TO vs. Non-TO
Stem state	TNS1	promoter-TSS (ENST00000646520.1)	-33	0.004181	-1.62	down
	BAIAP3	promoter-TSS (ENST00000628027.2)	-18	0.015623	-2.97	down
	PAMR1	promoter-TSS (ENST00000621476.4)	-191	1.23E-05	-4.34	down
	NFIX	promoter-TSS (ENST00000587760.5)	-921	0.007613	-1.47	down
	APCDD1	promoter-TSS (ENST00000578882.1)	-9	0.001803	-2.70	down
	ZFP3	promoter-TSS (ENST00000574352.1)	147	0.008388	-1.77	down
	ALOX15	promoter-TSS (ENST00000570836.5)	-513	0.006552	-5.64	down
	ATP2A1	promoter-TSS (ENST00000561547.5)	55	0.021148	-1.47	down
	BMP4	promoter-TSS (ENST00000558984.1)	-365	0.000296	-2.90	down
	NR4A1	promoter-TSS (ENST00000545748.5)	-610	0.000262	-2.67	down
	SFTA3	promoter-TSS (ENST00000518529.6)	-348	9.49E-05	-4.93	down
	NGFR	promoter-TSS (ENST00000504201.1)	-780	1.81E-07	-1.64	down
	NKX2-1	promoter-TSS (ENST00000498187.6)	69	0.0355	-5.39	down
	FRMD5	promoter-TSS (ENST00000484674.5)	317	0.000449	-3.37	down
	MNX1	promoter-TSS (ENST00000480284.1)	120	0.003431	-6.58	down
	COL6A2	promoter-TSS (ENST00000454245.1)	-82	0.044091	-7.49	down
	HCAR1	promoter-TSS (ENST00000432564.2)	5	0.001076	-4.79	down
	WNK2	promoter-TSS (ENST00000427277.6)	-483	0.014241	-2.31	down
	PHYHD1	promoter-TSS (ENST00000421063.6)	24	0.042853	-1.11	down
	C2orf74	promoter-TSS (ENST00000420918.3)	-53	8.55E-06	-2.38	down
	PGGHG	promoter-TSS (ENST00000409479.5)	-406	8.04E-05	-2.09	down
	IFITM1	promoter-TSS (ENST00000408968.3)	56	9.8E-05	-2.97	down
	ITGB2	promoter-TSS (ENST00000397857.5)	-139	0.000977	-4.47	down
	NRP1	promoter-TSS (ENST00000395995.5)	-281	0.001018	-1.15	down
	PANX2	promoter-TSS (ENST00000395842.2)	-710	0.043984	-1.44	down
	IGF2	promoter-TSS (ENST00000381406.8)	-190	0.006076	-1.78	down
	PAQR7	promoter-TSS (ENST00000374296.3)	-527	0.017417	-1.02	down
	WNT2B	promoter-TSS (ENST00000369684.4)	-42	0.037642	-1.07	down
	SV2A	promoter-TSS (ENST00000369146.7)	-145	0.010278	-2.63	down
	CIART	promoter-TSS (ENST00000369095.5)	-346	0.015809	-1.48	down
	LGR6	promoter-TSS (ENST00000367278.7)	-514	0.012292	-4.43	down
	CCDC88B	promoter-TSS (ENST00000359902.2)	-745	0.011935	-1.63	down
	WNK3	promoter-TSS (ENST00000354646.6)	-256	0.026961	-3.72	down
	PAK5	promoter-TSS (ENST00000353224.9)	-91	0.040812	-5.12	down
	EFS	promoter-TSS (ENST00000351354.3)	-435	0.023909	-1.10	down
	TRPC6	promoter-TSS (ENST00000348423.8)	-13	3.01E-05	-7.75	down
	NRG2	promoter-TSS (ENST00000340391.7)	-160	0.000327	-3.31	down
	VWA1	promoter-TSS (ENST00000338660.5)	-49	0.000741	-1.54	down
	B4GALNT4	promoter-TSS (ENST00000329962.10)	-214	1.05E-05	-1.88	down
	FAIM2	promoter-TSS (ENST00000320634.7)	-71	0.019572	-4.18	down
	HEG1	promoter-TSS (ENST00000311127.8)	-646	0.004292	-1.51	down
	AMOT	promoter-TSS (ENST00000304758.5)	-309	0.01086	-4.81	down
	SIX2	promoter-TSS (ENST00000303077.6)	-265	0.009051	-2.41	down
	KRT8	promoter-TSS (ENST00000293308.11)	-720	2.17E-17	-3.28	down
	PLEKHH2	promoter-TSS (ENST00000282406.8)	95	0.00657	-1.02	down
	NTRK2	promoter-TSS (ENST00000277120.7)	-537	0.018174	-4.82	down
	PSD2	promoter-TSS (ENST00000274710.3)	-75	0.024297	-6.13	down
	CABLES1	promoter-TSS (ENST00000256925.11)	-5	0.02386	-2.02	down
	ALDH3A1	promoter-TSS (ENST00000225740.10)	4, 14	1.51E-07	-2.12	down
	PPP2R2C	promoter-TSS (ENST00000506140.5)	68	0.032996	1.26	up
	TNFSF18	promoter-TSS (ENST00000404377.3)	-143	0.000986	2.53	up
	PRSS3	promoter-TSS (ENST00000379405.3)	-173	0.003301	1.63	up

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Differentiated state	AC074143.1	promoter-TSS (ENST00000518227.1)	62	0.023879	-1.60	down
	ADGRB2	promoter-TSS (ENST00000373658.7)	-136	0.019904	-1.53	down
