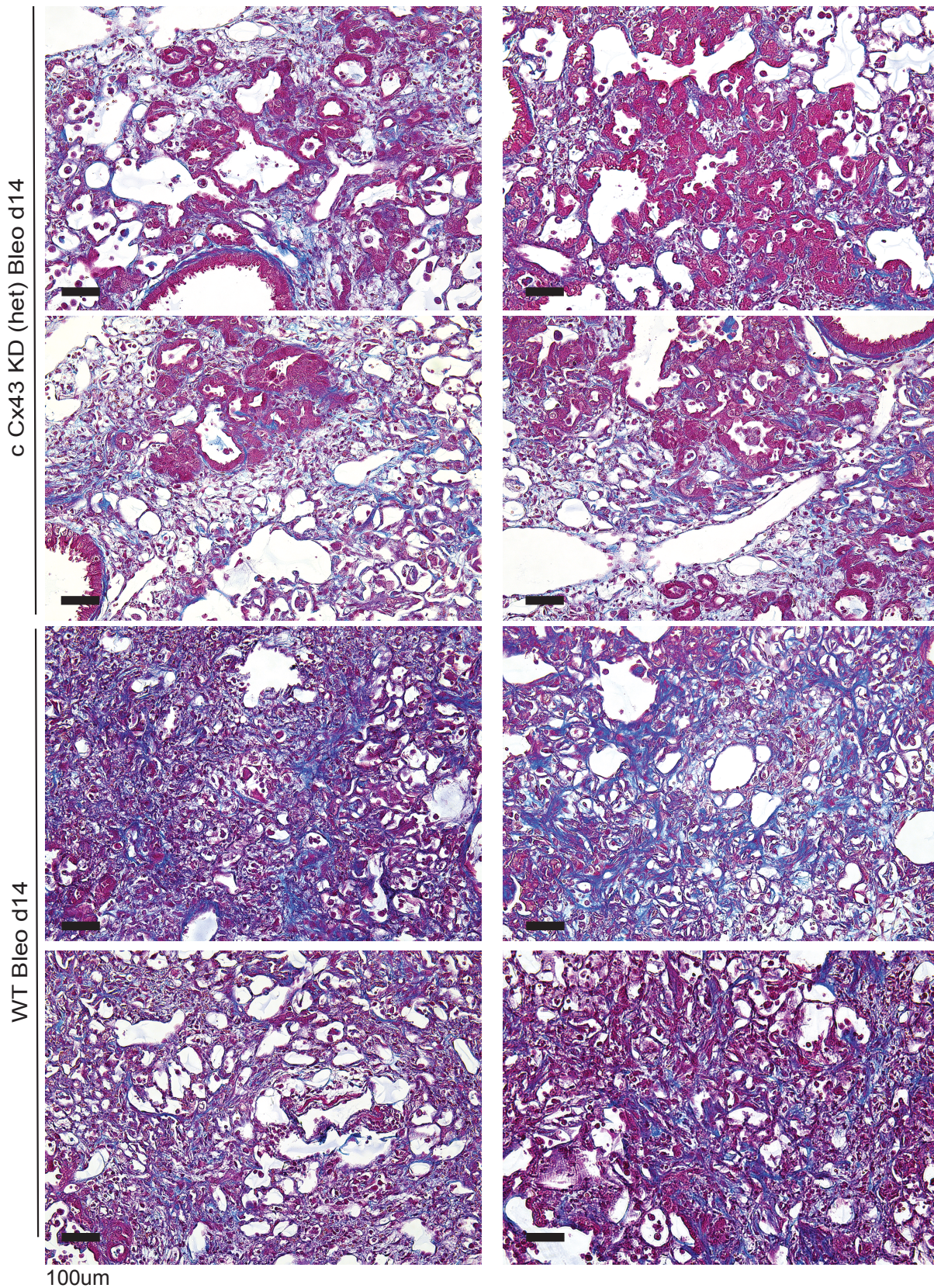


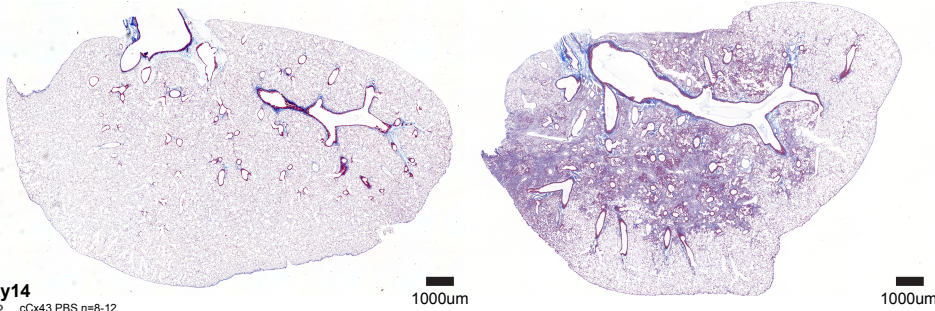
SUPPLEMENTAL FIGURE 1. Positive controls for Cx43 immunostaining in adult mouse lung. Immunostaining to detect Cx43 (red) in 3µm paraffin sectioned adult mouse lung tissue. **A.** Illustrated the endothelial layer of an arteriole as well as macrophages (Mac). **B,C.** Illustrated Cx43 expression in the alveolar-capillary unit. **B1,2; C1,2.** enlarged from selected areas. Scale = 20µm.



