Supplementary Fig. 1

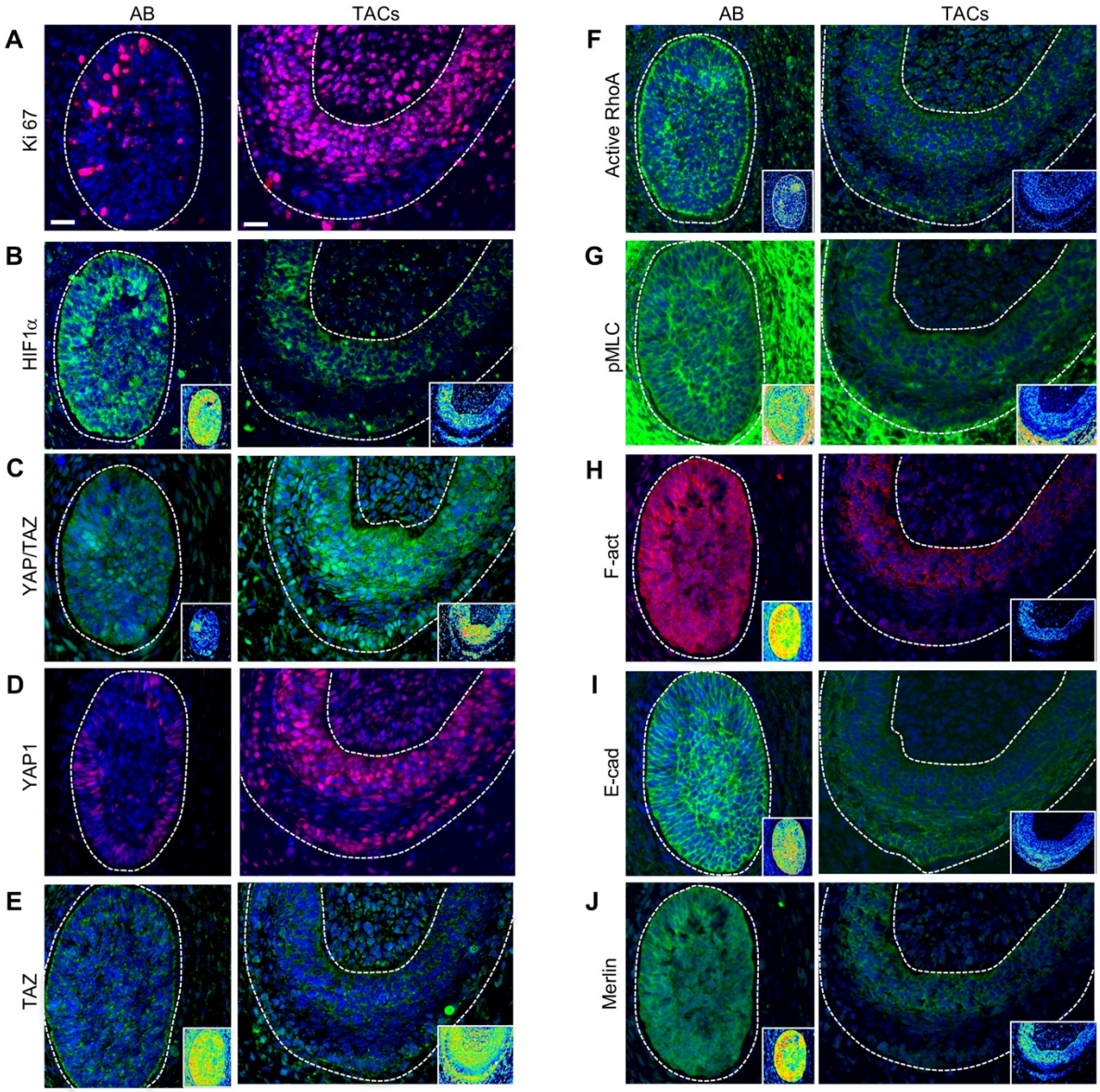

Figure S1. Immunostaining of adjacent frontal sections of mouse incisor *in vivo*

(A-J) Immunostaining of Ki67, HIF1α, YAP/TAZ, YAP1, TAZ, Active RhoA, pMLC, F-actin, E-cadherin, and Merlin in adjacent frontal sections of apical bud (AB) region (left) and TACs region (TACs) (right) of the same P3 mouse lower incisor. The nucleus is stained with DAPI (blue). Insets are pseudo-color images; dashed line delimits the dental epithelium. Scale bars: 20 μm.

