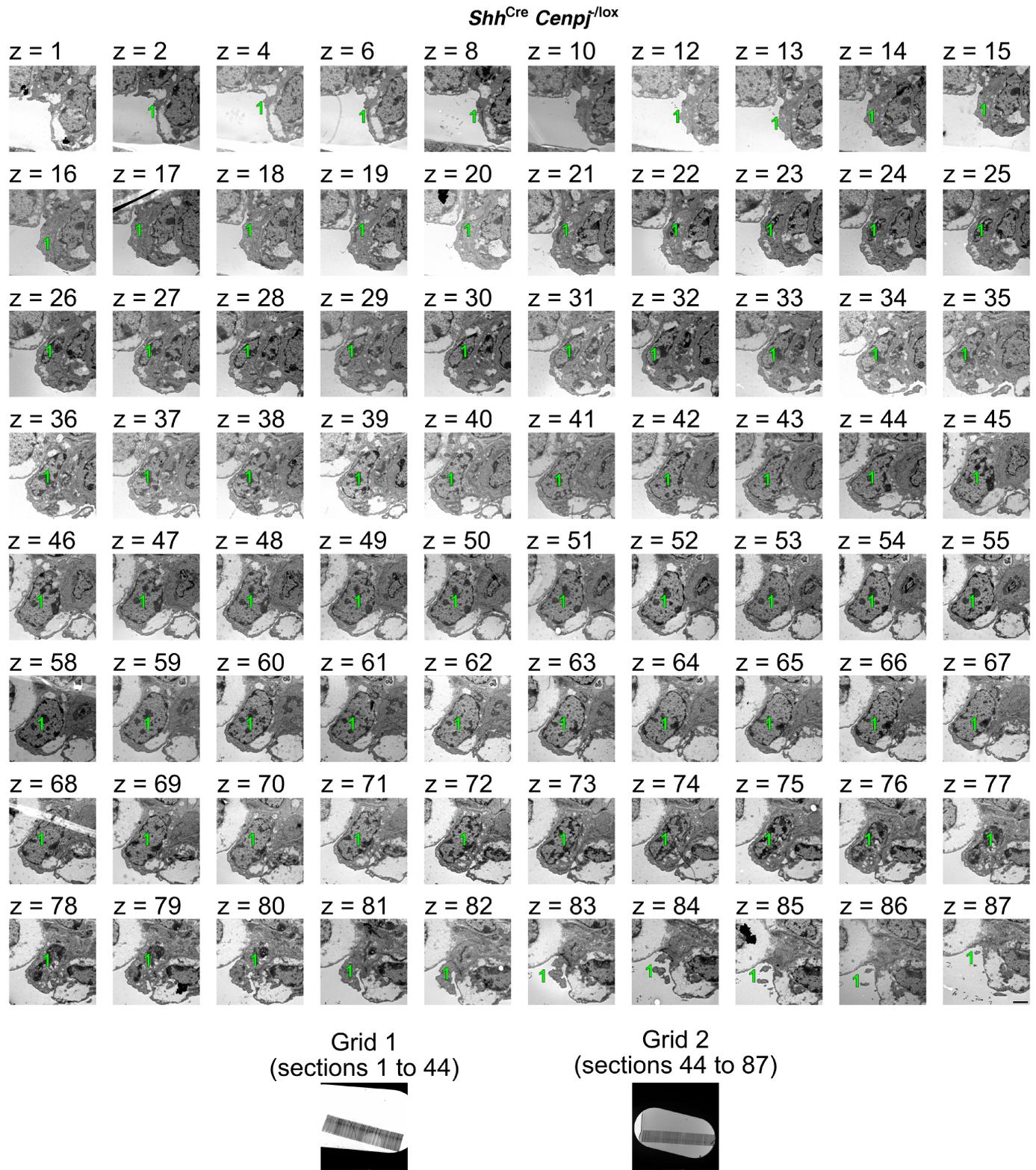
