Figure S1

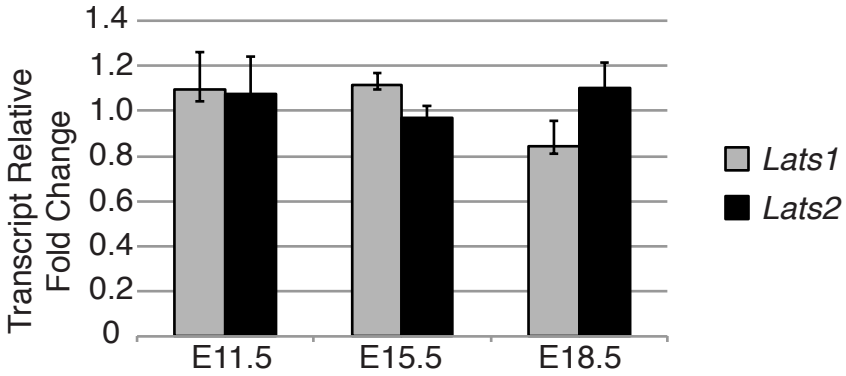

Figure S1. *Lats1* and *Lats2* relative mRNA levels remained unchanged throughout development.

(A) qRT-PCR quantification of mRNA levels of *Lats1* and *Lats2* relative to *β-Actin* (*Actb*) in control lungs at E11.5, E15.5 and E18.5. Data are presented as mean +/- SEM.

Figure S2

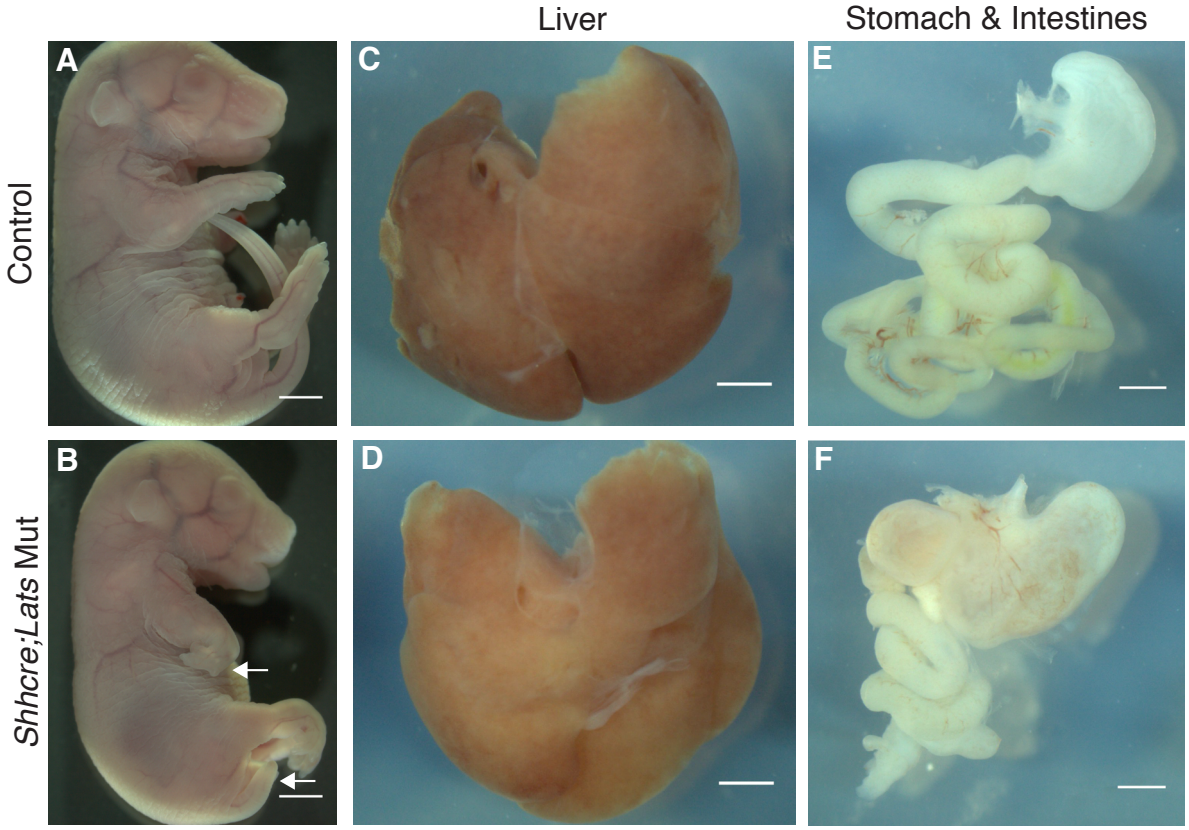

Figure S2. *Shhcre;Lats* mutants showed gross morphological defects. (A,B) Whole embryo images of control and the *Shhcre;Lats* mutant at E18.5 showed limb and tail defects (arrows). (C, D) Liver size in controls and *Shhcre;Lats* mutants appeared similar, likely due to low cre activity in the liver. (E,F) The stomach was larger but the intestine was shorter in the *Shhcre;Lats* mutants compred to the control. Scale bars: 50μm.