	ALDH3A1	promoter-TSS (ENST00000225740.10)	4, 14	0.000446	-3.45	down
	ALPL	promoter-TSS (ENST00000540617.5)	-93	0.011294	-2.23	down
	ANKRD24	promoter-TSS (ENST00000262970.9)	40	0.021459	-1.28	down
	ANKUB1	promoter-TSS (ENST00000446160.6)	13	0.000173	-2.39	down
	APCDD1	promoter-TSS (ENST00000578882.1)	-9	0.001778	-2.84	down
	BAIAP3	promoter-TSS (ENST00000628027.2)	-18	0.023153	-1.91	down
	BMP8A	promoter-TSS (ENST00000331593.5)	-319	0.018854	-1.70	down
	C2orf74	promoter-TSS (ENST00000420918.3)	-53	0.004271	-2.28	down
	CBY1	promoter-TSS (ENST00000355830.10)	95	8.97E-05	-1.79	down
	CCR10	promoter-TSS (ENST00000591765.1)	-120	0.001471	-2.98	down
	COA3	promoter-TSS (ENST00000588408.5)	573	0.005453	-1.63	down
	EFS	promoter-TSS (ENST00000351354.3)	-435	0.011481	-1.25	down
	FAIM2	promoter-TSS (ENST00000320634.7)	-71	2.78E-05	-4.25	down
	FAM183A	promoter-TSS (ENST00000335282.4)	-272	1.09E-05	-3.55	down
	FOXJ1	promoter-TSS (ENST00000322957.6)	-125	0.003167	-2.29	down
	FRMPD2	promoter-TSS (ENST00000305531.3)	-16	0.033067	-1.93	down
	GLB1L	promoter-TSS (ENST00000409640.5)	72	0.000195	-2.32	down
	GPR162	promoter-TSS (ENST00000428545.6)	-24	0.002601	-3.20	down
	GSTM4	promoter-TSS (ENST00000369833.5)	-16	0.002384	-1.97	down
	HHEX	promoter-TSS (ENST00000282728.9)	-103	0.042015	-1.91	down
	ICAM4	promoter-TSS (ENST00000393717.2)	-424	0.023663	-1.20	down
	IGFBP6	promoter-TSS (ENST00000549628.1)	-414	0.016203	-2.67	down
	ITPKA	promoter-TSS (ENST00000260386.6)	11	0.00934	-1.62	down
	KCNB1	promoter-TSS (ENST00000371741.5)	-283	0.037904	-1.51	down
	KCNH3	promoter-TSS (ENST00000257981.6)	-690	0.005005	-2.28	down
	KCNJ16	promoter-TSS (ENST00000615244.4)	-167	0.033686	-3.92	down
	KIF18B	promoter-TSS (ENST00000587309.5)	12	3.94E-10	-4.30	down
	KRT8	promoter-TSS (ENST00000293308.11)	-720	0.010438	-1.46	down
	LGR6	promoter-TSS (ENST00000367278.7)	-514	0.012392	-3.85	down
	LMNA	promoter-TSS (ENST00000532414.2)	125	0.028175	-1.58	down
	MPPED1	promoter-TSS (ENST00000443721.1)	-31	1.1E-05	-5.53	down
	NPAS1	promoter-TSS (ENST00000449844.6)	466	0.003975	-1.94	down
	NTRK2	promoter-TSS (ENST00000277120.7)	-537	0.011582	-2.62	down
	NUPR1	promoter-TSS (ENST00000395641.2)	-45	0.008744	-1.99	down
	PAQR5	promoter-TSS (ENST00000563004.2)	458	0.003522	-1.70	down
	PLEKHO1	promoter-TSS (ENST00000369124.4)	-12	0.014104	-1.83	down
	PLIN4	promoter-TSS (ENST00000633942.1)	-828	0.033122	-1.19	down
	POLR2J	promoter-TSS (ENST00000393794.4)	-121	0.013957	-1.89	down
	PPM1N	promoter-TSS (ENST00000401593.5)	-451	0.031517	-1.45	down
	PPP1R1B	promoter-TSS (ENST00000579000.5)	-127	0.000441	-3.36	down
	RBM24	promoter-TSS (ENST00000425446.6)	131	0.03824	-1.65	down
	RBP7	promoter-TSS (ENST00000294435.7)	53	0.003665	-3.42	down
	REC8	promoter-TSS (ENST00000611366.4)	56	0.035379	-4.05	down
	RND2	promoter-TSS (ENST00000587250.3)	-379	8.98E-05	-2.55	down
	RNF157	promoter-TSS (ENST00000319945.10)	-401	0.004983	-2.61	down
	SEMA4A	promoter-TSS (ENST00000368286.6)	74	0.013837	-1.09	down
	SHISA8	promoter-TSS (ENST00000621082.1)	-355	0.000244	-3.49	down
	SIX2	promoter-TSS (ENST00000303077.6)	-265	0.000579	-2.25	down
	SMKR1	promoter-TSS (ENST00000462322.2)	60	1E-05	-3.84	down
	SOX5	promoter-TSS (ENST00000546136.5)	-2	0.002097	-3.29	down
	STMN1	promoter-TSS (ENST00000399728.5)	9	0.001221	-1.51	down
	SV2A	promoter-TSS (ENST00000369146.7)	-145	0.015212	-3.39	down
	TEKT2	promoter-TSS (ENST00000446354.2)	150	0.000143	-3.22	down
	TFF3	promoter-TSS (ENST00000291525.11)	-20	1.89E-07	-3.70	down
	TRPC6	promoter-TSS (ENST00000348423.8)	-13	0.000826	-4.68	down
	TTLL6	promoter-TSS (ENST00000393382.7)	100	0.022268	-2.15	down