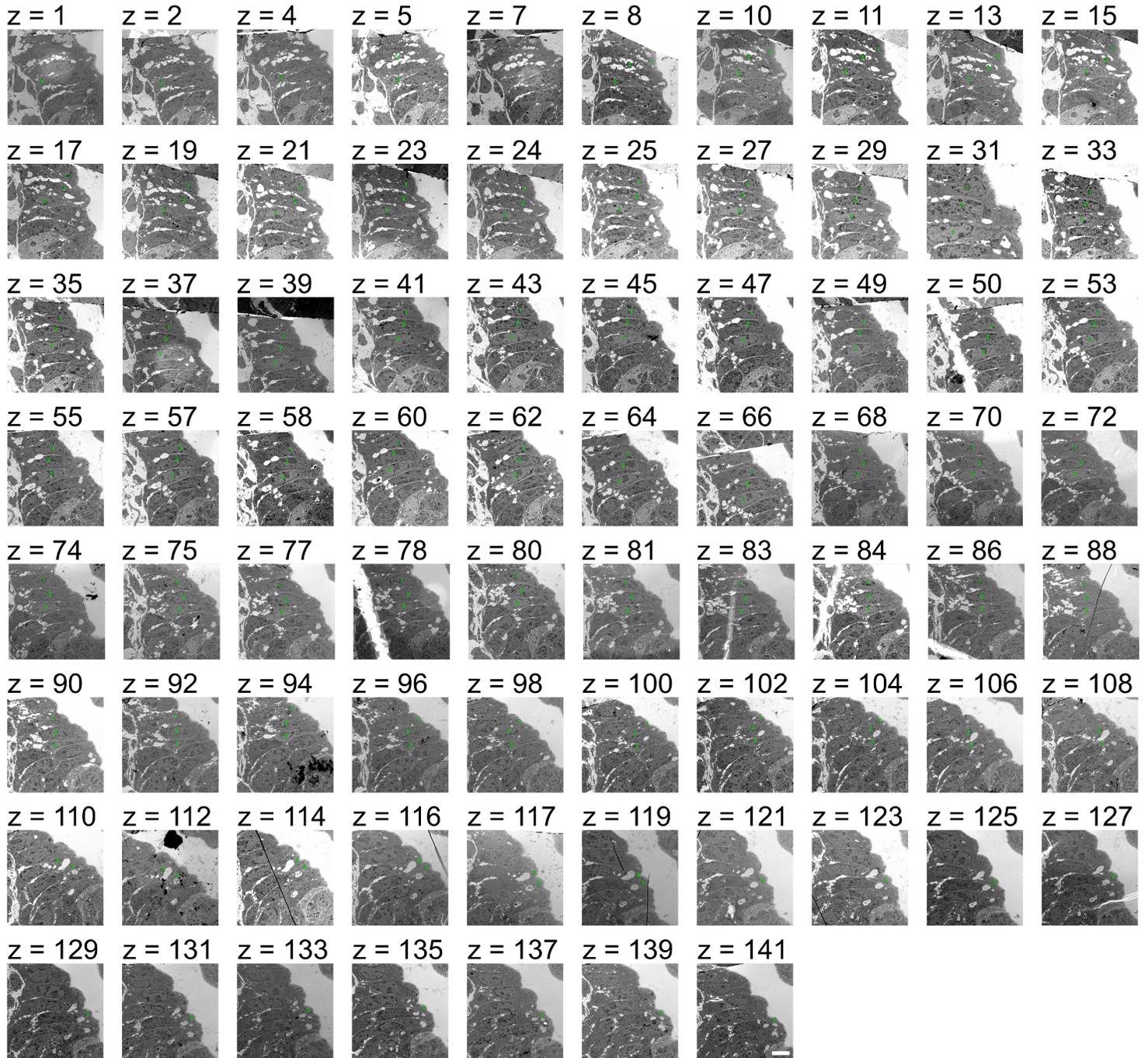