Supplementary Fig.2

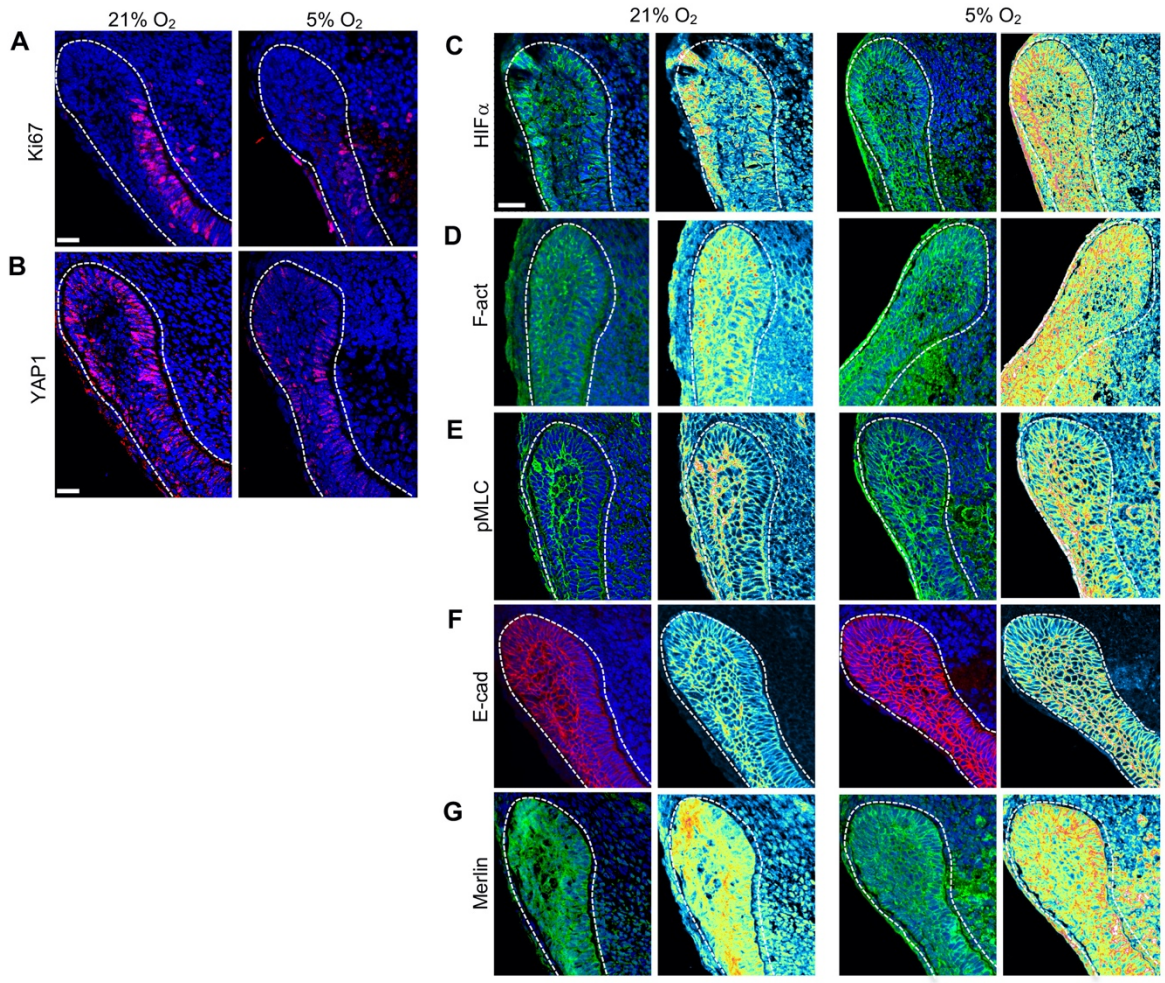

Figure S2. Immunostaining of adjacent sagittal sections of cultured mouse incisors in hypoxia

(A-G) Immunostaining of Ki67, YAP1, HIF1α, F-actin, pMLC, E-cadherin, and Merlin in adjacent sagittal sections of the apical bud cultured in normoxia and hypoxia. The nucleus is stained with DAPI (blue). (C-G) Right images are pseudo-color images of left images; dashed line delimits the dental epithelium. Scale bars: 20 μm.

