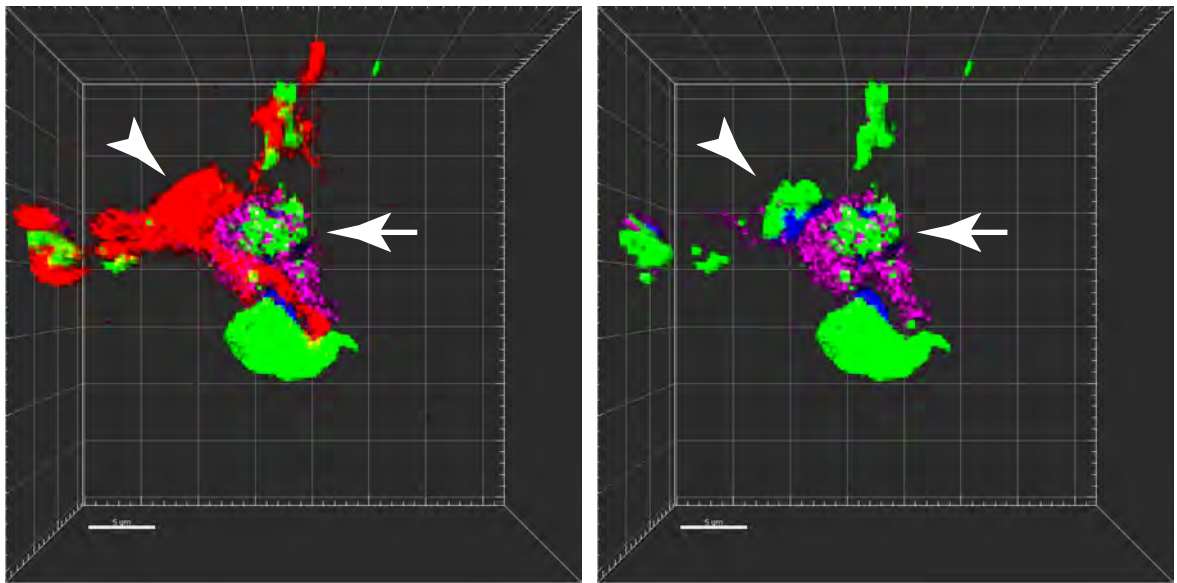
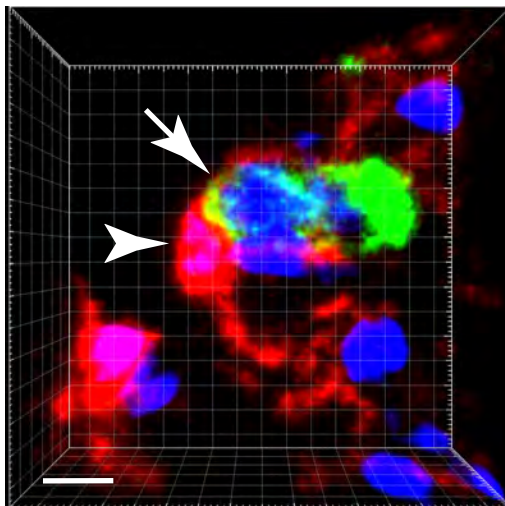


A



RFP pSmad1/5/8 LAMP-3

B



RFP Lamp-3

Fig. S1. Cellular Morphology of TASCs (Type 2 - associated stromal cells)

(A) *Pdgfra-CreER^{T2}; Rosa26-tdTomato* mice were treated with Tmx and lungs were fixed 4 days later. Images show that a representative *Pdgfra*⁺ cell (RFP antibody, arrowhead) closely adjacent to an AT2 (LAMP-3⁺, magenta, arrow) has long cellular extensions. Both cells in the niche are pSmad1/5/8⁺ (green) (B) A second example of a *Pdgfra*⁺ lineage labeled TASC (arrowhead) adjacent to AT2 cells (arrow). 3D rotation shown in movie 1.