Supplementary Table 4. List of genes with increased chromatin accessibility at exon region and their expressions at stem state and differentiated state

Gene expression linked to peaks up in TO	Gene ID	Peak Annotation	Distance to TSS	p-value	Fold Change (log2)	TO vs. Non-TO
Stem state	SDCBP2	exon (ENST00000614659.1, exon 4 of 4)	6912	0.001338	1.73	up
	TNFSF14	exon (ENST00000599359.1, exon 2 of 5)	161	0.017341	5.37	up
	ADGRE2	exon (ENST00000596991.6, exon 19 of 20)	33237	0.029884	2.05	up
	VNN2	exon (ENST00000525270.5, exon 2 of 8)	130	0.007287	6.87	up
	CWH43	exon (ENST00000513409.1, exon 6 of 16)	11877	0.000112	2.52	up
	FAM3D	exon (ENST00000482387.6, exon 17 of 17)	-75644	0.004619	4.43	up
	MUC4	exon (ENST00000463781.7, exon 2 of 25)	21603	0.015398	5.23	up
	SPINK5	exon (ENST00000398454.5, exon 4 of 28)	8213	0.000721	1.10	up
	GCNT3	exon (ENST00000396065.2, exon 3 of 3)	6744	0.02974	3.72	up
	PIK3AP1	exon (ENST00000371109.3, exon 1 of 10)	115	0.020077	1.79	up
	ESR1	exon (ENST00000338799.9, exon 1 of 9)	901	0.011128	2.55	up
	STX3	exon (ENST00000307552.3, exon 1 of 1)	111	0.009271	1.21	up
	ACER1	exon (ENST00000301452.4, exon 1 of 6)	169	0.016538	4.46	up
	GPRIN1	exon (ENST00000261944.9, exon 27 of 32)	19688	0.045576	1.04	up
	HLF	exon (ENST00000376352.6, exon 18 of 18)	-98065	0.003667	-2.67	down
	LOX	exon (ENST00000339397.4, exon 8 of 8)	50017	8.60E-05	-3.09	down
	CAVIN2	exon (ENST00000304141.4, exon 2 of 2)	11535	3.48E-05	-1.69	down
Differentiated state	ADGRE2	exon (ENST00000596991.6, exon 19 of 20)	33237	0.011349	1.86	up
	BMP3	exon (ENST00000282701.2, exon 1 of 3)	625	6.42E-08	2.77	up
	EMP1	exon (ENST00000256951.9, exon 5 of 5)	7210	0.004608	1.10	up
	ESR1	exon (ENST00000338799.9, exon 1 of 9)	901	0.008816	2.68	up
	FKBP14	exon (ENST00000222803.9, exon 4 of 4)	13614	0.000662	1.44	up
	IRAK3	exon (ENST00000457197.2, exon 4 of 11)	22300	0.000296	1.84	up
	ISM2	exon (ENST00000216484.6, exon 12 of 12)	-9928	0.00078	2.42	up
	LAMA3	exon (ENST00000399516.7, exon 33 of 74)	-14929	5.21E-09	2.94	up
	MGAM	exon (ENST00000549489.6, exon 11 of 48)	34593	0.033523	2.63	up
	NRG1	exon (ENST00000356819.7, exon 12 of 12)	44474	0.014837	1.26	up
	NTM	exon (ENST00000374791.7, exon 1 of 8)	360	0.038128	3.22	up
	PCDHA13	exon (ENST00000625195.1, exon 1 of 2)	127	0.030017	3.86	up
	PPARG	exon (ENST00000643888.1, exon 7 of 9)	54510	0.007546	1.32	up
	SATB2	exon (ENST00000428695.5, exon 1 of 7)	207	0.026141	1.53	up
	SEC24D	exon (ENST00000511481.5, exon 13 of 16)	37072	0.048046	1.16	up
	STX3	exon (ENST00000307552.3, exon 1 of 1)	111	0.003332	1.04	up
	TNFSF14	exon (ENST00000599359.1, exon 2 of 5)	161	0.002289	3.62	up
	DEGS2	exon (ENST00000544450.6, exon 11 of 11)	21019	0.003834	-2.36	down
	EFHC1	exon (ENST00000360726.3, exon 3 of 3)	-16338	0.005452	-1.86	down
	ERICH3	exon (ENST00000612390.4, exon 3 of 3)	10371	0.040271	-2.40	down
	FANK1	exon (ENST00000368676.8, exon 19 of 19), (ENST00000368679.8, exon 23 of 23)	66975, 39130	1.78E-06	-2.53	down
	FBF1	exon (ENST00000592193.6, exon 3 of 28)	4524	0.004857	-1.49	down
	IL22RA1	exon (ENST00000327535.5, exon 4 of 7)	-18526	0.003463	-1.83	down
	LCA5L	exon (ENST00000485895.6, exon 5 of 5)	5677	0.011146	-1.79	down
	MYLK3	exon (ENST00000394809.8, exon 1 of 13)	387	0.006472	-2.60	down
	NCAPH	exon (ENST00000427946.5, exon 7 of 17)	17568	0.011858	-2.33	down
	NTRK2	exon (ENST00000376208.5, exon 14 of 14)	203993	0.011582	-2.62	down
	SYNE3	exon (ENST00000557275.5, exon 17 of 17)	41904	0.04791	-1.67	down
	TCTEX1D1	exon (ENST00000371037.8, exon 22 of 25)	-13116	0.030144	-2.20	down

Supplementary Table 5. List of genes with decreased chromatin accessibility at exon region and their expressions at stem state and differentiated state