Supplementary Fig.3

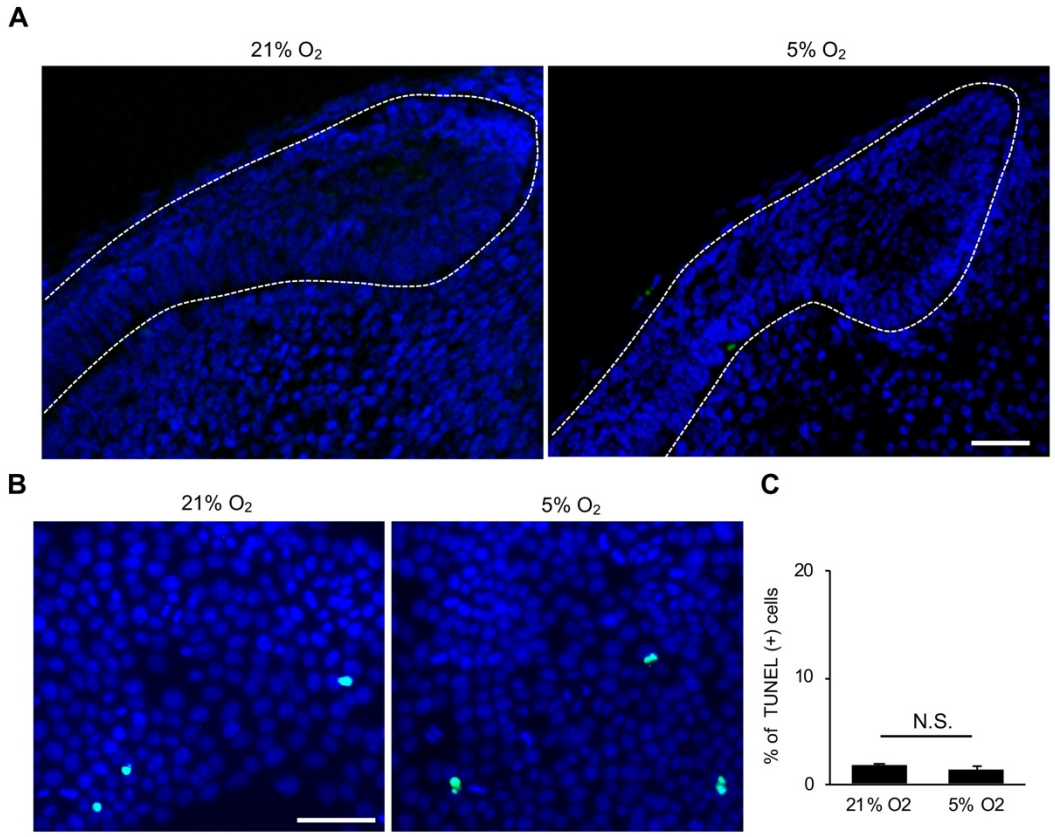

Figure S3. Effect of hypoxia on apoptosis in cultured mouse incisors and mHAT9d cells. (A) Terminal deoxynucleotidyl transferase (TdT)-mediated dUTP-biotin nick-end labeling (TUNEL) staining assay of the apical bud cultured in normoxia (left) and hypoxia (right) for 2 days. (B, C) TUNEL staining assay of mHAT9d cells incubated in normoxia (21% O_2) or hypoxia (5% O_2) for 1 day. Representative images demonstrate TUNEL-positive nuclei (green color). The nucleus is stained with DAPI (blue). Percentages (%) of TUNEL-positive cells relative to DAPI-positive total nuclei are indicated in the histogram; n = 4. N.S., non-significant. Scale bars: (A) 30 μm; (B) 50 μm.