# Supplemental Figures

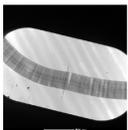


**Figure S1. Serial section transmission electron microscopy of *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>/lox</sup>*) lung epithelial cells, Related to Figure 1. Scale bar, 2  $\mu$ m.**

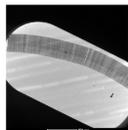
*Shh*<sup>Cre</sup> *Cenpj*<sup>-/lox</sup>



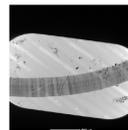
Grid 1  
(sections 1 to 7)



Grid 2  
(sections 8 to 66)



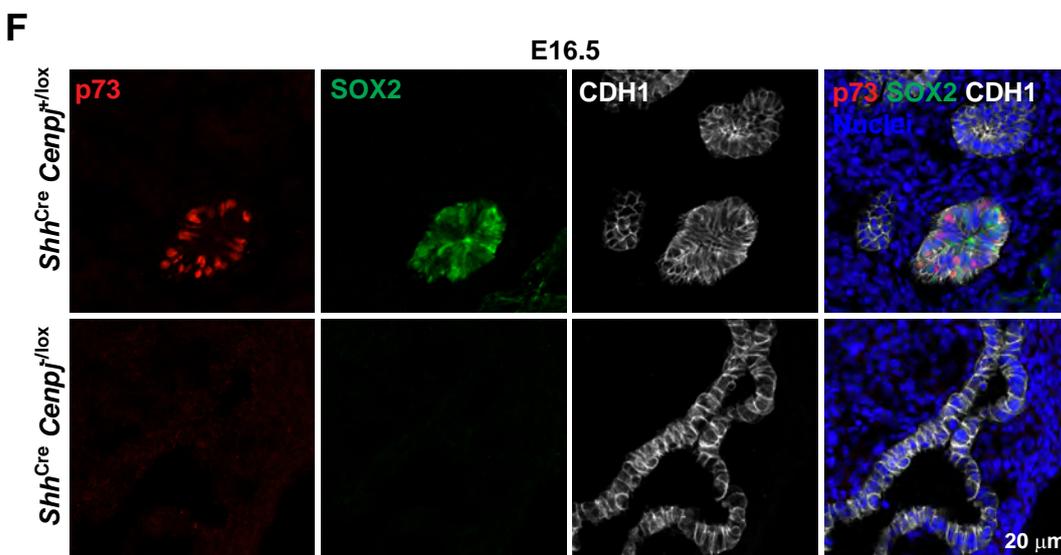
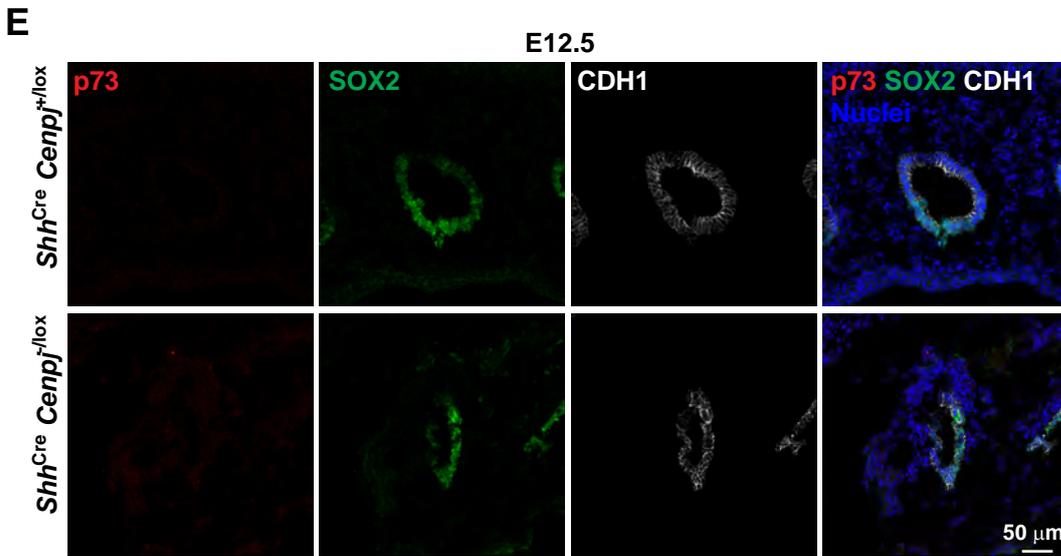
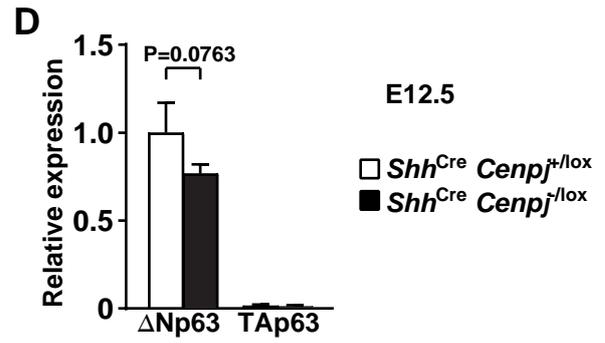
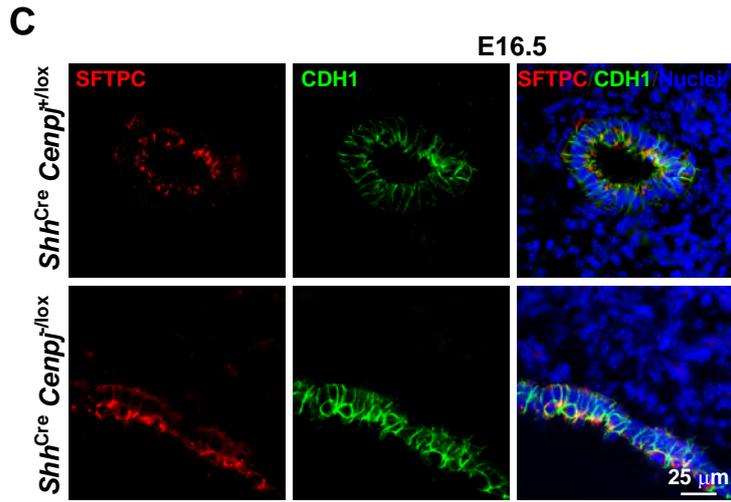
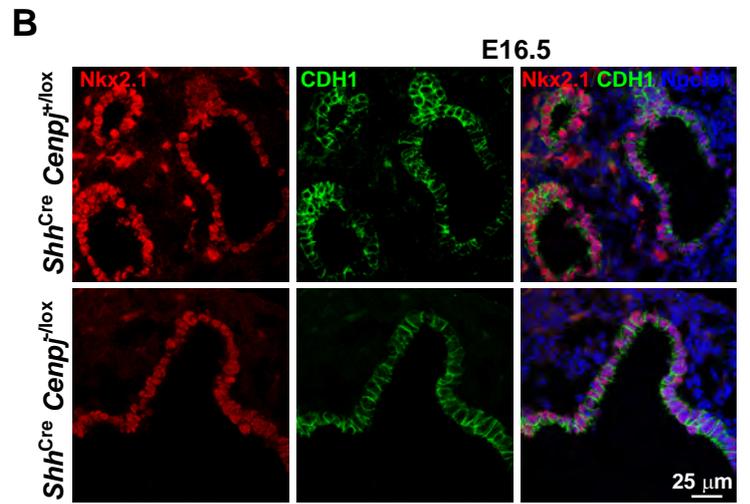
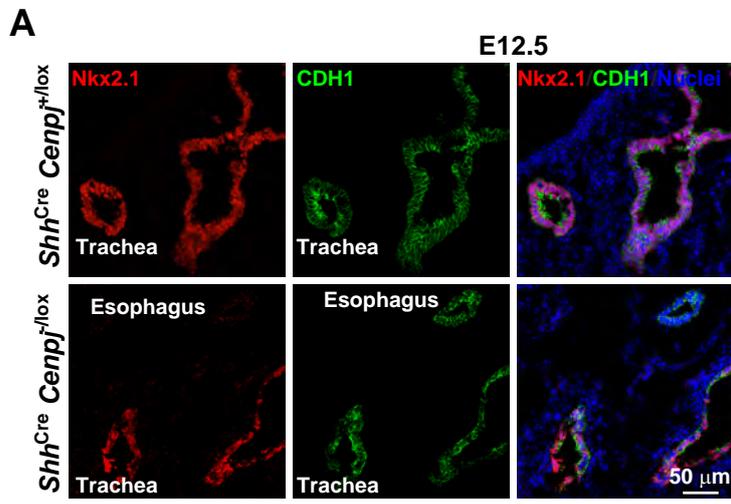
Grid 3  
(sections 68 to 116)