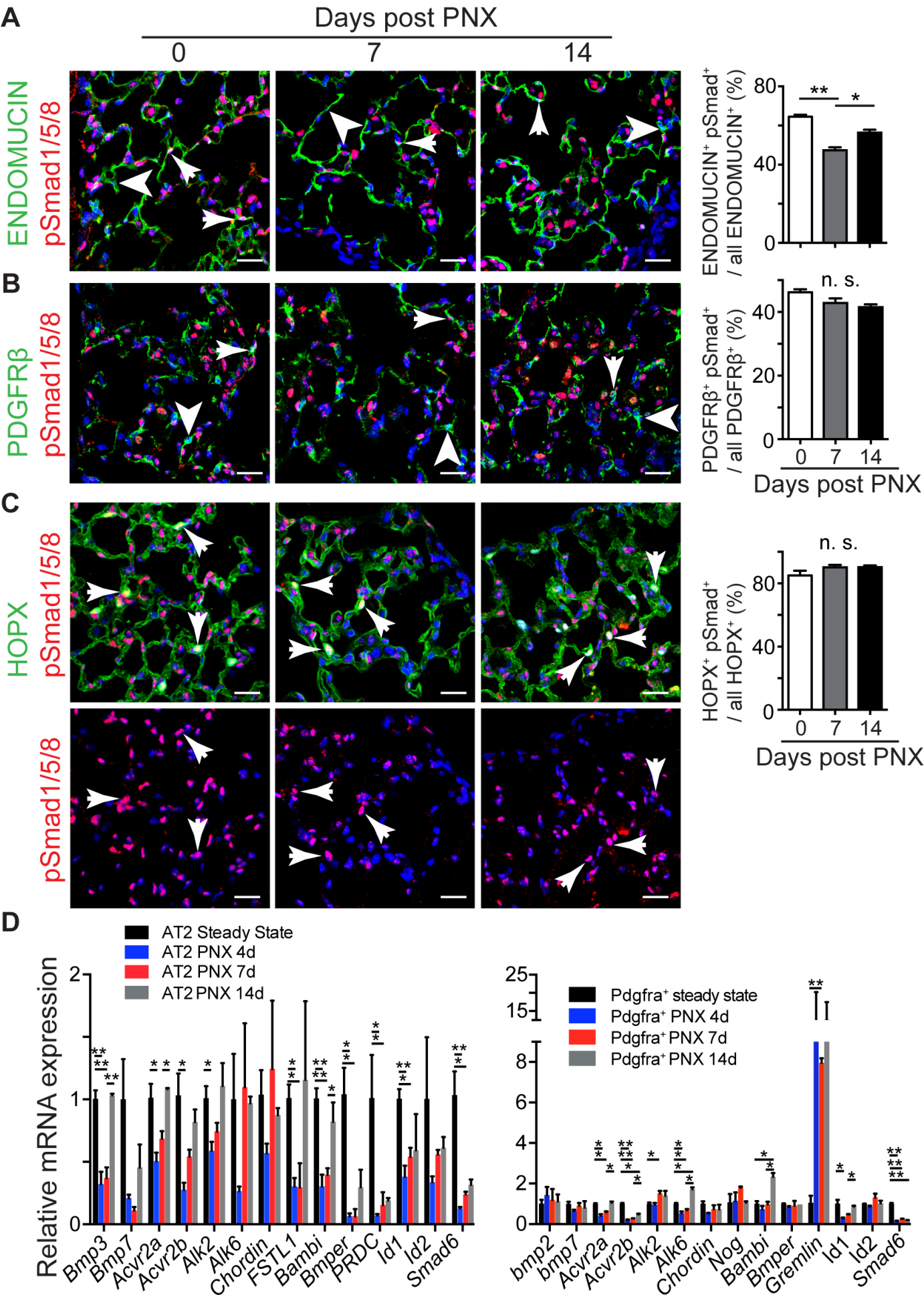


Fig. S2. BMP signaling during alveolar regrowth *in vivo*

Expression of pSmad1/5/8 (red) in (A) Endomucin⁺ (B) PDGFRβ⁺ and (C) HOPX⁺ cells at steady state and after PNx. Only nuclei that could be unambiguously assigned to a specific cell were scored as either positive for pSmad (arrows) or negative (arrowhead). Scale bars 20 μm. (D) qPCR for BMP signaling genes in AT2s and Pdgfrα⁺ cells at steady state and times after PNx. The mRNA expression levels of PNx samples were normalized to steady state levels. Data shown are mean ± SEM. *p < 0.05, **p < 0.01.