Supplementary Fig.4

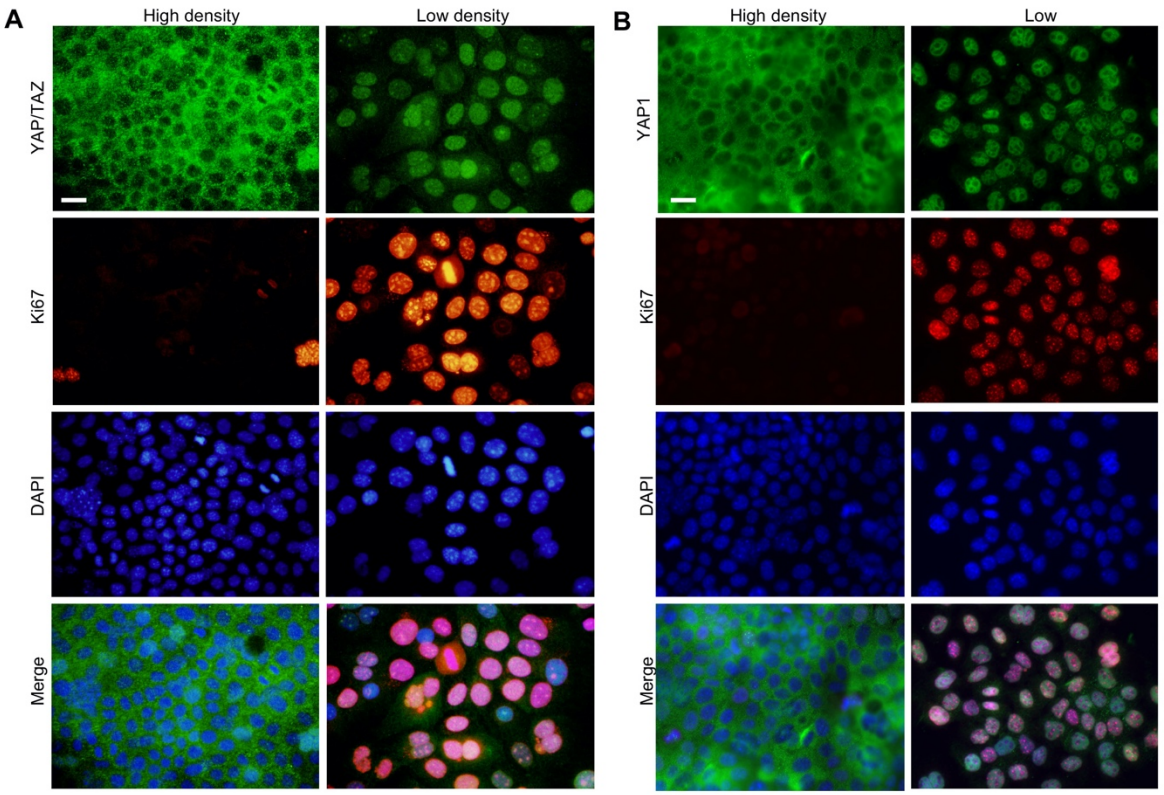

Figure S4. Cell-density-dependent expression of YAP/TAZ and ki67 in mHAT9d cells.

Immunostaining of YAP/TAZ and Ki67 (A), and YAP1 and Ki67 (B) in high-density (left) and low-density (right) mHAT9d cells under normoxia (21% O_2). Scale bars: 20 μm.