Gene expression linked to peaks down in TO	Gene ID	Peak Annotation	Distance to TSS	p-value	Fold Change (log2)	TO vs. Non-TO
Stem state	GNAT1	exon (ENST00000232461.7, exon 8 of 9)	3172	0.04349328	-4.27	down
	BMP4	exon (ENST00000245451.8, exon 1 of 4)	257	2.75708E-05	-2.72	down
	PRPH	exon (ENST00000257860.8, exon 6 of 9)	3849	0.013755449	-4.61	down
	WNT10A	exon (ENST00000258411.7, exon 1 of 4)	118	0.017549088	-1.05	down
	PHYHD1	exon (ENST00000259324.5, exon 4 of 4)	-3444	0.002430617	-1.15	down
	IGFBP4	exon (ENST00000269593.4, exon 1 of 4)	343	0.013647231	-1.53	down
	WNT3A	exon (ENST00000284523.1, exon 1 of 4)	144	0.000203853	-2.11	down
	SOSTDC1	exon (ENST00000307068.4, exon 1 of 2)	128	0.002798447	-4.11	down
	CCDC8	exon (ENST00000307522.4, exon 1 of 1)	254	0.000165404	-3.15	down
	GGT5	exon (ENST00000327365.8, exon 1 of 12)	498	1.70261E-12	-4.43	down
	METTL7A	exon (ENST00000332160.4, exon 1 of 2)	162	0.000470109	-1.68	down
	CKB	exon (ENST00000348956.6, exon 1 of 8)	148	0.003734738	-1.60	down
	SUSD2	exon (ENST00000358321.3, exon 1 of 15)	181	1.98678E-07	-3.35	down
	NRG2	exon (ENST00000361474.5, exon 1 of 10)	332	0.00075442	-2.72	down
	TREX2	exon (ENST00000370211.8, exon 8 of 10)	-7882	0.025254889	-1.24	down
	LDOC1	exon (ENST00000370526.3, exon 1 of 1)	266	1.04493E-06	-4.72	down
	SMOC1	exon (ENST00000381280.4, exon 1 of 12)	231	2.2141E-06	-1.69	down
	RUNX3	exon (ENST00000399916.5, exon 2 of 6)	138	0.028468019	-2.66	down
	RBM38	exon (ENST00000417346.1, exon 1 of 2)	386	0.000912418	-1.17	down
	HCAR1	exon (ENST00000432564.2, exon 1 of 1)	4545	0.003119762	-2.92	down
	PROB1	exon (ENST00000434752.3, exon 1 of 1)	1529	0.004149771	-1.09	down
	RNF165	exon (ENST00000588679.1, exon 1 of 1)	271	3.08181E-10	-2.52	down
	MYO15B	exon (ENST00000610510.4, exon 1 of 63)	1077	0.026822784	-1.20	down
	TPRG1	exon (ENST00000617246.4, exon 11 of 11)	-65461	0.000119316	-1.21	down
	PRODH	exon (ENST00000638240.1, exon 6 of 6)	-10702	0.035269387	-2.84	down

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Differentiated state	DOK7	exon (ENST00000340083.5, exon 3 of 7)	10172	0.000405461	-1.37	down
	DOK7	exon (ENST00000340083.5, exon 7 of 7)	9813	0.000405461	-1.37	down
	ESPN	exon (ENST00000636330.1, exon 11 of 11)	7221	0.001509439	-1.52	down
	ESPN	exon (ENST00000636330.1, exon 8 of 11)	689	0.001509439	-1.52	down
Differentiated state	DMRT3	exon (ENST00000190165.2, exon 1 of 2)	114	0.008928564	-3.33	down
	MAMSTR	exon (ENST00000222145.8, exon 5 of 12)	-9517	0.014971701	-1.87	down
	LGR6	exon (ENST00000255432.11, exon 1 of 18)	117	0.012391622	-3.85	down
	PRPH	exon (ENST00000257860.8, exon 6 of 9)	3849	0.038094502	-2.18	down
	PIMREG	exon (ENST00000262483.12, exon 20 of 20)	10881	8.54161E-09	-4.52	down
	UBE2S	exon (ENST00000264552.13, exon 4 of 4)	7192	0.000996521	-2.64	down
	RCN3	exon (ENST00000270645.7, exon 1 of 7)	267	0.015963982	-1.93	down
	WNT3A	exon (ENST00000284523.1, exon 1 of 4)	144	0.007349871	-2.47	down
	HRASLS5	exon (ENST00000301790.4, exon 1 of 6)	186	0.008114229	-2.35	down
	CCDC8	exon (ENST00000307522.4, exon 1 of 1)	254	0.021311823	-2.13	down
	DEF6	exon (ENST00000316637.6, exon 7 of 11)	20520	0.002836985	-1.19	down
	PSAPL1	exon (ENST00000319098.6, exon 1 of 1)	4304	0.000181007	-3.11	down
	GPR62	exon (ENST00000322241.5, exon 1 of 1)	1023	0.015472082	-4.30	down
	C11orf65	exon (ENST00000323468.9, exon 8 of 8)	-5329	0.027419126	-1.30	down
	HMG20B	exon (ENST00000333651.10, exon 8 of 10)	4002	0.047601065	-1.00	down
	CAPS	exon (ENST00000339485.3, exon 2 of 2)	-1510	1.26422E-05	-4.04	down