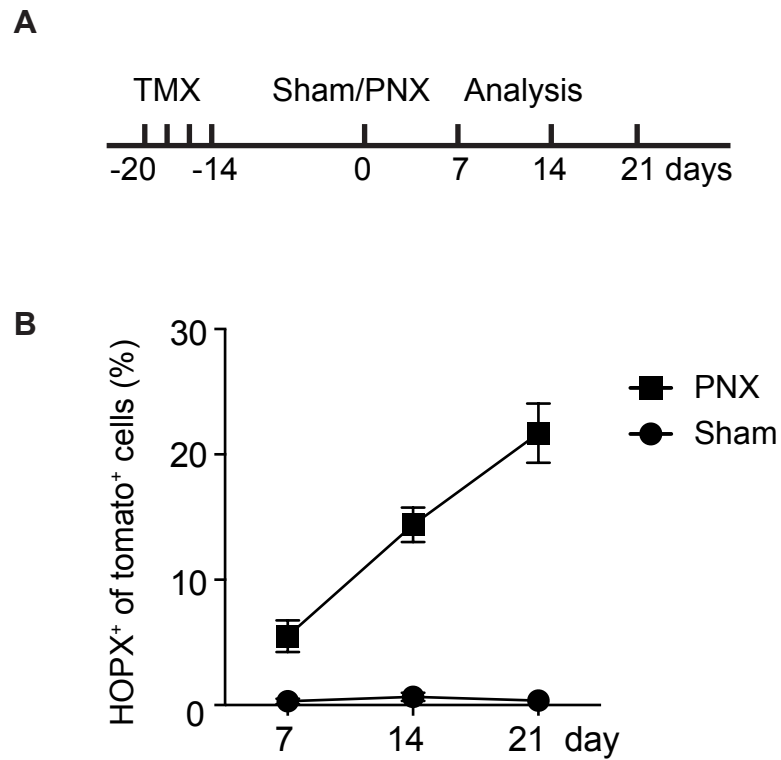


Fig. S3. AT2 differentiation into AT1s during alveolar regrowth

(A) *Sftpc-CreER^{T2}*; Rosa26-tdTomato mice were treated with Tmx two weeks before sham surgery or PNX and lungs fixed 7d, 14d, and 21d later. (B) Number of lineage labeled AT2-derived AT1s was determined using RFP and HOPX immunofluorescence as shown in Fig.5. $n \geq 3$ animals/group.

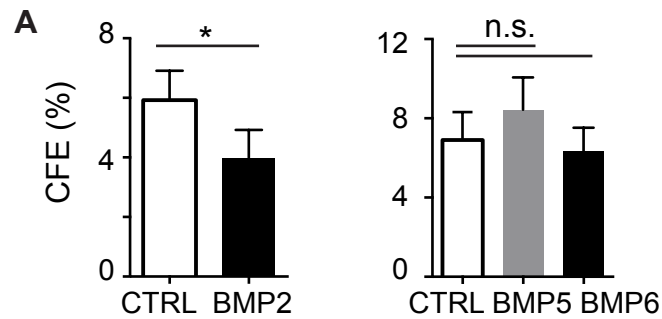


Fig. S4. Effect of BMP ligands on AT2 organoid culture

(A) AT2 organoid culture in the presence of BMP ligands (all 50 ng/ml). While adding BMP2 reduces CFE, no effect was seen with BMP5 and BMP6.