Grid 4  
(sections 117 to 141)



**Figure S2. Serial section transmission electron microscopy of *Cenpj* loss of function (*Shh*<sup>Cre</sup> *Cenpj*<sup>-/lox</sup>) intestinal epithelial cells, Related to Figure 1. Scale bar, 2  $\mu$ m.**



**Figure S3. Centrioles are not required for distal epithelial lung fate, but required for bronchiolar epithelial formation, Related to Figure 2.**

(A) Immunostaining of Nkx2.1 (red), CDH1 (green) and nuclei (blue) in E12.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung sections. Scale bar, 50  $\mu$ m.

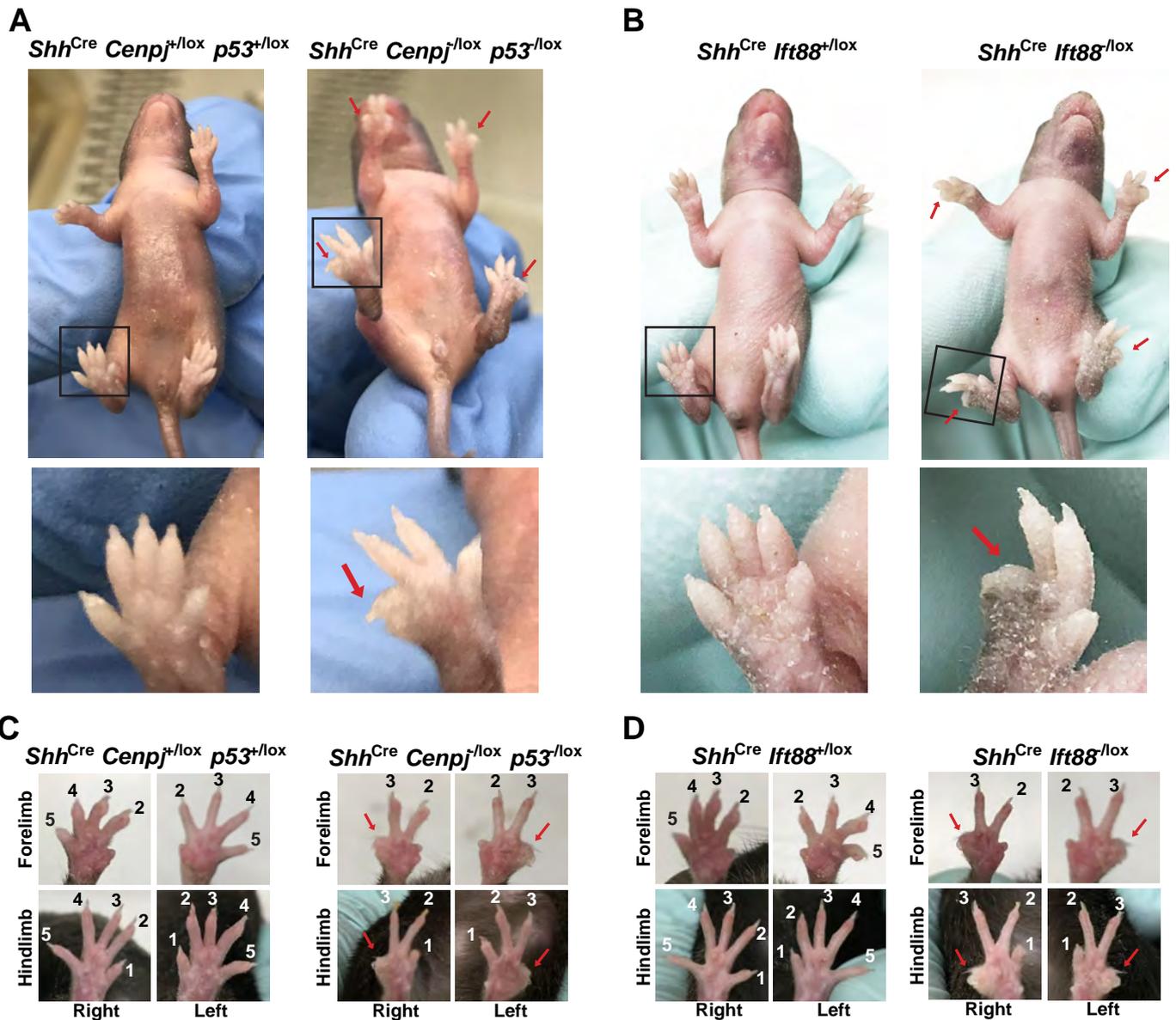
(B) Immunostaining of Nkx2.1 (red), CDH1 (green) and nuclei (blue) in E16.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung sections. Scale bar, 25  $\mu$ m.

(C) Immunostaining of SFTPC (red), CDH1 (green) and nuclei (blue) in E16.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung sections. Scale bar, 25  $\mu$ m.

(D) RT-qPCR analysis of DeltaN p63 and TAp63 isoform expression in E12.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung and trachea. n=4 and 3 for control and *Cenpj* loss of function respectively.

(E) Immunostaining of p73 (red), SOX2 (green), CDH1 (grey) and nuclei (blue) in E12.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung sections. Scale bar, 50  $\mu$ m.

