

## Supplemental Information

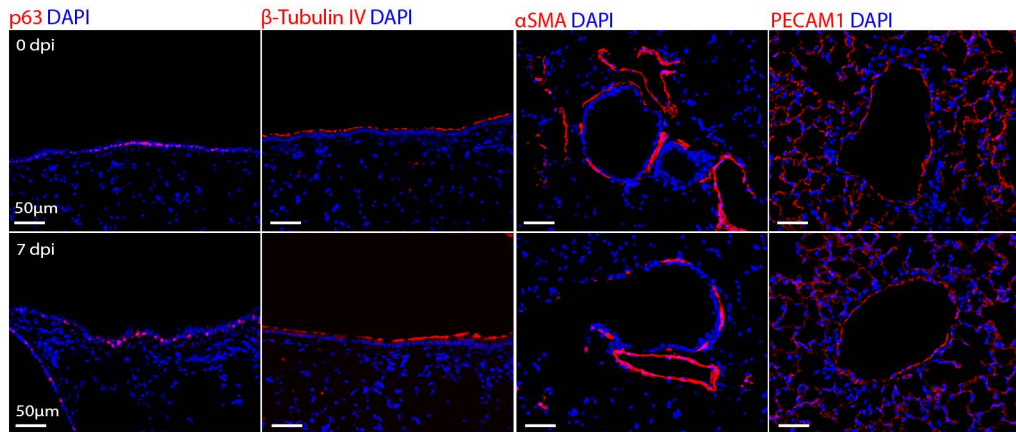
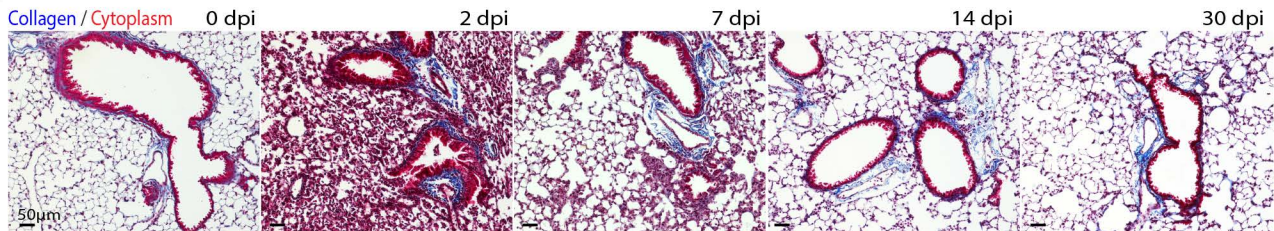
**Figure S1. Tissue damage and resolution in *Sp*-infected mouse lung.** (A) Histological analysis of lung sections at 7 dpi using indicated antibodies (red) with nuclear counterstain (DAPI, blue). P63 (basal cells),  $\beta$ -tubulin IV (ciliated cells),  $\alpha$ SMA (perivascular and peribronchiolar smooth muscle, and fibroblasts at the alveolar entrance ring), PECAM1 (vascular endothelial cells), respectively. (B) Masson's trichrome stained lung sections at 0, 2, 7, 14, 30 dpi. Scale bar, 50  $\mu$ m.

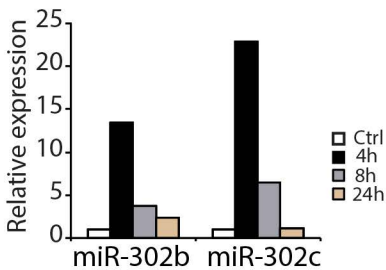
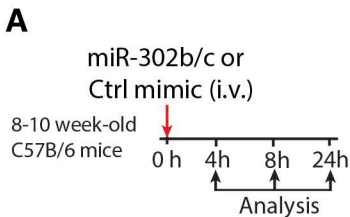
**Figure S2. Expression of miR-302b/c mimics in the lung and tissue histology after systemic treatment with mimics.** (A) Experimental design and qRT-PCR showing miR-302b/miR-302c levels in the lung at various time points after intravenous (i.v.) treatment of mimics. (B) Masson's trichrome staining showing fibrotic tissue formation and resolution from lungs with control mimics (Ctrl mimics)- or miR-302b/c mimics (miR-302b/c)-treated mice at indicated dpi (n=3 per group and time point). Scale bar, 50  $\mu$ m.