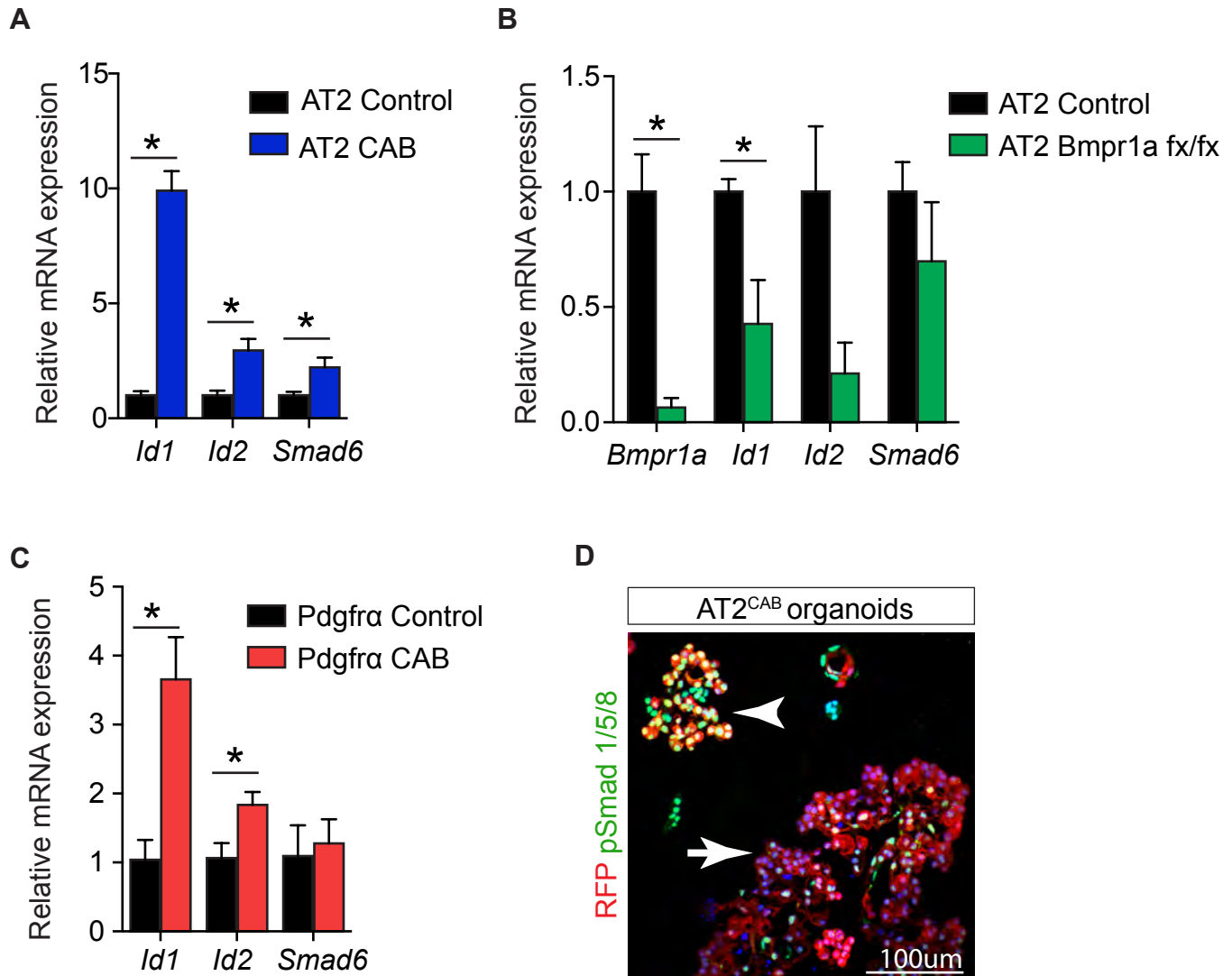


Fig. S5. Validation of enhanced and inhibited BMP signaling

qPCR analysis for BMP downstream targets in (A) AT2^{CTRL} and AT2^{CAB}, (B) AT2^{CTRL} and AT2^{Bmpr1a fx/fx} and (C) Pdgfra^{CTRL} and Pdgfra^{CAB} cells. Data shown are mean \pm SEM. * $p < 0.05$. (D) Typical high pSmad1/5/8 expression in a lineage labeled AT2^{CAB}-derived organoid (arrowhead). Levels were typically lower in the few large organoids (arrow), suggesting these were derived from AT2s that had recombined the Rosa26-tdTomato but not the Rosa26-caBmpr1a allele. $n = 3$ animals/group. Data shown as mean \pm SEM. Scale bar 100 μ m.

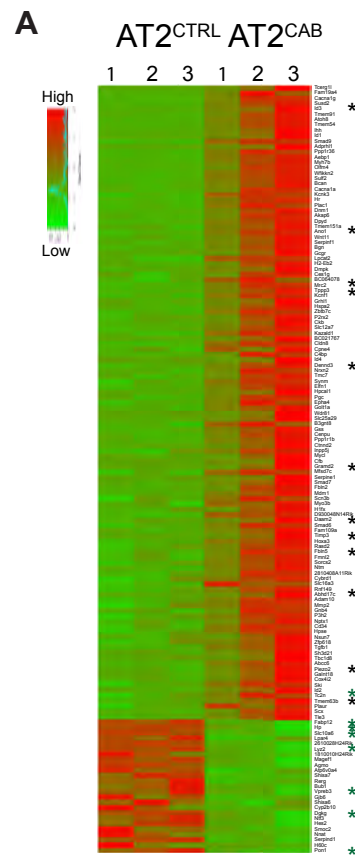


Fig. S6. RNA sequencing analysis of AT2^{CTRL} and AT2^{CAB} Heatmap showing 119 genes upregulated more than two-fold in AT2^{CAB} compared with AT2^{CTRL}. Of these genes, 12 are normally preferentially expressed in AT1 cells (black star). Of the 25 genes preferentially downregulated more than 2 fold in AT2^{CAB} cells, 8 are preferentially expressed in AT2 cells (green star). P-adj < 0.05.