(F) Immunostaining of p73 (red), SOX2 (green), CDH1 (grey) and nuclei (blue) in E16.5 control (*Shh<sup>Cre</sup> Cenpj<sup>+/-lox</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/-lox</sup>*) lung sections. Scale bar, 20  $\mu$ m.



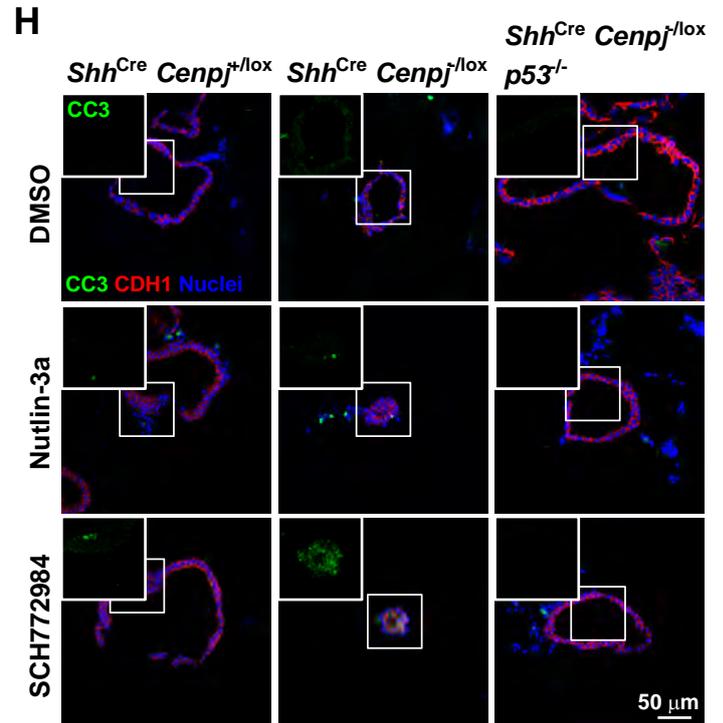
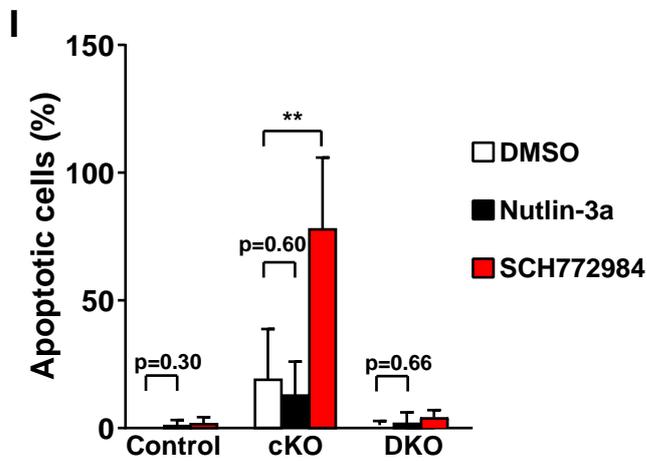
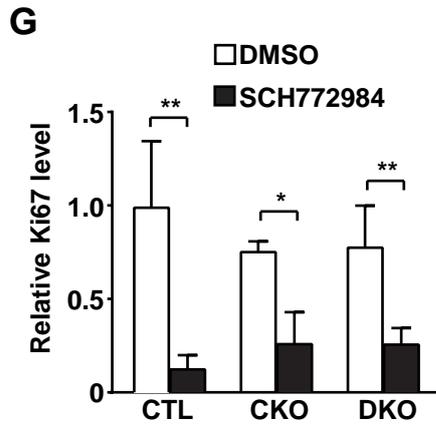
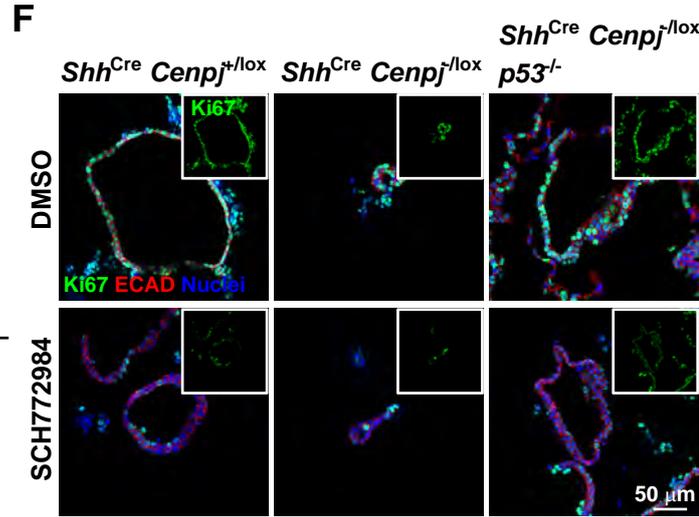
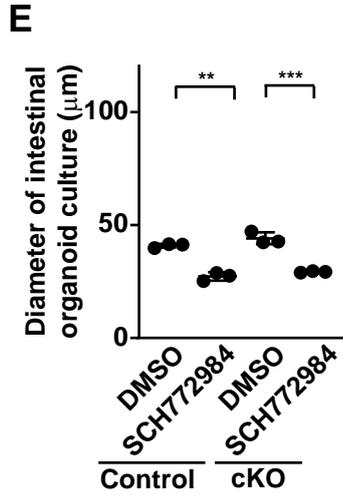
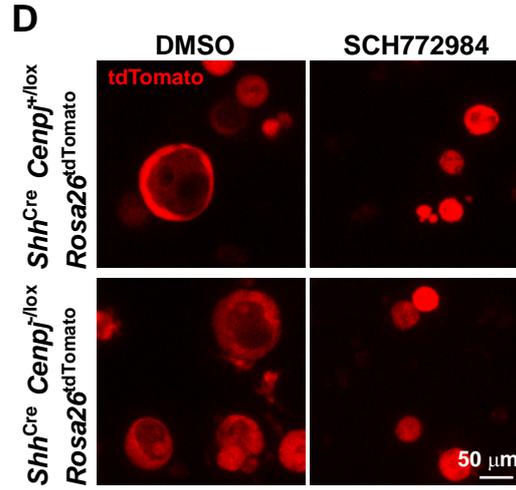