Figure S3

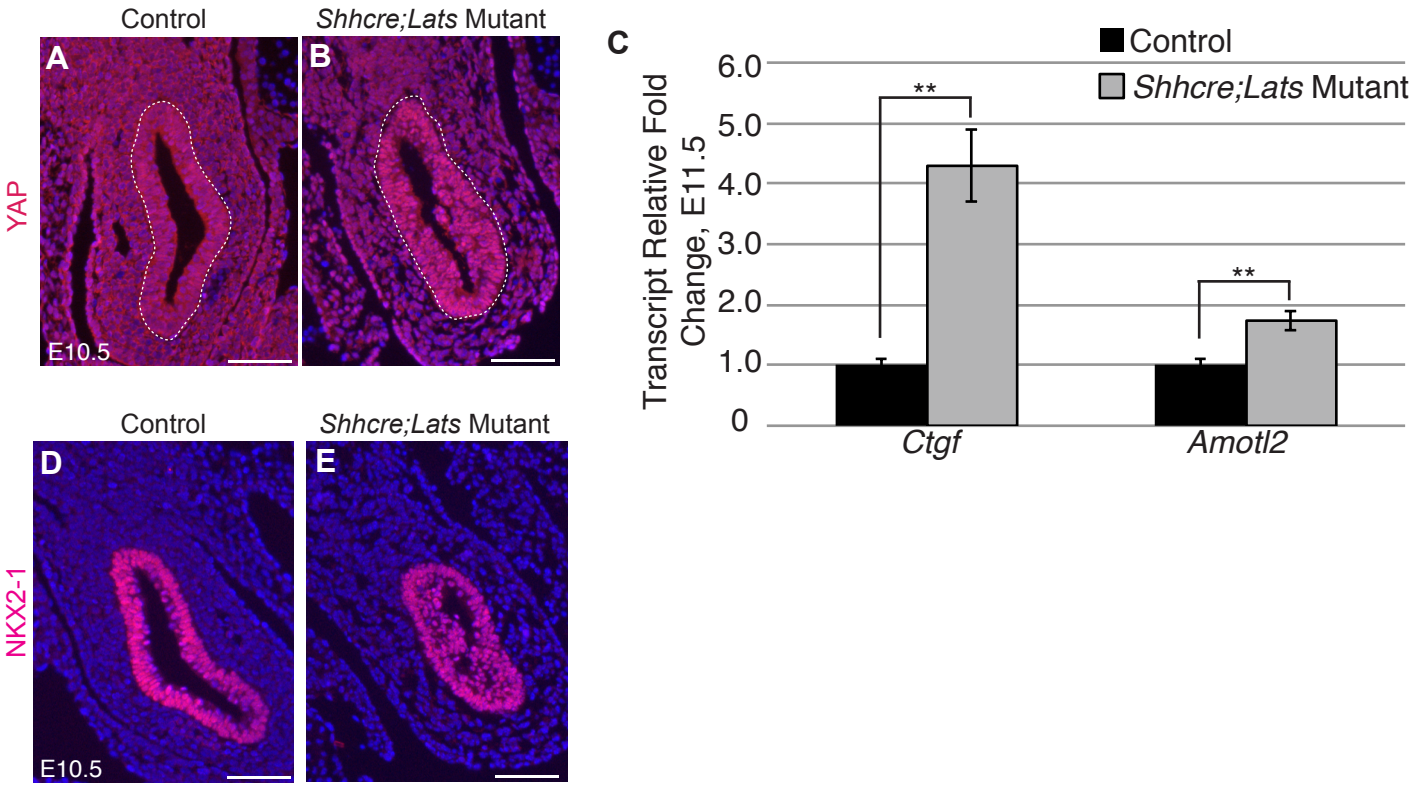

Figure S3. *Shhcre;Lats* mutants showed increased nuclear YAP at E10.5. (A,B) Immunofluorescent detection of YAP (red) in control and *Shhcre;Lats* mutant lungs at E10.5, showing intense nuclear staining in the mutant epithelium. (C) qRT-PCR quantification of relative mRNA levels of *Ctgf* and *Amotl2* in *Shhcre;Lats* mutant lungs at E11.5. **: $p<0.01$. Data are presented as mean +/- SEM. (D,E) Immunofluorescent detection of NKX2-1 (red) in control and *Shhcre;Lats* mutant lungs at E10.5, showing presence of signal in the mutant. Scale bars: 50μm.