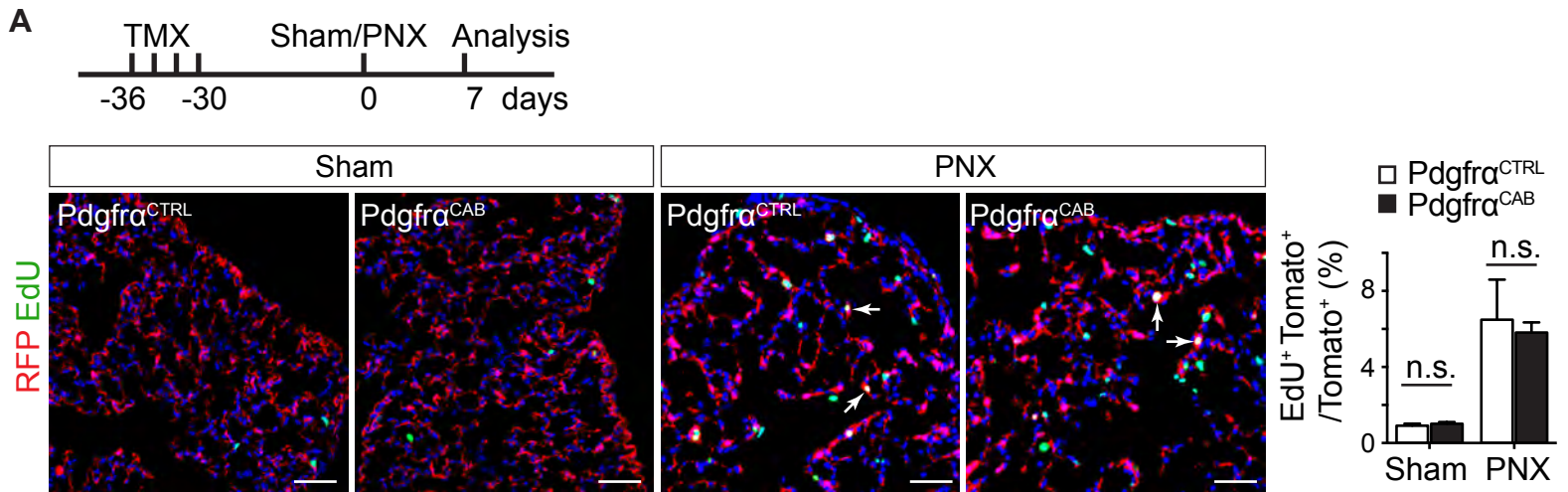


Fig. S7. Enhanced BMP signaling in Pdgfra stromal cells has no effect on their proliferation

(A) Tmx was used to lineage label and conditionally activate Bmpr1a in Pdgfra⁺ cells. Pdgfra^{CTRL} and Pdgfra^{CAB} lungs were fixed 7 days post sham or PNx surgery. Immunofluorescence analysis of RFP (lineage label) and EdU showed no significant differences of proliferation in stromal cells of Pdgfra^{CTRL} and Pdgfra^{CAB} lungs. $n \geq 3$ animals/group. Data shown as mean \pm SEM. Scale bars 50 μ m.