	IFT27	exon (ENST00000340630.9, exon 5 of 7)	12156	0.000165931	-2.66	down
	CKB	exon (ENST00000348956.6, exon 1 of 8)	148	1.79983E-05	-2.56	down
	PLEKHA4	exon (ENST00000355496.9, exon 8 of 17)	9515	0.004077529	-1.35	down
	ITPR1PL1	exon (ENST00000361124.5, exon 1 of 1)	4084	2.18949E-05	-2.68	down
	ABCA4	exon (ENST00000370225.3, exon 33 of 50)	41336	0.037652708	-1.21	down
	LDOC1	exon (ENST00000370263.3, exon 1 of 1)	266	0.00679574	-2.83	down
	CFP	exon (ENST00000376983.7, exon 5 of 7)	-7695	0.006550587	-2.66	down
	ZBTB48	exon (ENST00000377674.8, exon 8 of 11)	8052	0.013524327	-1.59	down
	SERP2	exon (ENST00000379179.7, exon 1 of 3)	106	0.03630176	-1.72	down
	SPEF1	exon (ENST00000379756.3, exon 7 of 7)	3460	0.000514229	-3.48	down
	SLC47A1	exon (ENST00000395585.5, exon 1 of 19)	116	0.048438318	-3.72	down
	RBM38	exon (ENST00000417346.1, exon 1 of 2)	386	0.002178803	-1.53	down
	ISOC2	exon (ENST00000438389.6, exon 5 of 5)	8401	0.002990006	-2.68	down
	MMP23B	exon (ENST00000505820.6, exon 20 of 20)	-1643	0.02507483	-4.87	down
	NDUFA9	exon (ENST00000527518.1, exon 4 of 4)	16196	0.035511362	-1.61	down
	MYO15B	exon (ENST00000610510.4, exon 1 of 63)	1077	0.010998191	-1.93	down
	PRR5	exon (ENST00000617066.4, exon 1 of 8)	128	0.048949757	-1.49	down
	TPRG1	exon (ENST00000617246.4, exon 11 of 11)	-65461	0.02411273	-1.53	down
	PRODH	exon (ENST00000638240.1, exon 6 of 6)	-10702	0.040648883	-2.72	down
	BMP4	exon (ENST00000245451.8, exon 1 of 4)	257	0.004487366	1.89	up
	EFHD1	exon (ENST00000264059.7, exon 1 of 4)	614	0.022659204	3.07	up
	GAL	exon (ENST00000265643.3, exon 1 of 6)	225	0.039827589	4.59	up
	MYOM3	exon (ENST00000270800.1, exon 7 of 7)	-8239	7.24585E-05	2.42	up
	CXCL8	exon (ENST00000307407.7, exon 1 of 4)	131	0.001728359	3.12	up
	SPOCK2	exon (ENST00000317376.8, exon 2 of 12)	228	1.51222E-15	5.48	up
	SLC39A14	exon (ENST00000356766.10, exon 23 of 23)	-11881	0.000272043	1.87	up
	DKK3	exon (ENST00000396505.6, exon 2 of 8)	625	3.17259E-07	2.19	up
	NAT8L	exon (ENST00000423729.2, exon 3 of 3)	4783	0.002674438	5.83	up
	CPAMD8	exon (ENST00000443236.5, exon 1 of 42)	242	0.000416259	1.96	up
	BIRC3	exon (ENST00000615299.4, exon 3 of 10)	7144	0.000404694	2.52	up

Supplementary Table 6. List of genes with decreased chromatin accessibility at intron region and their expressions at differentiated state

Gene expression linked to peaks down in TO	Gene ID	Peak Annotation	Distance to TSS	p-value	Fold Change (log2)	TO vs. Non-TO
Differentiated state	FOXP1	intron (ENST00000475937.5, intron 10 of 19)	31578	0.039143	-1.61	down
	FOXP1	intron (ENST00000475937.5, intron 11 of 19)	57529			down
	FOXP1	intron (ENST00000475937.5, intron 2 of 19)	55389			down
	FOXP1	intron (ENST00000475937.5, intron 2 of 19)	59619			down
	FOXP1	intron (ENST00000475937.5, intron 5 of 19)	2804			down
	FOXP1	intron (ENST00000475937.5, intron 5 of 19)	9227			down
	FOXP1	intron (ENST00000647725.1, intron 6 of 25)	-13861			down
	ZBTB7C	intron (ENST00000590800.5, intron 1 of 4)	25014	0.045913	-1.28	down
	ZBTB7C	intron (ENST00000590800.5, intron 3 of 4)	63961			down
	ZBTB7C	intron (ENST00000590800.5, intron 3 of 4)	3689			down
	ZBTB7C	intron (ENST00000590800.5, intron 3 of 4)	-2207			down
	ZBTB7C	intron (ENST00000590800.5, intron 3 of 4)	17744			down
	LGR6	intron (ENST00000367278.7, intron 1 of 17)	-3719	0.0123916	-3.85	down
	LGR6	intron (ENST00000367278.7, intron 3 of 17)	15253			down
	LGR6	intron (ENST00000439764.2, intron 1 of 15)	8298			down
	LGR6	intron (ENST00000439764.2, intron 1 of 15)	399			down
	IL2RB	intron (ENST00000216223.9, intron 1 of 9)	4082	0.0232101	-3.29	down
	IL2RB	intron (ENST00000216223.9, intron 2 of 9)	6112			down