Figure S4

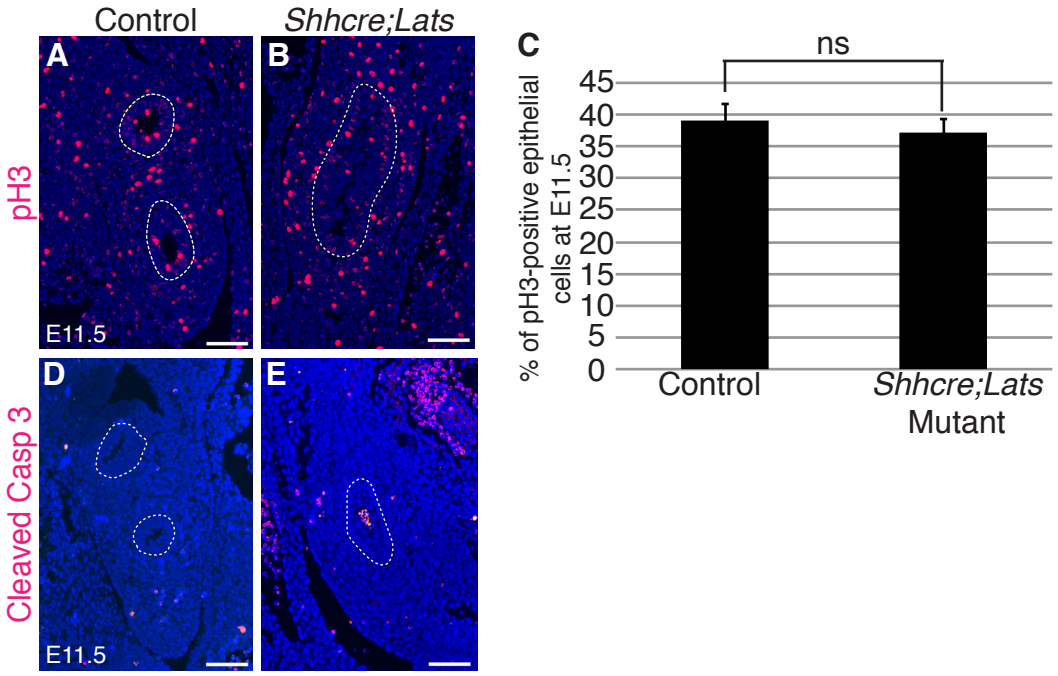

Figure S4. *Shhcre;Lats* mutants showed normal proliferation, but increased cell death at E11.5.

(A,B) Immunofluorescent detection of phospho-histone H3 (red) in control and *Shhcre;Lats* mutant lungs at E11.5, showing similar signals in the mutant as compared to control. Dotted circles outline the epithelium. (C) Quantification of percentage of epithelial cells positive for phospho-histone H3. ns: not significant. Data are presented as mean +/- SEM. (D,E) Immunofluorescent detection of cleaved caspase 3 (red) in control and *Shhcre;Lats* mutant lungs at E11.5, showing increased signal in the lumen of the mutant epithelium. Dotted line outlines the epithelium. Scale bars: 50μm.

Figure S5

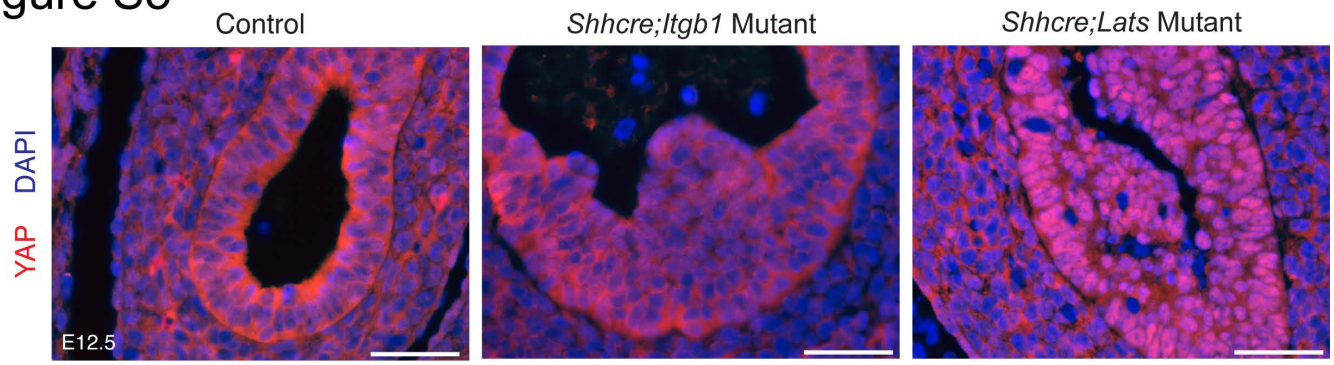

Figure S5. *Shhcre;Itgb1* mutants do not express YAP exclusively in the nucleus, unlike in *Shhcre;Lats* mutants.