Supplementary Fig.5

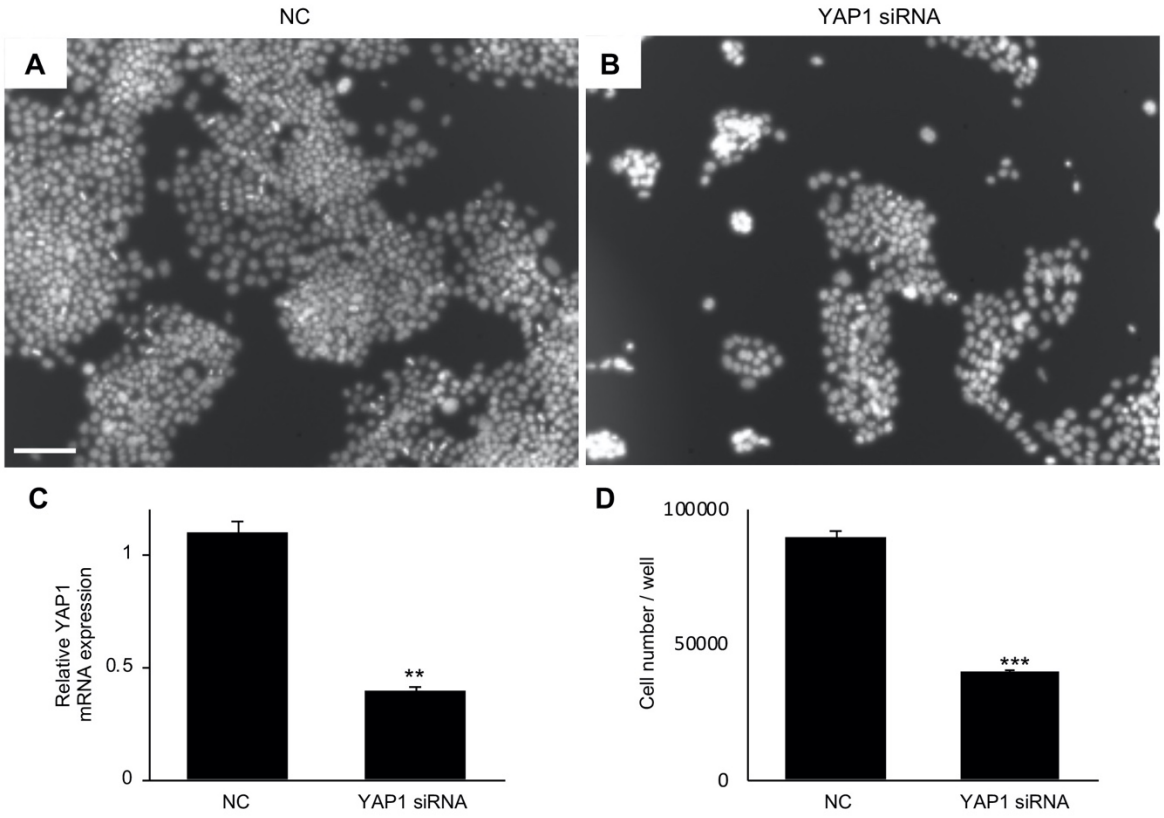

Figure S5. Effect of knocking down YAP1 expression on cell proliferation in mHAT9d cells. (A-B) DAPI staining of low-density mHAT9d cells transfected with non-specific control siRNA (NC) or siRNA specific for YAP1. (C) Expression of YAP1 mRNA in mHAT9d cells transfected with NC or siRNA specific for YAP1; n = 3. Data are represented as mean ± SEM. (D) The cells were counted 3 days after YAP1 siRNA transfection; n = 3. Data are represented as mean ± SEM. Scale bars: 100 μm.

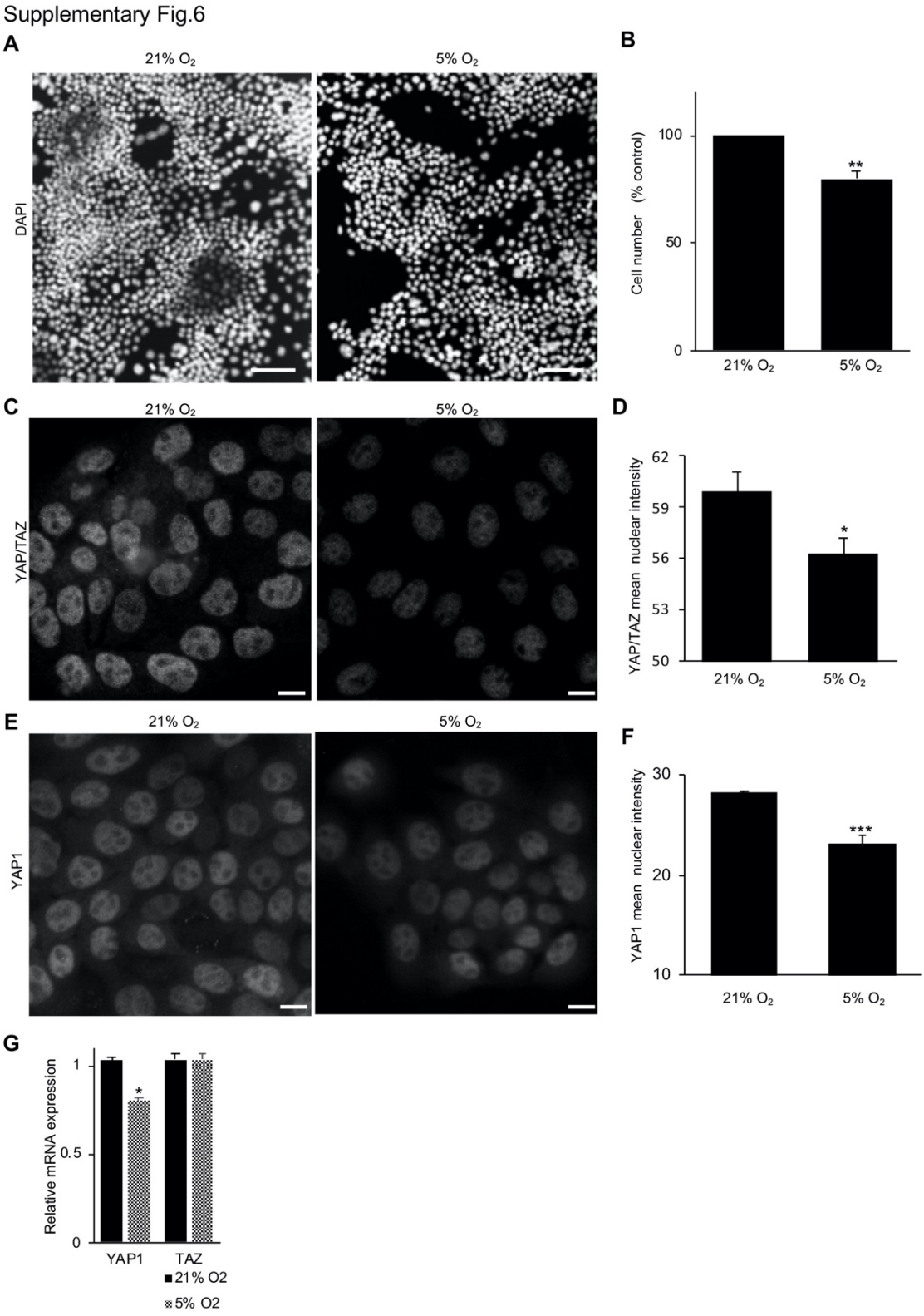

Figure S6. Effect of hypoxia on cell proliferation and YAP/TAZ expression in mHAT9d cells.