**Figure S3. Effects on cell apoptosis in *Sp*-infected lung with miR-302b/c mimics treatment.** (A) Histological analysis and (B) quantification of apoptotic cells measured by TUNEL staining (green) at indicated dpi. Quantification data are means  $\pm$  SEM (n=10 per group and time point). (C) Representative flow cytometry plots assessing cleaved Caspase-3 expressions from Epcam<sup>+</sup> cells in lung with control mimics- (black line) or miR-302b/c- treated (red line) mice at 7 dpi. (D) Group data quantify number of Epcam<sup>+</sup>Caspase-3<sup>+</sup> cells (n=3 per group and time point). (E) qRT-PCR analysis of *Dapk1*, *Stk17b*, *Bax* at the indicated dpi from isolated lung epithelial cells. Data are means  $\pm$  SEM (n=10 per group) \**P* < 0.05 versus control mimic treated lungs (Student's *t* test). Scale bar, 50  $\mu$ m.

**Figure S4. Cell proliferation in *Sp*-infected lung with miR-302b/c mimics treatment.**

Histological analysis and quantification of lung sections showing proliferating (EdU, green) (**A**) basal cells (anti-p63, red), (**B**) ciliated cells (anti- $\beta$ -Tubulin IV, red), (**C** and **D**) club cells (anti-CC10, red), (**E** and **F**) smooth muscle cells (anti- $\alpha$ SMA, red), (**G** and **H**) macrophages (anti-F4/80, red), (**I** and **J**) endothelial cells (anti-PECAM1, red). White arrowhead points to nucleus of cell type specific proliferating cells. Scale bar, 50  $\mu$ m. Data are means  $\pm$  SEM (**D**, **F**, **H**, **J**: n=3 per group). \* $P < 0.05$  versus control mimic- treated lungs using Student's  $t$  test. **A**, **B**, **C**, **E**, **G**, **I**: left, un-infected normal lung; middle, control mimics-treated lung at 7 dpi; right, miR-302b/c-treated lung at 7 dpi.

**A****B**

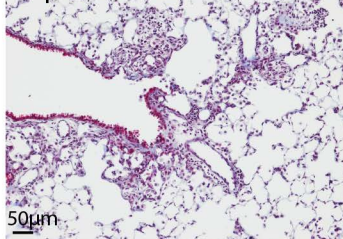


**B**

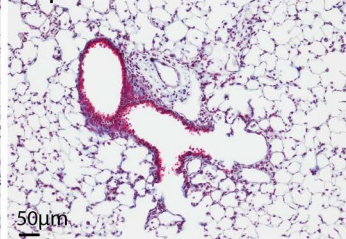
Ctrl mimics

miR-302b/c

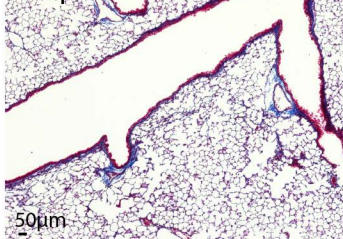
7 dpi



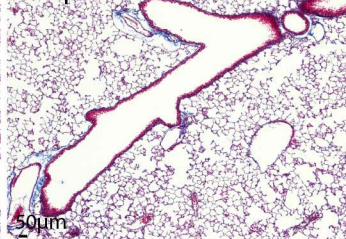
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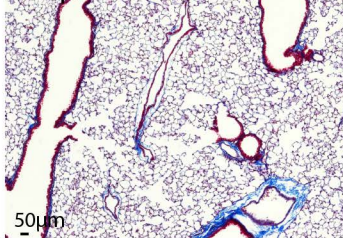
14 dpi