(A-C) Immunofluorescent detection of YAP (red) and in E12.5 control, *Shhcre;Itgb1* and *Shhcre;Lats* lungs showing strong nuclear YAP expression in the epithelium of *Shhcre;Lats* mutants but not in *Shhcre;Itgb1* mutants. Scale bars: 50μm.

Figure S6

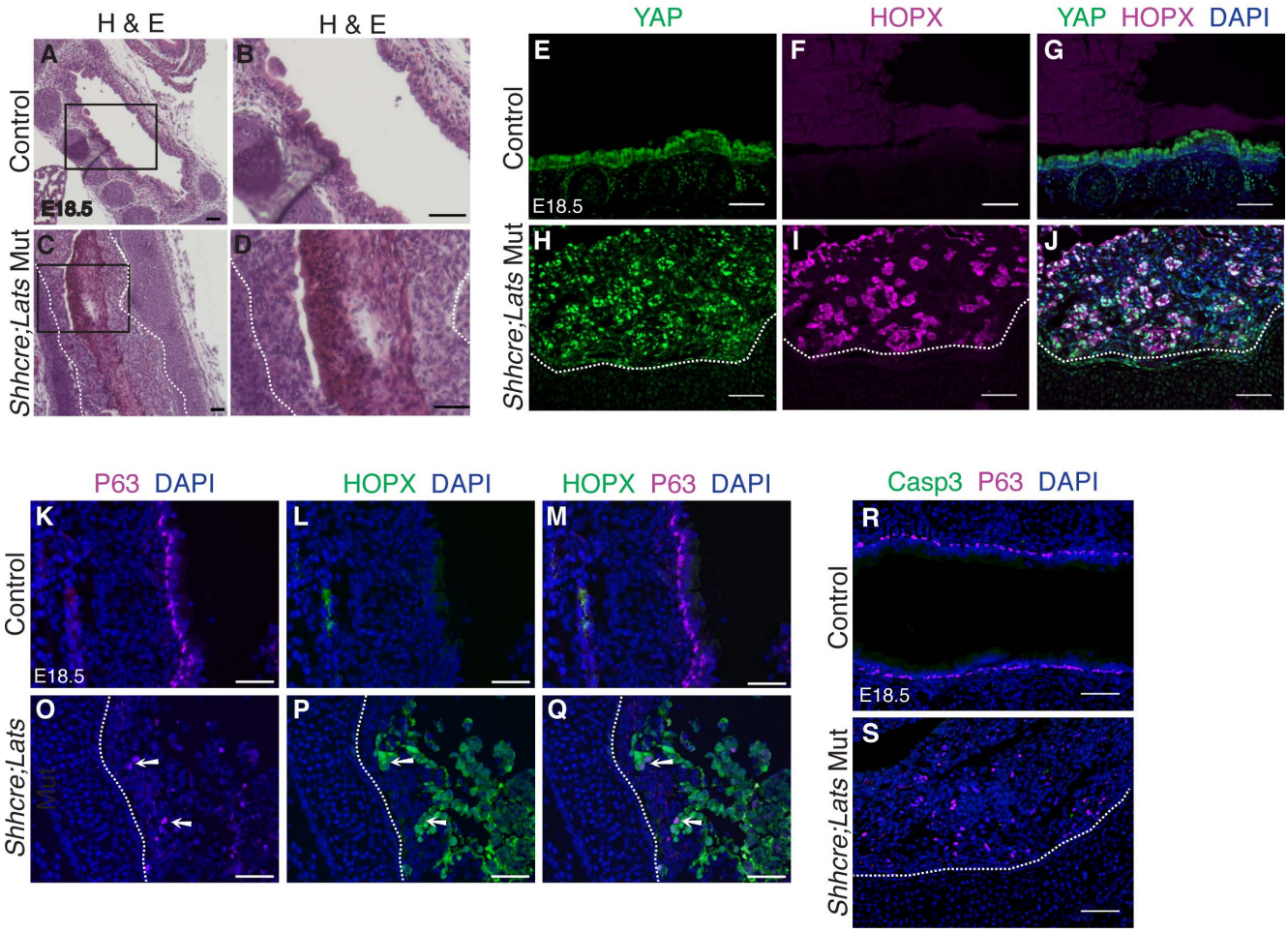

Figure S6. *Shhcre;Lats* mutants showed increased expression of AEC1 markers in the trachea at E18.5.

(A-B) Hematoxylin and Eosin staining of control and *Shhcre;Lats* mutant tracheas at E18.5. Boxed regions in A and C are magnified in B and D, which represent the general regions shown in the rest of the figure. In the mutant, the epithelium, delineated by white dashed lines, shows a large number of protruded cells that almost filled the lumen. (E-J) Immunofluorescent detection of YAP (green) and HOPX (magenta) in control and *Shhcre;Lats* mutant tracheas at E18.5, showing many YAP+ cells also express AEC1 marker HOPX in the *Shhcre;Lats* mutant tracheal epithelium, delineated by white dashed lines. (K-Q) Immunofluorescent detection of KRT5 (green) and P63 (magenta) in control and *Shhcre;Lats* mutant tracheas at E18.5, showing increased number and disorganization of KRT5+ and P63+ cells in the lumen of the mutant. White dashed lines delineate epithelium. (R,S) Immunofluorescent detection of cleaved Caspase 3 (green) and P63 (magenta) in control and *Shhcre;Lats* mutant tracheas at E18.5, showing presence and disorganization of P63+ cells, and few apoptotic cells in the mutant. White dashed lines delineate epithelium. Scale bars: 50μm.

