



Supplemental Figure S7 (related to Fig. 5). **Validation of direct TAp73 target genes**

(A) At the earliest stages of ciliation on ALI D2, p73 and FoxJ1 are already co-expressed in the nuclei of suprabasal MCCs, and then maintained until full differentiation at D14 (see Fig. 5A). Confocal immunofluorescence images of WT MTECs at D2. DAPI counterstain.

(B) p73 is expressed in p63-negative suprabasal cells. Immunofluorescence for p63 (red) and p73 (green) of WT tracheosphere organoids grown as 3D in matrigel at ALI D14. DAPI counterstain. Lateral view.

(C) TAp73-deficient airways show marked, albeit not complete, loss of FoxJ1 protein. Representative bronchi from WT vs. TAp73KO mice analyzed by IHC (n=3 each).

(D) Compared to WT littermates, lungs of TAp73KO mice exhibit downregulation of the core ciliogenesis transcription factors FoxJ1 and Rfx2, and of representative ciliary motility and structural genes like axonemal Dyneins *Dnahc5*, *Dnahc3*, *Dnali1*, *Rsph4a* (radial spoke head), *Hydin* (central pair-associated) and *Spata18* (aka *Spetex-1*). qRT-PCR on lung tissues from 3 mo (n= 6-7 mice per genotype) and 6 mo (n=3 mice per genotype) old animals.

(E) Expression of FoxJ protein is strongly downregulated in lung lysates of p73KO mice. Immunoblot (n=3 mice each). β -actin as loading control.

(F) Expression of Dnali1 protein is strongly downregulated in lung lysates of TAp73KO mice. Immunoblot (n=3 mice each). β -actin as loading control.

(G) Validation of the pan-p73 antibody used for endogenous p73 ChIP from mouse tracheae. Immunoblot of lung extracts from WT, p73KO and TAp73KO mice. β -actin as loading control.

(H) Endogenous p73 directly binds to regulatory regions of core ciliogenesis genes. Targeted ChIP assays from 30 mouse tracheae. Immunoprecipitations with pan-p73 specific antibody vs. IgG control.

(I) Human TAp73 α and TAp73 β directly bind to regulatory regions of core ciliogenesis genes. Targeted ChIP assays in Saos2 cells. Immunoprecipitations with TAp73-specific antibody vs. IgG control. Data derived from 3 independent experiments per gene. Error bars represent standard error of the mean (SEM).