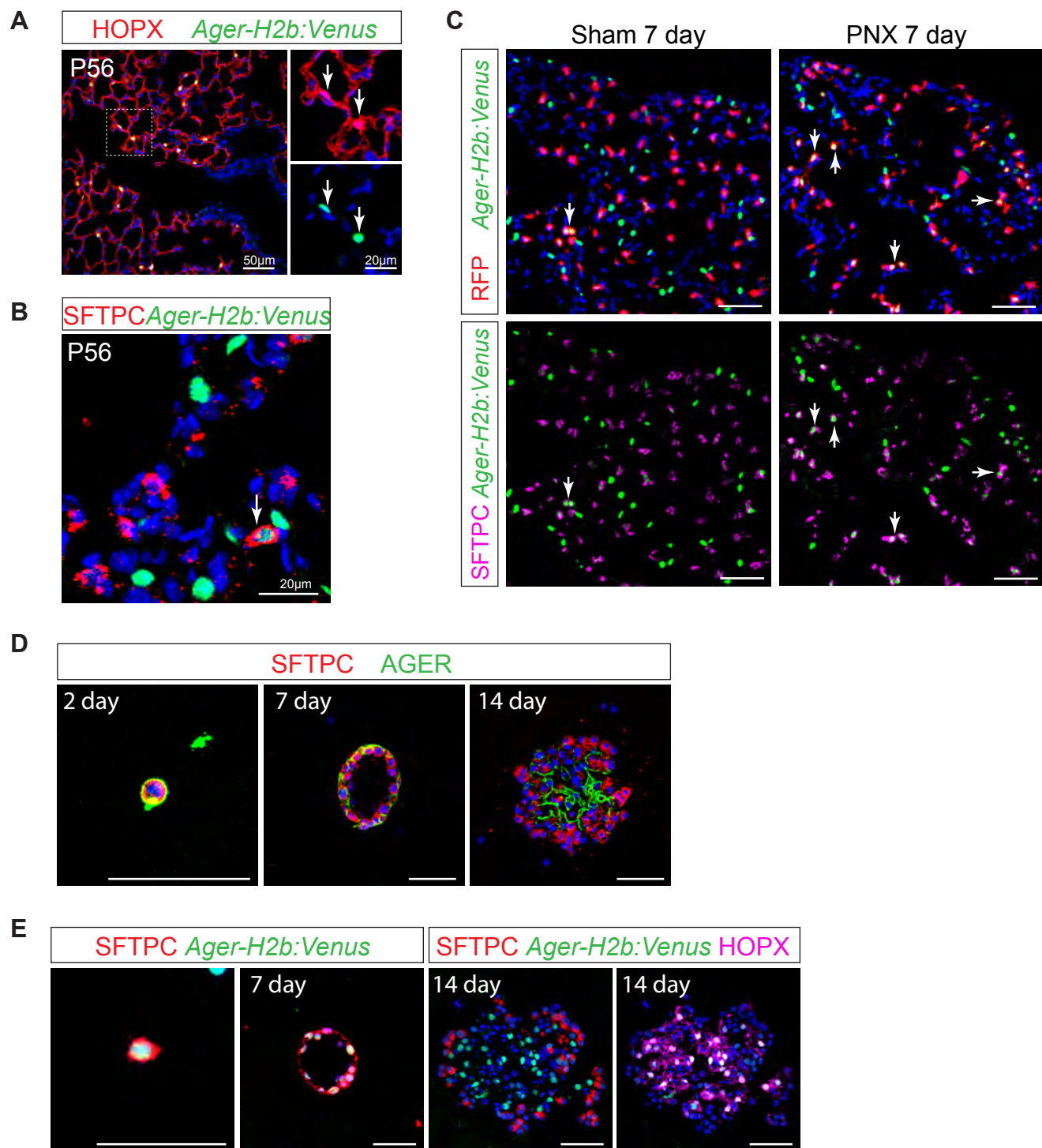
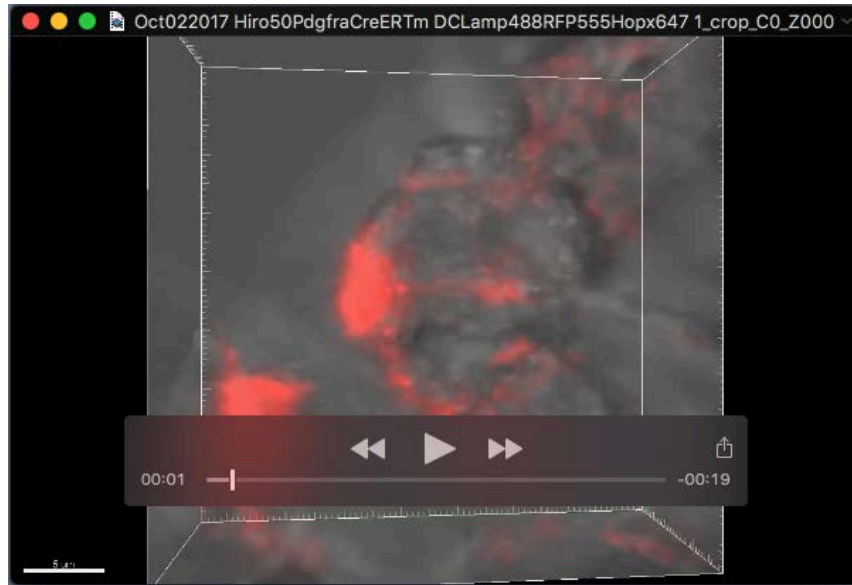


Fig. S8. SFTPC and AGER dual positive cells in regeneration systems including PNX and organoid cultures

(A) Evidence that a new knock-in allele, *Ager-H2b:Venus*, labels AT1s, as judged by co-expression (using antibodies to GFP) with HOPX in nuclei. (B) Note that < 1% of SFTPC⁺ cells express a high *Ager* signal (arrow) at steady state (P56). (C) Tmx treated *Sftpc-CreER^{T2}*; *Rosa26-tdTomato*; *Ager-H2b:Venus* mice were analyzed 7 days post sham and PNX surgery. Arrows indicate lineage labeled (RFP⁺) AT2s that are SFTPC⁺ Ager⁺. The number of these double positive cells increases in the post-PNX lung (20%), compared to sham (2.5%) and steady state (< 1%). (D) Analysis of sections of AT2 cultures using antibodies for SFTPC, AGER, H2B:Venus (GFP) and HOPX. Nearly all cells are SFTPC⁺ AGER⁺ double positive at 2 and 7 days while the number is reduced at 14 days. At 14 day, *Ager*⁺ HOPX⁺ AT1s are found internal to the sphere while SFTPC⁺ AT2s are located towards the periphery. Scale bars 50 μ m.