Figure S7

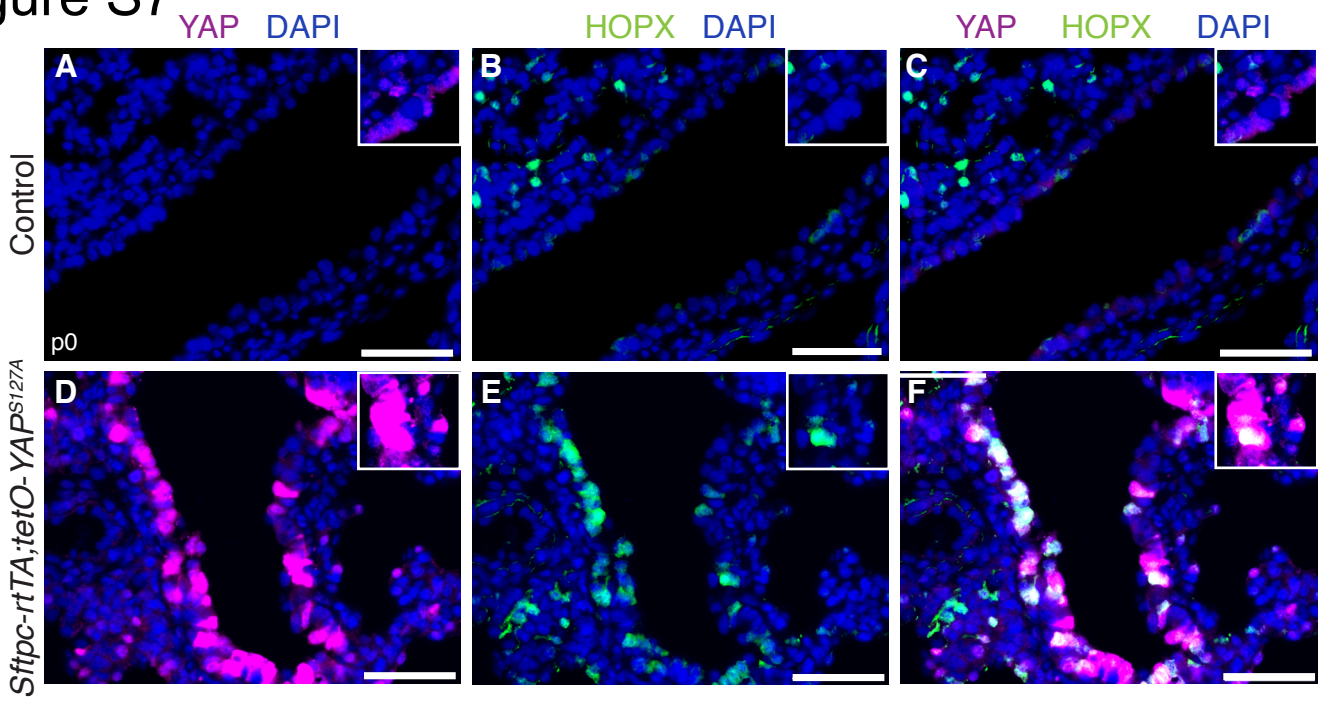

Figure S7. *Sftpc-rtTA;tetO-YAP*^{S127A} mutants showed ectopic HOPX expression in the airway epithelium.

(A-F) Immunofluorescent detection of HOPX (green) and YAP (magenta) in control and *Sftpc-rtTA;tetO-YAP*^{S127A} mutant lungs at p0, showing ectopic HOPX+ cells in the airway of trangenics. Insets show same staining adjusted for longer exposure to illustrate low YAP expression in control and high YAP expression in the mutant. Scale bars: 50μm.