	IL2RB	intron (ENST00000216223.9, intron 9 of 9)	18308			down
	PRODH	intron (ENST00000334029.6, intron 1 of 13)	1866	0.0406489	-2.72	down
	PRODH	intron (ENST00000334029.6, intron 2 of 13)	6505			down
	PRODH	intron (ENST00000640084.1, intron 2 of 3)	-2236			down
	GRM4	intron (ENST00000374177.7, intron 1 of 8)	760	0.0106985	-2.27	down
	GRM4	intron (ENST00000374177.7, intron 1 of 8)	-4412			down
	GRM4	intron (ENST00000538487.6, intron 1 of 10)	643			down
	RPL37A	intron (ENST00000446558.5, intron 3 of 3)	41227	0.0014269	-2.25	down
	RPL37A	intron (ENST00000446558.5, intron 3 of 3)	52776			down
	RPL37A	intron (ENST00000446558.5, intron 3 of 3)	34741			down
	SERPINF1	intron (ENST00000254722.8, intron 3 of 7)	8366	0.0032762	-1.65	down
	SERPINF1	intron (ENST00000305513.11, intron 5 of 10)	31351			down
	TRPV4	intron (ENST00000261740.6, intron 1 of 15)	-6104	0.022084	-1.12	down
	TRPV4	intron (ENST00000261740.6, intron 1 of 15)	-4403			down
	KRT8	intron (ENST00000293308.11, intron 1 of 8)	1519	0.010438	-1.46	down
	KRT8	intron (ENST00000552551.5, intron 2 of 8)	2845			down
	CYP2S1	intron (ENST00000310054.8, intron 1 of 8)	495	0.0072782	-1.34	down
	CYP2S1	intron (ENST00000310054.8, intron 2 of 8)	2754			down
	ELN	intron (ENST00000320492.11, intron 4 of 28)	11549	0.0008747	-3.69	down
	ELN	intron (ENST00000414324.5, intron 1 of 30)	4279			down
	NTRK2	intron (ENST00000323115.8, intron 11 of 16)	181509	0.0115815	-2.62	down
	NTRK2	intron (ENST00000395882.5, intron 6 of 12)	41203			down
	PLA2G4E	intron (ENST00000399518.3, intron 1 of 19)	15962	0.0028415	-2.39	down
	PLA2G4E	intron (ENST00000399518.3, intron 1 of 19)	19624			down
	UMODL1	intron (ENST00000400424.6, intron 1 of 22)	1292	0.0143468	-2.40	down
	UMODL1	intron (ENST00000400424.6, intron 2 of 22)	7841			down
	MRV11	intron (ENST00000541483.5, intron 1 of 19)	-2547	0.0013676	-2.29	down
	MRV11	intron (ENST00000541483.5, intron 1 of 19)	-7299			down
	FAIM2	intron (ENST00000550890.5, intron 4 of 10)	5835	2.782E-05	-4.25	down
	FAIM2	intron (ENST00000550890.5, intron 9 of 10)	13946			down
	DMRT3	intron (ENST00000569227.1, intron 3 of 4)	-63286	0.0089286	-3.33	down
	DMRT3	intron (ENST00000569227.1, intron 4 of 4)	-16794			down
	ELFN2	intron (ENST00000613079.4, intron 1 of 2)	7579	0.0341975	-1.00	down
	ELFN2	intron (ENST00000613079.4, intron 1 of 2)	660			down
	STPG1	intron (ENST0000003583.12, intron 3 of 7)	33895	0.0009024	-1.14	down
	GALK1	intron (ENST00000200181.7, intron 26 of 39)	17176	0.0351854	-1.82	down
	SLC22A4	intron (ENST00000200652.3, intron 4 of 9)	28033	0.0237632	-1.31	down
	FOXN1	intron (ENST00000226247.2, intron 3 of 7)	4134	1.679E-05	-3.37	down
	RPL10A	intron (ENST00000229769.2, intron 8 of 9)	-6987	7.965E-05	-1.42	down

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Differentiated state	MAPRE3	intron (ENST00000233121.6, intron 1 of 6)	699	0.0030833	-1.12	down
	QTRT1	intron (ENST00000250237.9, intron 3 of 9)	5310	0.0270079	-1.25	down
	EEF1AKMT1	intron (ENST00000255305.10, intron 9 of 22)	-40441	0.0086936	-1.32	down
	HRASLS2	intron (ENST00000255695.1, intron 1 of 3)	2568	1.667E-06	-3.08	down
	KCNH3	intron (ENST00000257981.6, intron 7 of 14)	8919	0.0050047	-2.28	down
	PSMB7	intron (ENST00000259457.7, intron 5 of 7)	15632	0.0419781	-1.39	down
	GMPR	intron (ENST00000259727.4, intron 1 of 8)	4771	0.0227813	-1.04	down
	CYSTM1	intron (ENST00000261811.5, intron 1 of 2)	7274	0.0008925	-1.30	down
	TRMU	intron (ENST00000262738.7, intron 15 of 34)	55388	0.0371333	-1.63	down
	RAB36	intron (ENST00000263116.6, intron 2 of 10)	2464	0.0017616	-2.26	down
	CLDN5	intron (ENST00000263201.5, intron 13 of 18)	13385	0.0012544	-3.74	down