(A) DAPI staining of low-density mHAT9d cells cultured in normoxia (left) and hypoxia (right) for 3 days. (B) Quantification of cell number; n=4. Data are represented as mean ± SEM. (C) Immunostaining of YAP/TAZ in normoxia (left) and hypoxia (right) for 3 days. (D) Quantification of the intensity of nuclear YAP/TAZ fluorescence; n=4. (E) Immunostaining of YAP1 in normoxia (left) and hypoxia (right) for 3 days. (F) Quantification of the nuclear YAP1 fluorescence intensity; n = 4. (G) Expression of YAP1 and TAZ mRNA in mHAT9d cells cultured in normoxia and hypoxia; n = 4. Data are represented as mean ± SEM. Scale bars: (A) 100 μm; (C, E) 20 μm.

Supplementary Fig.7

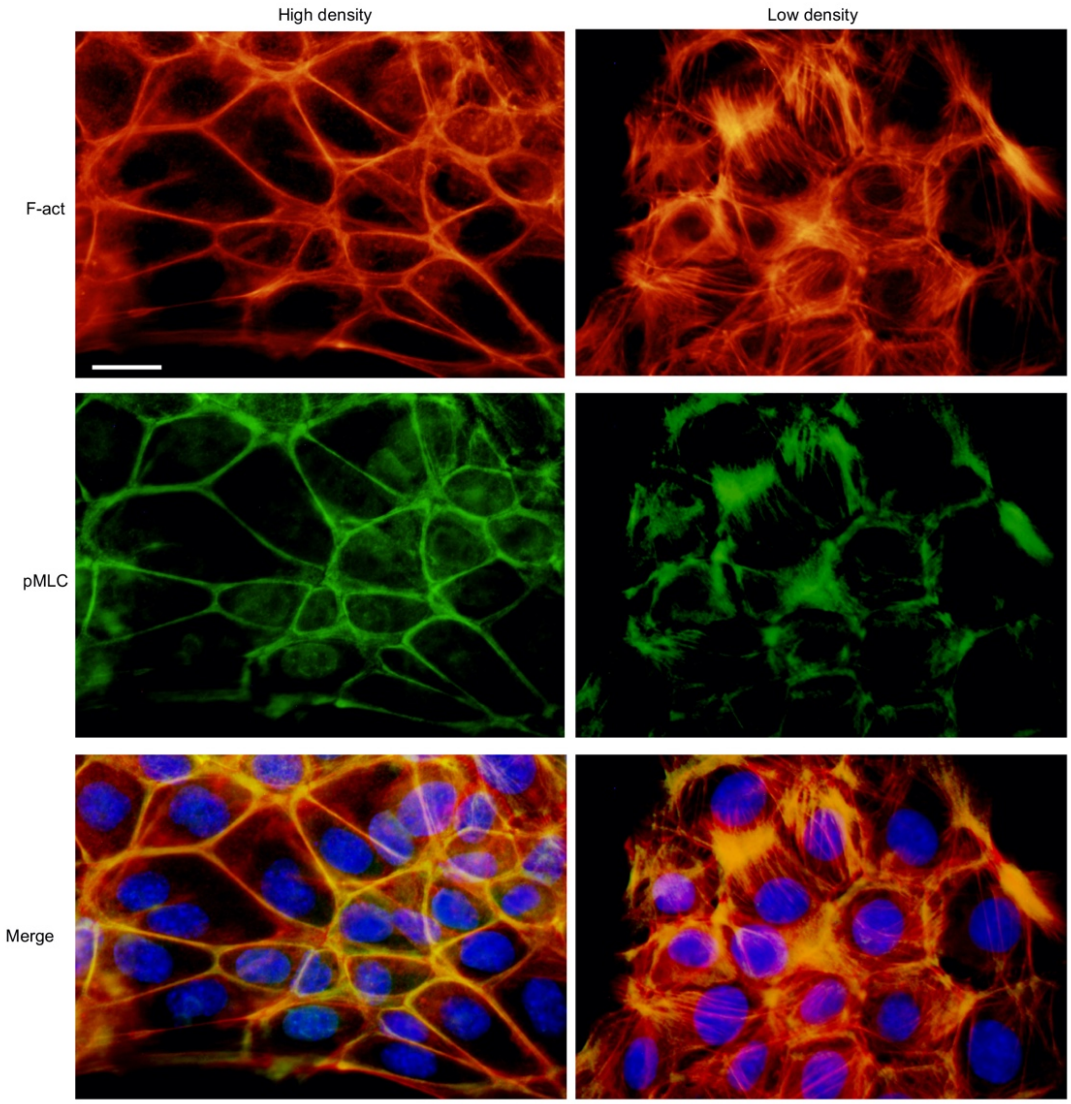

Figure S7. Cell-density-dependent expression of F-actin and pMLC in mHAT9d cells.