Figure S8

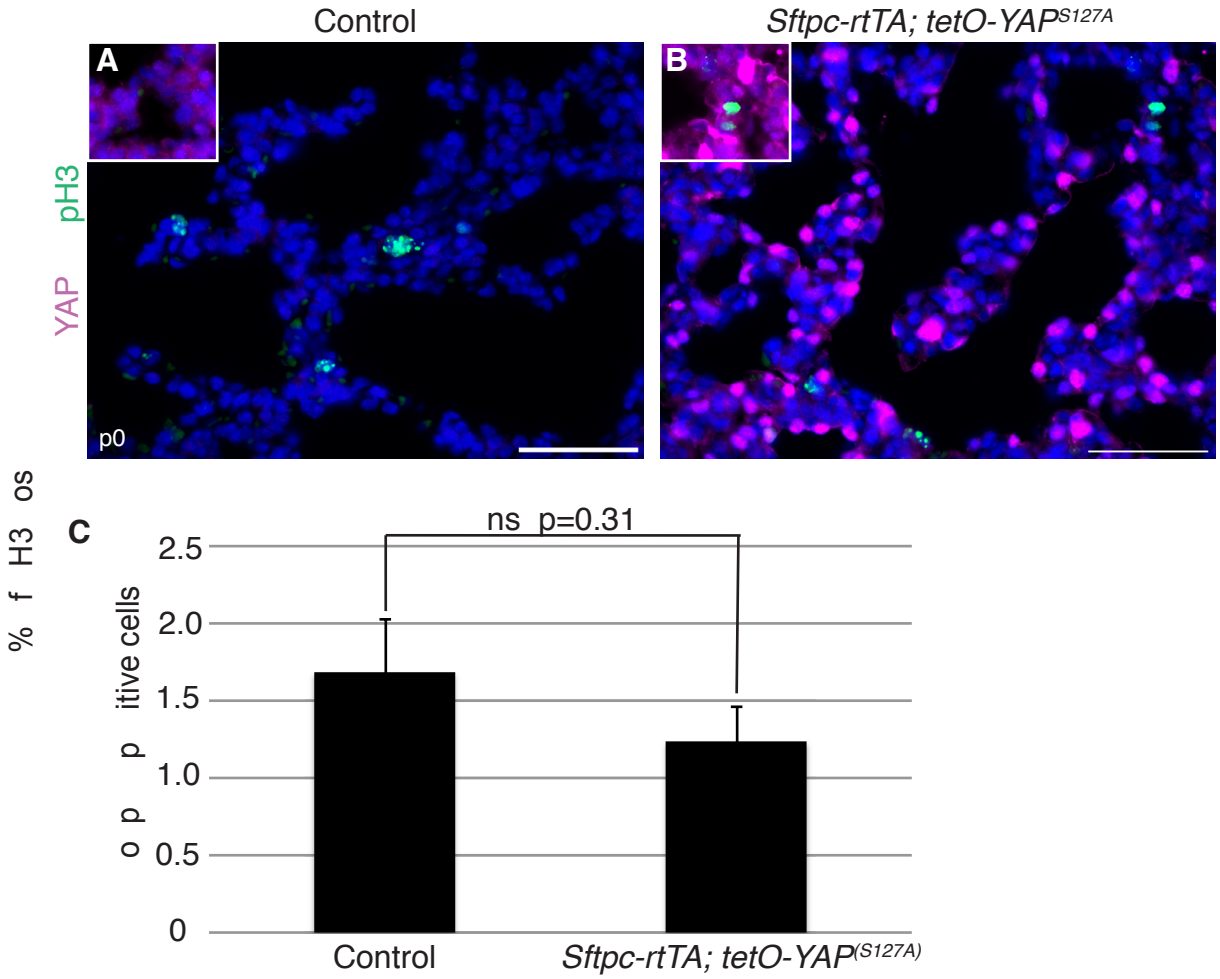

Figure S8. *Sftpc-rtTA;tetO-YAP*^{S127A} mutants did not show increased cell proliferation. (A,B) Immunofluorescent detection of phospho-Histone H3 (green) and YAP (magenta) in control and *Sftpc-rtTA;tetO-YAP*^{S127A} mutant lungs at p0. Insets show same staining adjusted for longer exposure to illustrate low YAP expression in control and high YAP expression in the mutant. Scale bars: 50μm. (C) Percentage of DAPI cells positive for phospho-Histone H3 (Control: 1.68 +/- 0.35% , Mutant: 1.25 +/- 0.23%, p=0.31). ns: not significant. Data are presented as mean +/- SEM.