Movie 1. 3D rotation of AT2-TASC

Long cellular extensions of a TASC (red) closely adjacent to an AT2 (green).

Table S1. Primer sequences

Primers	forward	reverse
qPCR		
Bmp2	5'-CAG AAG CCC AGT TGC TGC TC-3'	5'-AAC ACT AGA AGA CAG CGG GTC C-3'
Bmp4	5'-GGA ACA GGG CTT CCA CCG TA-3'	5'-ACT GCA GGG CTC ACA TCG AA-3'
Bmp5	5'-GGG TAT TGT GGG CTT CCT CT-3'	5'-TTT CCC GTC TCT CAT GGT TC-3'
Bmp6	5'-CAG AGT CGC AAC CGG TCC AC-3'	5'-TGC AAT GAT CCA GTC CTG CCA-3'
Bmp7	5'-CAA GAC GCC AAA GAA CCA AG-3'	5'-CAG CTC ATG TTT CTT GCA GG-3'
Bmpr2	5'-CCT TGA CCT GGA TAA CCT GAA G-3'	5'-TTA CAG CAA CTG GAC GCT C-3'
Bmpr1a	5'-CCT GAT TGA CCA GTC CCA AA-3'	5'-CTT TAC CAA CCT GCC GAA CC-3'
Bmpr1b	5'-ACT CTA CGG TAC TGC AGG GC-3'	5'-GCG CTT CGA TGG CTT AGC TT-3'
Fst	5'-CAA GGT TGG CAG AGG TCG CT-3'	5'-AGA AGC ACG CCA GAA GAG CA-3'
Fstl1	5'-AGC CAT CAA CAT CAC CAC TTA T-3'	5'-AGT TTC CAG TCA GCG TTC TC-3'
Gremlin	5'-AAG CGA GAT TGG TGC AAA AC-3'	5'-TGA AAG GAC CCT TCC TCC TT-3'
Gremlin2	5'-GGA TGT TCT GGA AGC TCT CG-3'	5'-GAT CTG GTG ATG CCA CCT CT-3'
Noggin	5'-ACG TCA AAA GTT ACC CGG CTT-3'	5'-CCA TGC GAA GGG TAC TGG GA-3'
Chordin	5'-CGA GGG GCT CAT ATG CTG CT-3'	5'-GGC AAT CTG TCA TAG CGG GC-3'
Acvr2a	5'-GCG TTC GCC GTC TTT CTT ATC-3'	5'-GTT GGT TCT GTC TCT TTC CCA AT-3'
Acvr2b	5'-GGC CAT GTA CCG TCT GGT-3'	5'-TGG CTG TTC GGT TTG AGC-3'
Acvr1(Alk2)	5'-CAT CAG GAA GTG GCT CCG GT-3'	5'-TCC CGA CAC ACT CCA ACA GG-3'
Bambi	5'-CTG TGA TAG CGG TTC CCA TT-3'	5'-TGG TGT CCG TGA AAG CTG TA-3'
Bmper	5'-GGT GAC TTG TAA GAG GGA GAA G-3'	5'-GTT TGC CAC TTG AAG GAA CTG-3'
Id1	5'-GGC GAG ATC AGT GCC TTG-3'	5'-AAG GGC TGG AGT CCA TCT G-3'
Id2	5'-ATG AAA GCC TTC AGT CCG GTG-3'	5'-AGC AGA CTC ATC GGG TCG T-3'
Smad6	5'-AAT TCT CAG ATG CCA GCA TG-3'	5'-AGG TAG GTC GTA GAA GAT GC-3'