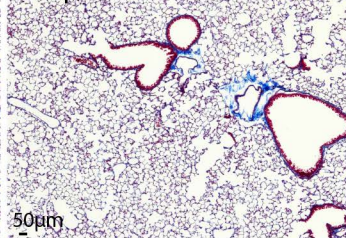
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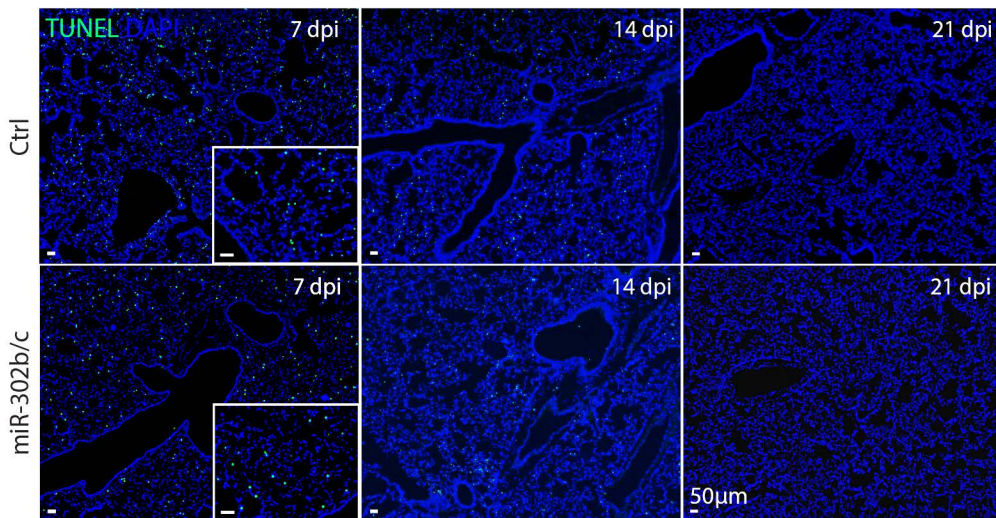
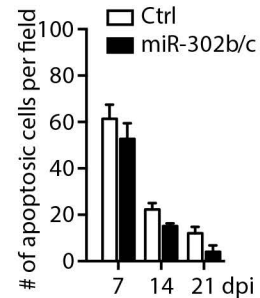
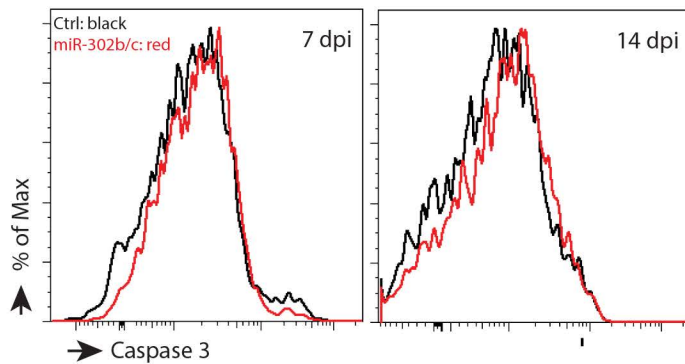
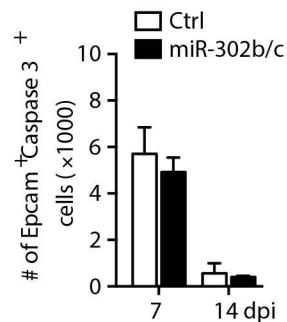
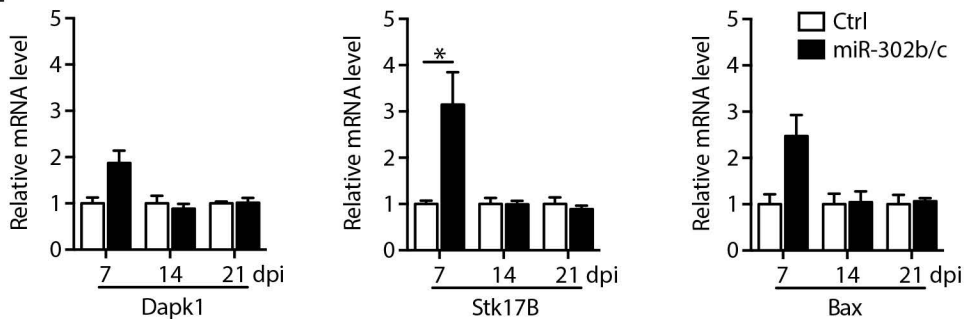
21 dpi