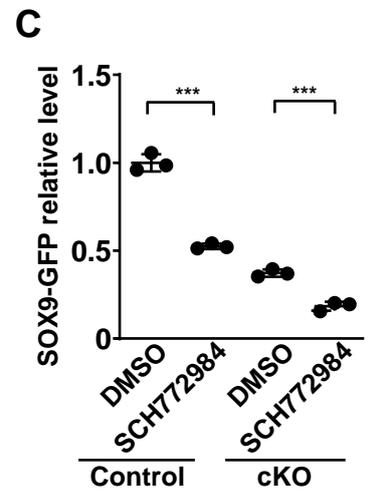
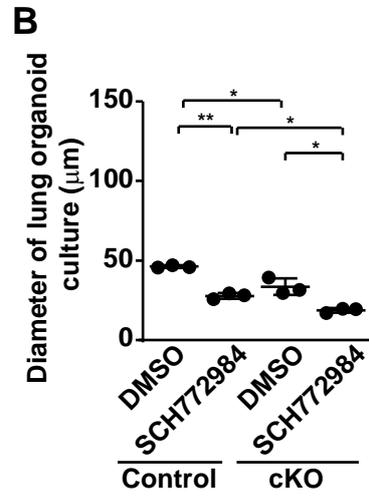
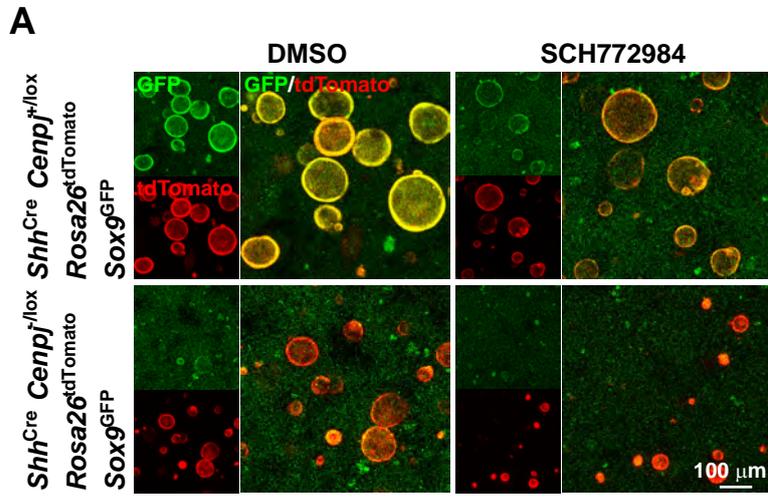
**Figure S4. p53 deletion does not restore limb development in  $Shh^{Cre} Cenpj^{+/lox}$  mice, Related to Figure 2 and Figure 3.**

(A) Images of P7 control ( $Shh^{Cre} Cenpj^{+/lox} p53^{+/lox}$ ),  $Cenpj$  and  $p53$  combined loss of function ( $Shh^{Cre} Cenpj^{+/lox} p53^{-/lox}$ ) mice. Higher magnification of right hind paw (boxed) was shown below. Arrows indicated the abnormal digits.