Phalloidin staining (F-actin) and immunostaining for pMLC in high-density (left) and low-density (right) mHAT9d cells under normoxia (21% O_2). Scale bars: 20 μm.

Supplementary Fig.8

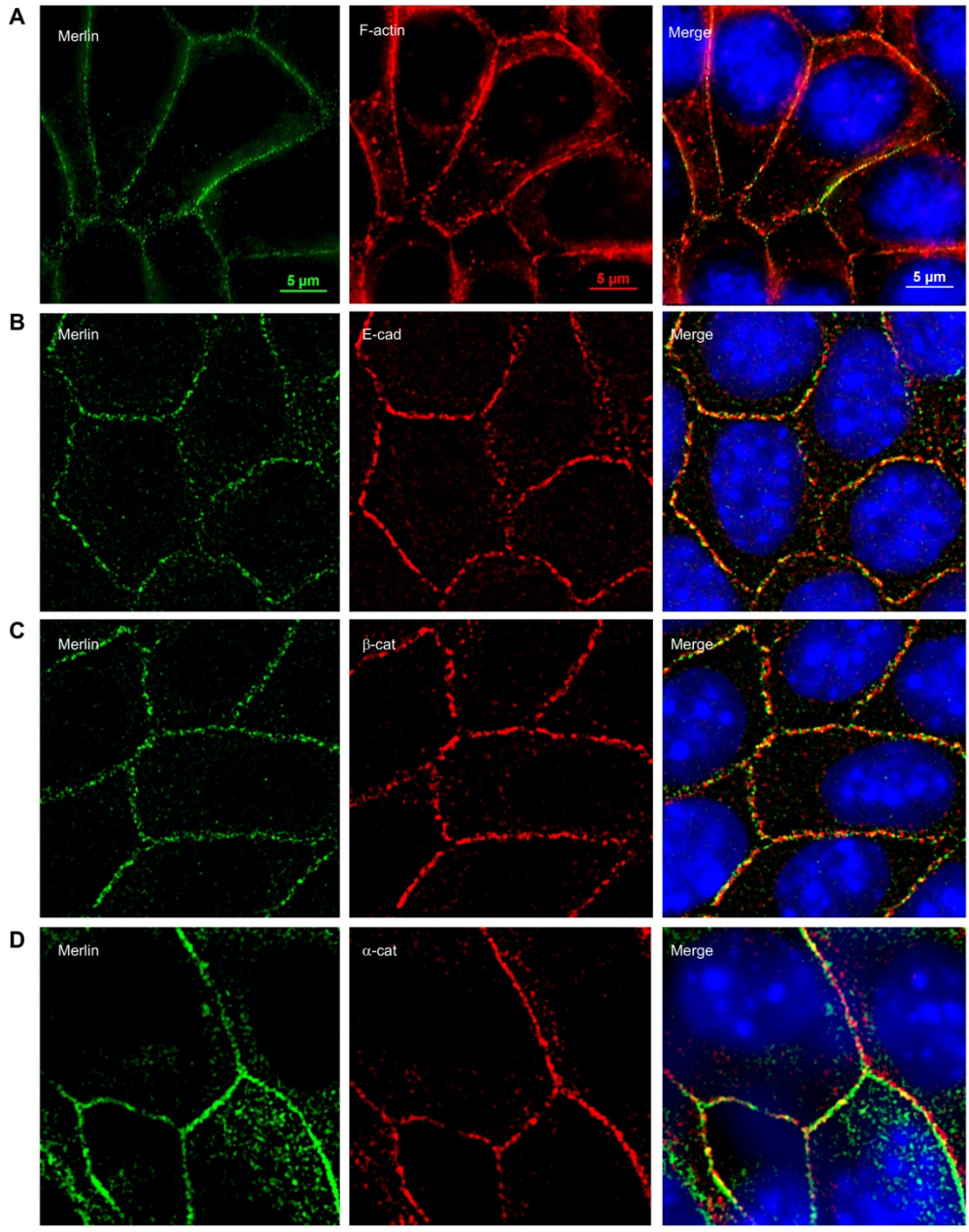

Figure S8. Co-expression of AJ protein in mHAT9d cells.