Figure S9

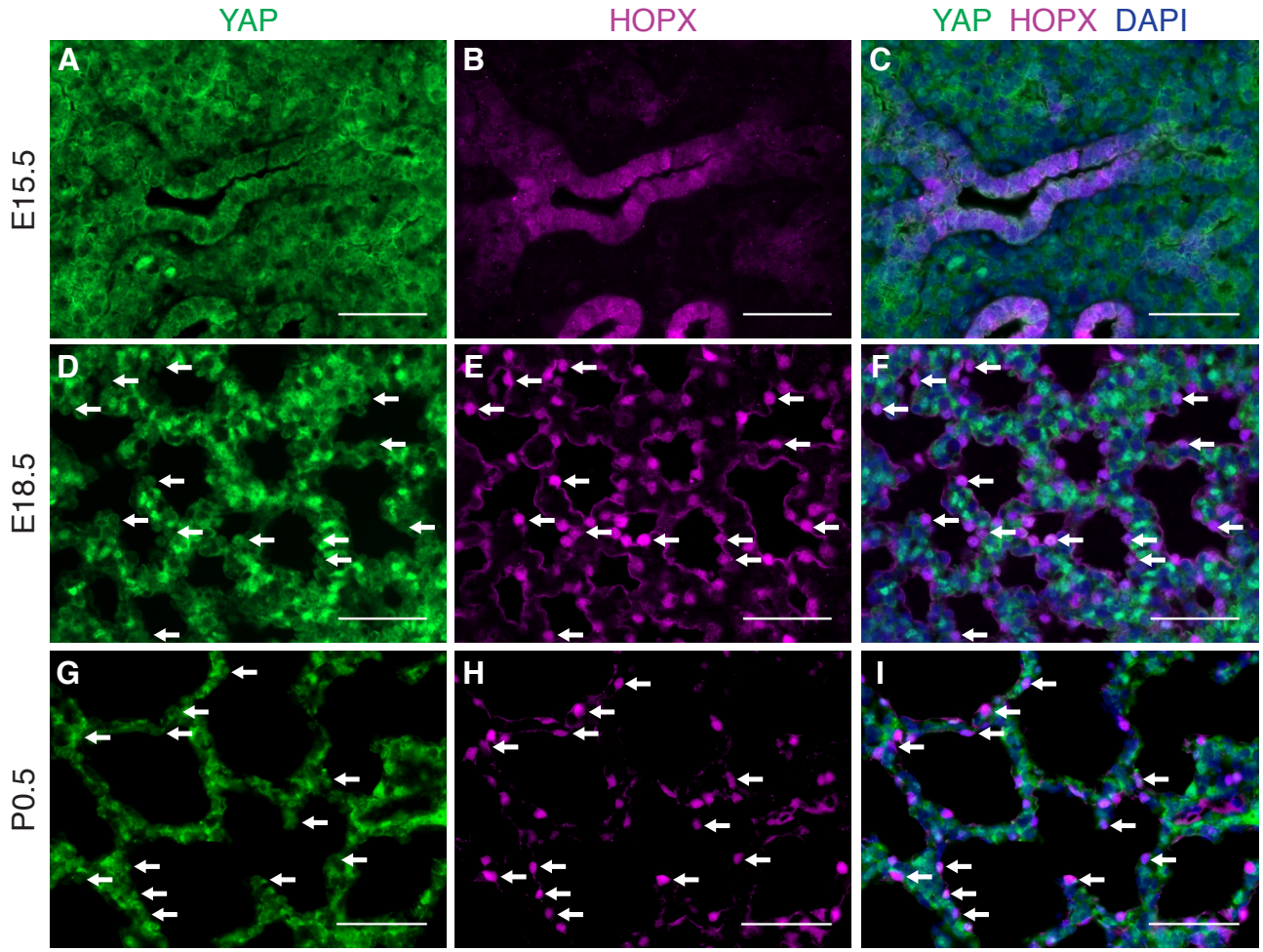

Figure S9. Nuclear YAP was detected in AEC1s in the normal lung.

(A-I) Immunofluorescent detection of YAP (green) and HOPX (magenta) in control lungs at E15.5, E18.5 and p0. At E18.5 and P0, but not E15.5, there are cells with nuclear YAP and HOPX expression (arrows). Scale bars: 50μm.