	CALR3	intron (ENST00000269881.7, intron 3 of 8)	7301	0.0486552	-4.91	down
	WDR66	intron (ENST00000288912.8, intron 8 of 21)	31493	2.801E-06	-1.57	down
	PPP1R16A	intron (ENST00000292539.8, intron 1 of 10)	-2063	0.0003827	-2.08	down
	POC1A	intron (ENST00000296484.6, intron 9 of 10)	47230	0.0002618	-2.62	down
	MAP1A	intron (ENST00000300231.5, intron 1 of 5)	770	0.0182915	-2.34	down
	TKFC	intron (ENST00000301764.11, intron 5 of 26)	-6962	0.0004774	-1.30	down
	SPATA24	intron (ENST00000302060.9, intron 7 of 7)	-11275	0.0045507	-1.79	down
	ABR	intron (ENST00000302538.9, intron 2 of 22)	-2175	0.0099194	-2.78	down
	ASPSCR1	intron (ENST00000306739.8, intron 4 of 15)	14172	0.0305452	-1.66	down
	SCNN1B	intron (ENST00000307331.9, intron 2 of 13)	20841	0.010799	-1.48	down
	LKAAEAR1	intron (ENST00000308906.6, intron 1 of 1)	604	6.696E-06	-4.77	down
	SOBP	intron (ENST00000317357.9, intron 1 of 6)	2860	0.024268	-1.88	down
	HYAL1	intron (ENST00000320295.12, intron 1 of 5)	2096	0.028551	-1.74	down
	CCDC34	intron (ENST00000328697.10, intron 1 of 5)	5598	5.178E-05	-1.68	down
	BMP8A	intron (ENST00000331593.5, intron 1 of 6)	9538	0.0188536	-1.70	down
	BRAT1	intron (ENST00000340611.8, intron 6 of 13)	13465	0.0249898	-1.27	down
	CCDC30	intron (ENST00000340612.5, intron 1 of 20)	4072	0.0492074	-1.47	down
	SERPINB4	intron (ENST00000341074.9, intron 4 of 7)	2800	0.0088926	-1.18	down
	SSBP4	intron (ENST00000348495.10, intron 4 of 16)	-4182	0.0004209	-2.04	down
	SLC47A2	intron (ENST00000350657.9, intron 8 of 17)	9434	0.0218463	-1.22	down
	SPTBN4	intron (ENST00000352632.7, intron 3 of 35)	20826	0.0025147	-2.55	down
	NR2E3	intron (ENST00000355327.7, intron 8 of 17)	-115506	0.0140028	-2.69	down
	BOC	intron (ENST00000355385.7, intron 4 of 19)	47646	0.001236	-1.28	down
	DTNBP1	intron (ENST00000355917.7, intron 6 of 8)	8179	0.034845	-1.42	down
	OSCP1	intron (ENST00000356637.9, intron 1 of 10)	1616	3.272E-05	-2.65	down
	ASTN2	intron (ENST00000361209.6, intron 16 of 21)	45326	0.0115199	-1.17	down
	UBE2T	intron (ENST00000367278.7, intron 6 of 17)	49495	1.795E-05	-1.46	down
	MYB	intron (ENST00000367814.8, intron 1 of 14)	4036	0.0162834	-1.89	down
	SEMA4A	intron (ENST00000368284.5, intron 6 of 12)	6945	0.0138373	-1.09	down
	PMVK	intron (ENST00000368467.3, intron 2 of 4)	4697	0.0062004	-1.86	down
	PSMD4	intron (ENST00000368884.7, intron 1 of 9)	4778	0.0171525	-1.47	down
	BEND5	intron (ENST00000371833.3, intron 4 of 5)	35188	0.042724	-2.14	down
	CEL	intron (ENST00000372080.6, intron 7 of 10)	5709	2.152E-05	-1.49	down
	RSPH9	intron (ENST00000372165.8, intron 1 of 5)	352	4.689E-05	-3.68	down
	CCDC24	intron (ENST00000372318.7, intron 5 of 8)	2645	0.0007492	-2.10	down
	ANGPTL2	intron (ENST00000373425.7, intron 1 of 4)	10000	0.0006579	-4.14	down
	ADGRB2	intron (ENST00000373655.6, intron 1 of 32)	975	0.019904	-1.53	down
	PIGU	intron (ENST00000374820.6, intron 5 of 10)	52376	0.0239794	-1.62	down
	CROCC	intron (ENST00000375541.9, intron 3 of 36)	3667	0.0005887	-2.04	down

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Differentiated state	AQP7	intron (ENST00000377425.8, intron 2 of 6)	2743	0.0079073	-2.17	down
	FOLR1	intron (ENST00000378140.3, intron 2 of 2)	-8258	0.0279488	-1.69	down
	NWD1	intron (ENST00000379808.7, intron 1 of 16)	2986	0.0212596	-2.32	down
	CCDC57	intron (ENST00000392347.5, intron 14 of 16)	18421	0.000774	-1.81	down
	ANKRD39	intron (ENST00000393537.4, intron 1 of 3)	2914	0.0448068	-1.52	down
	RAB17	intron (ENST00000409822.1, intron 1 of 4)	8317	0.0391141	-1.23	down
	CDCA7	intron (ENST00000410019.3, intron 1 of 7)	597	0.0108253	-3.76	down