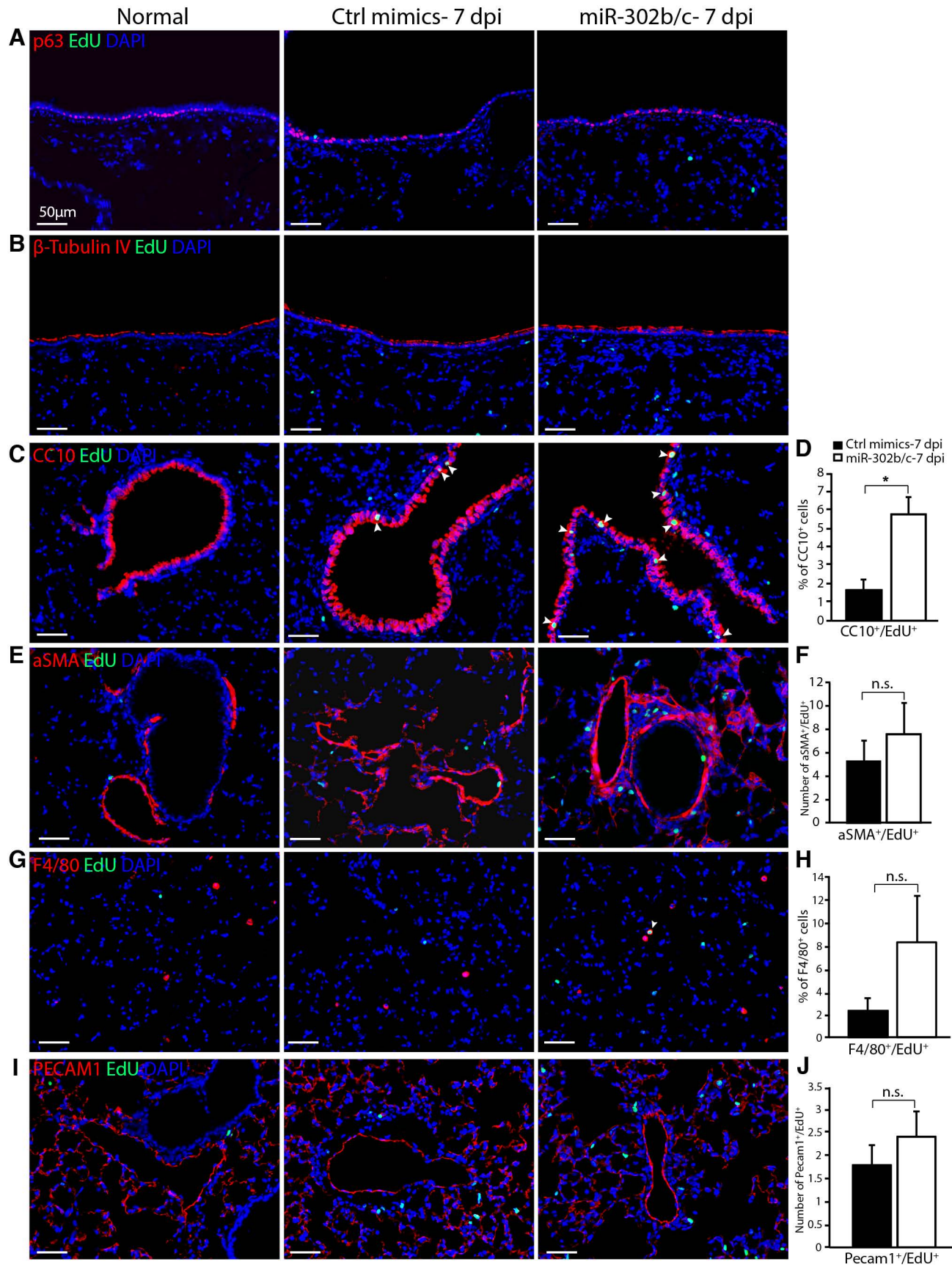
21 dpi



Collagen/ Cytoplasm

**A****B****C****D****E**





**Table S1. qRT-PCR primer sequences used in this study.**

<b>Gene name</b>	<b>Forward</b>	<b>Reverse</b>
<b>Pdpn (T1a)</b>	GGTGCCCCCAGGTATAGAAG	ACGCTCTCTCTGCGTTGGTA
<b>Sftpc (SPC)</b>	ACCCTGTGTGGAGAGCTACCA	TTTGCGGAGGGTCTTTCT
<b>Scgb1a1 (CC10)</b>	ATACCCTCCCACAAGAGACCAGGATA	ACACAGGGCAGTGACAAGGCTTTA
<b>Dapk1</b>	GCTGAACATGGAGCTGACTT	CAAGGAGGGTCTTGATGACTTC
<b>Stk17B</b>	AATCTGCATGAGGTCTACGAA A	TCGGCTAACTCAGGTAAACAC
<b>Bax</b>	GTG GTT GCC CTC TTC TAC TTT	CAG CCC ATG ATG GTT CTG AT
<b>Cdkn1a (p21)</b>	TTGTACAAGGAGCCAGGCCAAGAT	ACTAAGTGCTTTGACACCCACGGT
<b>Ccnd1 (CyclinD1)</b>	TTCCTCTCCAAAATGCCAGA	AGGGTGGGTGGAAATGAAC
<b>Ccnd2 (CyclinD2)</b>	GAACCTGGCCGCAGTCACCC	CGACGGCGGGTACATGGCAA
<b>Ctgf</b>	AACCGCAAGATCGGAGTG	TGCTTTGGAAGGACTCACC
<b>Cyr61</b>	TGAGTTAATCGCAATTGGAA	GTGGTCTGAACGATGCATTT
<b>RacGap1</b>	CAGATCCAGTGACAATGTTCCA	TCCACCATCATGAACTGATTCC
<b>Nusap1</b>	GAGGAGGAAGAAGCACAAGAC	CTACTATCAGTTCCTTTCATCTCCAA
<b>Myh10</b>	GGAATTCGAGAGGCAGAACAA	AAGGCTCGCTTGGAATTTCTC
<b>Cks2</b>	CAGAGTCTAGGATGGGTTTCATTAC	TCCCAGCTGCACTTCATTT
<b>Brca2</b>	ATTTGAACGGCCCAGCAT	GGCTGGTAA ACCTGGAGTAAAG
<b>Bcl2</b>	GTGGATGACTGAGTACCTGAAC	GAGACAGCCAGGAGAAATCAA
<b>GAPDH</b>	TGCACCACCAACTGCTTAGC	GGCATGGACTGTGGTCATGAG