Figure S10

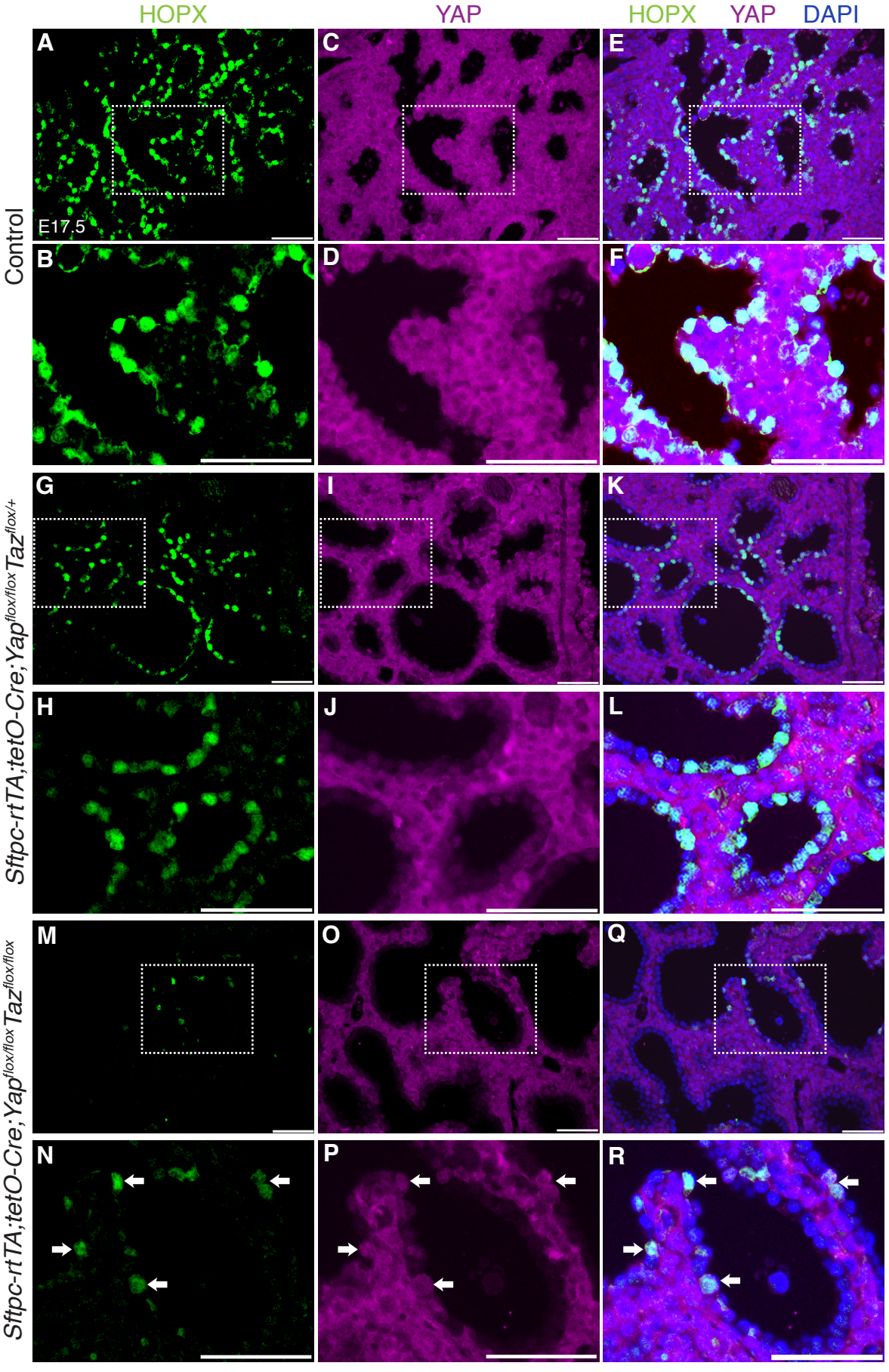

Figure S10. *Sftpc-rtTA;tetO-Cre;Yap$^{flox/flox}$;Taz$^{flox/flox}$* mutants showed that both *Yap* and *Taz* are essential for AEC1 differentiation.

(A-R) Immunofluorescent detection of HOPX (green) and YAP (magenta) in control, *Sftpc-rtTA;tetO-Cre;Yap$^{flox/flox}$;Taz$^{flox/+}$* mutant and *Sftpc-rtTA;tetO-Cre;Yap$^{flox/flox}$;Taz$^{flox/flox}$* mutant lungs at E17.5. Boxed areas are magnified in the rows immediately below. The *Sftpc-rtTA;tetO-Cre;Yap$^{flox/flox}$;Taz$^{flox/+}$* mutants showed an intermediate phenotype of slightly reduced HOPX+ cells. Arrows in the *Sftpc-rtTA;tetO-Cre;Yap$^{flox/flox}$;Taz$^{flox/flox}$* mutant indicated that the few remaining HOPX+ cells all had escaped recombination and retained YAP. Scale bars: 50μm.

Table S1. Primers used for qRT-PCR

Transcript	Forward Primer (5'-3')	Reverse Primer (5'-3')
Actb	CGGCCAGGTCATCACTATTGGCAAC	GCCACAGGATTCCATACCCAAGAAG
Ager	GTGGCTCAAATCCTCCCCAAT	CCTTCCCTCGCCTGTTAGTTG
Amotl2	AAGGGCTCGTATCCAGTGAG	CGTCTCTGCTGCCA TGTTT
Cdh1	CAAGGACAGCCTTCTTTTCG	TGGACTTCAGCGTCACTTTG
Ctgf	GCCCTAGCTGCCTACCGACT	AACAGGCGCTCCACTCTGTG
Hopx	CCACGCTGTGCCTCATCGCA	GGCCTGGCTCCCTAGTCCGT
Pdpn	CACCTCAGCAACCTCAGAC	AAGACGCCAACTATGATTCCAA
Sox2	GGAGAAAGAAGAGGAGAGAG	CTGGCGGAGAATAGTTGG
Sox9	CGTGGACATCGGTGAACTGA	GGTGGCAAGTATTGGTCAAACTC
Wnt5a	CAAATAGGCAGCCGAGAGAC	CTCTAGCGTCCACGAACTCC
Wnt7b	CAATGGTGGTCTGGTACCCAA	AGTCTCATGGTCCCTTTGTGGTT