Images show the double staining for Merlin with F-actin (A), E-cadherin (B), β-catenin (C), and α-catenin (D) of high-density mHAT9d cells. Scale bars: 5 μm.

Supplementary Fig.9

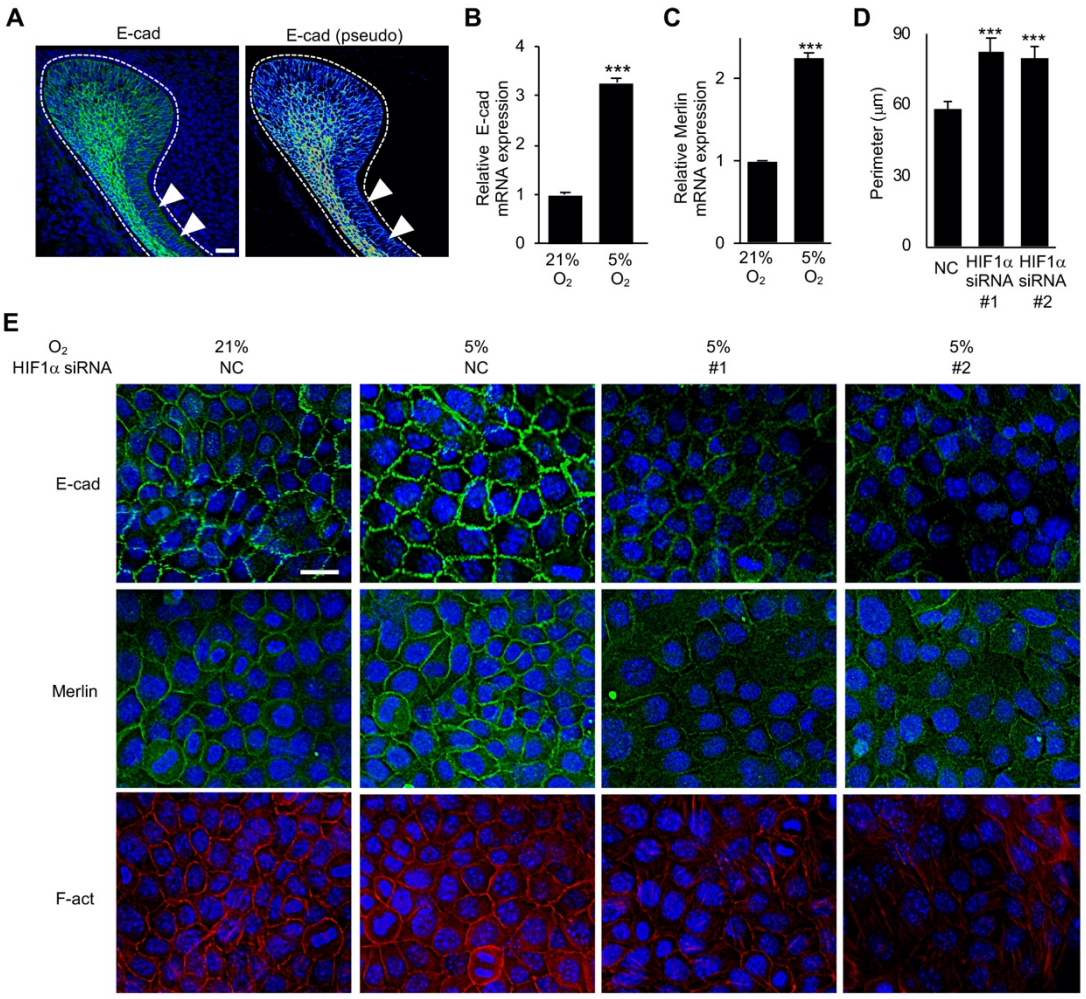

Figure S9. Effect of hypoxic signal on AJ proteins.

(A) Immunostaining of E-cadherin (E-cad) in a P3 mouse apical bud. (B, C) Expression of E-cadherin and Merlin mRNA in mHAT9d cells cultured in normoxia (21% 0_2) and hypoxia (5% O_2) for 1 day; n=3. Data are represented as mean ± SEM. (D) Average perimeter quantification of mHAT9d cells transfected with non-specific control siRNA (NC) or two different siRNA specific for HIF1α in hypoxia; n = 3. Data are represented as mean ± SEM. (E) Immunostaining of E-cadherin, Merlin, and Phalloidin staining (F-act) of high-density mHAT9d cells transfected with HIF1α siRNA in normoxia and hypoxia. Scale bars: (A) 30 μm; (E) 20 μm.