	FBXO15	intron (ENST00000419743.6, intron 1 of 9)	5908	0.000598	-2.90	down
	PIMREG	intron (ENST00000421306.7, intron 10 of 18)	26985	8.542E-09	-4.52	down
	NT5C3B	intron (ENST00000435506.6, intron 1 of 8)	162	0.0273074	-1.60	down
	ZNF487	intron (ENST00000437590.2, intron 1 of 3)	8320	1.418E-05	-1.72	down
	CYHR1	intron (ENST00000438911.6, intron 2 of 4)	6464	0.0452385	-1.15	down
	MPPED1	intron (ENST00000443721.1, intron 1 of 6)	12718	1.097E-05	-5.53	down
	IGFBP5	intron (ENST00000447289.1, intron 1 of 3)	-15507	0.0188297	-2.64	down
	ATP5MF	intron (ENST00000449683.5, intron 1 of 3)	5310	0.0073866	-2.13	down
	FAM166B	intron (ENST00000455600.1, intron 2 of 11)	9869	0.0006031	-2.90	down
	FAM178B	intron (ENST00000490605.2, intron 12 of 16)	-19015	0.0033887	-2.95	down
	TXNRD2	intron (ENST00000491939.6, intron 7 of 11)	20186	0.0295864	-1.48	down
	EFNA3	intron (ENST00000505139.1, intron 1 of 4)	-5374	0.0227855	-1.89	down
	TOP1MT	intron (ENST00000519148.5, intron 1 of 13)	4700	0.0276524	-1.06	down
	NAALADL1	intron (ENST00000526799.5, intron 2 of 7)	549	5.671E-05	-2.91	down
	NR1H3	intron (ENST00000529444.5, intron 5 of 8)	-4854	0.0012189	-2.04	down
	NPIPB6	intron (ENST00000532254.1, intron 1 of 6)	860	0.0059014	-2.88	down
	ANKRD65	intron (ENST00000537107.5, intron 2 of 3)	379	9.626E-05	-2.45	down
	KIF6	intron (ENST00000538893.5, intron 12 of 21)	-23482	0.0011879	-2.48	down
	CNBD2	intron (ENST00000538900.1, intron 7 of 10)	24426	0.0138565	-3.70	down
	PTMS	intron (ENST00000539187.5, intron 1 of 7)	-2091	0.0014826	-2.12	down
	FAM186A	intron (ENST00000543111.5, intron 4 of 7)	1621	0.0488133	-2.15	down
	SLC27A2	intron (ENST00000544960.1, intron 1 of 10)	2299	0.0456375	-1.71	down
	MESP1	intron (ENST00000560294.5, intron 13 of 16)	15970	0.0211654	-3.07	down
	LRRCA9	intron (ENST00000560369.5, intron 6 of 15)	16913	0.0001149	-1.74	down
	LRRCA36	intron (ENST00000563189.5, intron 2 of 10)	11863	0.0005613	-3.32	down
	SCX	intron (ENST00000569669.5, intron 3 of 15)	6560	0.0073543	-2.30	down
	PKMYT1	intron (ENST00000573944.5, intron 2 of 8)	2557	4.303E-17	-4.61	down
	ZNF232	intron (ENST00000574788.5, intron 4 of 37)	164	0.0001396	-1.41	down
	CLUAP1	intron (ENST00000576634.5, intron 5 of 11)	4541	2.443E-05	-1.83	down
	MBD3	intron (ENST00000585937.1, intron 2 of 6)	2798	0.0107518	-2.23	down
	KCNJ16	intron (ENST00000586462.1, intron 1 of 1)	953	0.033686	-3.92	down
	TMEM161A	intron (ENST00000587583.6, intron 11 of 11)	17815	0.0475359	-1.21	down
	FOXJ1	intron (ENST00000590137.1, intron 6 of 7)	-6687	0.0031671	-2.29	down
	PRKCSH	intron (ENST00000591462.5, intron 10 of 18)	10795	0.0499495	-1.34	down
	SPC24	intron (ENST00000592540.5, intron 1 of 4)	2678	1.877E-08	-4.10	down
	RFX2	intron (ENST00000592546.5, intron 5 of 16)	26743	0.0018349	-1.92	down
	KIF18B	intron (ENST00000593135.5, intron 1 of 15)	-4261	3.942E-10	-4.30	down
	PEX11G	intron (ENST00000593942.5, intron 1 of 6)	2646	0.0005022	-2.78	down
	BCAT2	intron (ENST00000599157.5, intron 4 of 7)	-8763	0.0007964	-1.18	down
	IL24	intron (ENST00000611909.4, intron 2 of 4)	1290	0.0081832	-2.34	down
	RAB44	intron (ENST00000612677.5, intron 4 of 13)	18839	0.0027756	-2.84	down
	SCARF2	intron (ENST00000622235.4, intron 1 of 10)	409	0.0004136	-2.43	down
	EFHC1	intron (ENST00000636379.1, intron 2 of 9)	3036	0.0054518	-1.86	down
	GAMT	intron (ENST00000640762.1, intron 1 of 5)	493	0.0420347	-1.58	down
	TPRG1	intron (ENST00000640853.1, intron 8 of 10)	-92361	0.0241127	-1.53	down
	DOK7	intron (ENST00000643608.1, intron 2 of 7)	7339	0.0004055	-1.37	down

Supplementary table 2-6, Fisher's exact tests were applied to identify the significance.