(B) Images of P7 control ( $Shh^{Cre} Ift88^{+/lox}$ ),  $Ift88$  loss of function ( $Shh^{Cre} Ift88^{-/lox}$ ) mice. Higher magnification of right hind paw (boxed) was shown below. Arrows indicated the abnormal digits.

(C) Images of the 4 paws of 6 months old control ( $Shh^{Cre} Cenpj^{+/lox} p53^{+/lox}$ ),  $Cenpj$  and  $p53$  combined loss of function ( $Shh^{Cre} Cenpj^{+/lox} p53^{-/lox}$ ) mice. Higher magnification of right hind paw (boxed) was shown below. Arrows indicated the abnormal digits.

(D) Images of the 4 paws of 6 months old control ( $Shh^{Cre} Ift88^{+/lox}$ ),  $Ift88$  loss of function ( $Shh^{Cre} Ift88^{-/lox}$ ) mice. Higher magnification of right hind paw (boxed) was shown below. Arrows indicated the abnormal digits.



**Figure S5. ERK inhibitor suppresses the growth of lung and intestinal organoids, Related to Figure 5.**

(A) Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) lung organoid cultures were treated with DMSO or 2.5  $\mu$ M SCH772984 for 24 hours, then imaged for GFP and tdTomato fluorescence. Scale bar, 100  $\mu$ m.

(B) Quantification of the diameter of control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) (cKO) lung organoid cultures in (A). n=3.

(C) Quantification of the Sox9-GFP level of control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> Rosa26<sup>tdTomato</sup> Sox9<sup>GFP</sup>*) (cKO) lung organoid cultures in (A). n=3

(D) Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup> Rosa26<sup>tdTomato</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> Rosa26<sup>tdTomato</sup>*) intestinal organoid cultures were treated with DMSO or 2.5  $\mu$ M SCH772984 for 24 hours, then imaged for tdTomato fluorescence. Scale bar, 50  $\mu$ m.

(E) Quantification of the diameter of control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup> Rosa26<sup>tdTomato</sup>*) and *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> Rosa26<sup>tdTomato</sup>*) (cKO) intestinal organoid cultures in (D). n=3

(F) Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup>*), *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup>*), and *Cenpj* and *p53* combined loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> p53<sup>-/-</sup>*) lung organoid culture were treated with DMSO or 2.5  $\mu$ M SCH772984 for 24 hours, then subjected to frozen section and stained for Ki67 (green), CDH1 (red) and nuclei (blue). Scale bar, 50  $\mu$ m.

(G) Quantification of the Ki67 level in Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup>*), *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup>*), and *Cenpj* and *p53* combined loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> p53<sup>-/-</sup>*) lung organoid culture in (F). n=4, 3 for control; n=2,3 for *Cenpj* loss of function; n=2, 6 for *Cenpj* and *p53* combined loss of function.

(H) Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup>*), *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup>*), and *Cenpj* and *p53* combined loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> p53<sup>-/-</sup>*) lung organoid culture were treated with DMSO, 10  $\mu$ M Nutlin-3a or 2.5  $\mu$ M SCH772984 for 24 hours, then subjected to frozen section and stained for cleaved Caspase 3 (CC3, green), CDH1 (red) and nuclei (blue). Scale bar, 50  $\mu$ m

(I) Quantification of the apoptotic cells in Control (*Shh<sup>Cre</sup> Cenpj<sup>+/lox</sup>*), *Cenpj* loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup>*)(cKO), and *Cenpj* and *p53* combined loss of function (*Shh<sup>Cre</sup> Cenpj<sup>-/lox</sup> p53<sup>-/-</sup>*)(DKO) lung organoid culture in (J). n=5, 4, 4 for control; n=4, 5, 5 for *Cenpj* loss of function; n=5, 4, 2 for *Cenpj* and *p53* combined loss of function.