SUPPLEMENTAL FIGURE 2. Representative images of ectopic basal cells in mouse lungs with heterozygous knockout of Cx43 in ABCG2 EPC. Representative enlarged trichrome stained mouse lung tissue sections from cCx43KO or WT mice. n=4,4. Scale =100µm.

A. cCx43 KO(het) PBS

cCx43 KO(het) Bleo



Day14

- cCx43 PBS n=8-12
- cCx43 Bleo n=15-18
- WT PBS n=6-17
- WT Bleo n=4-22

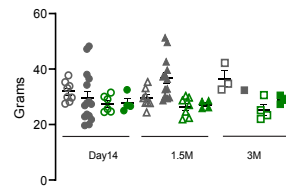
1.5 Months

- △ cCx43 PBS n=8
- ▲ cCx43 Bleo n=10-14
- △ WT PBS n=7-12
- ▲ WT Bleo n=4-9

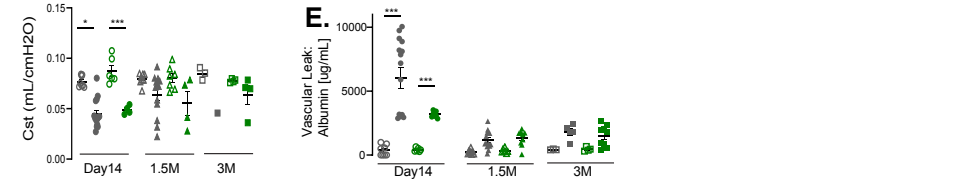
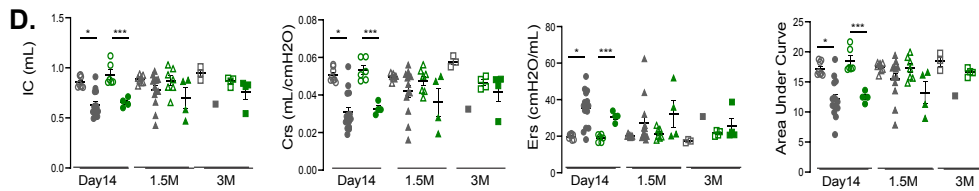
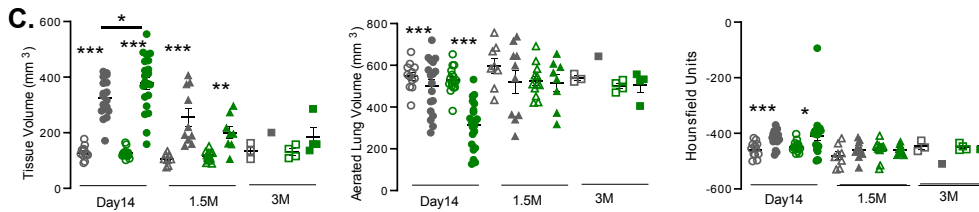
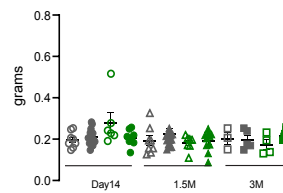
3 Months

- cCx43 PBS n=3
- cCx43 Bleo n=1-5
- WT PBS n=4
- WT Bleo n=4-9

B. Harvest Weights

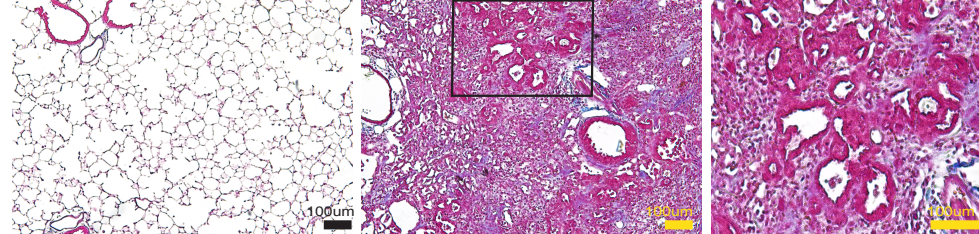


C. RV/LV+S

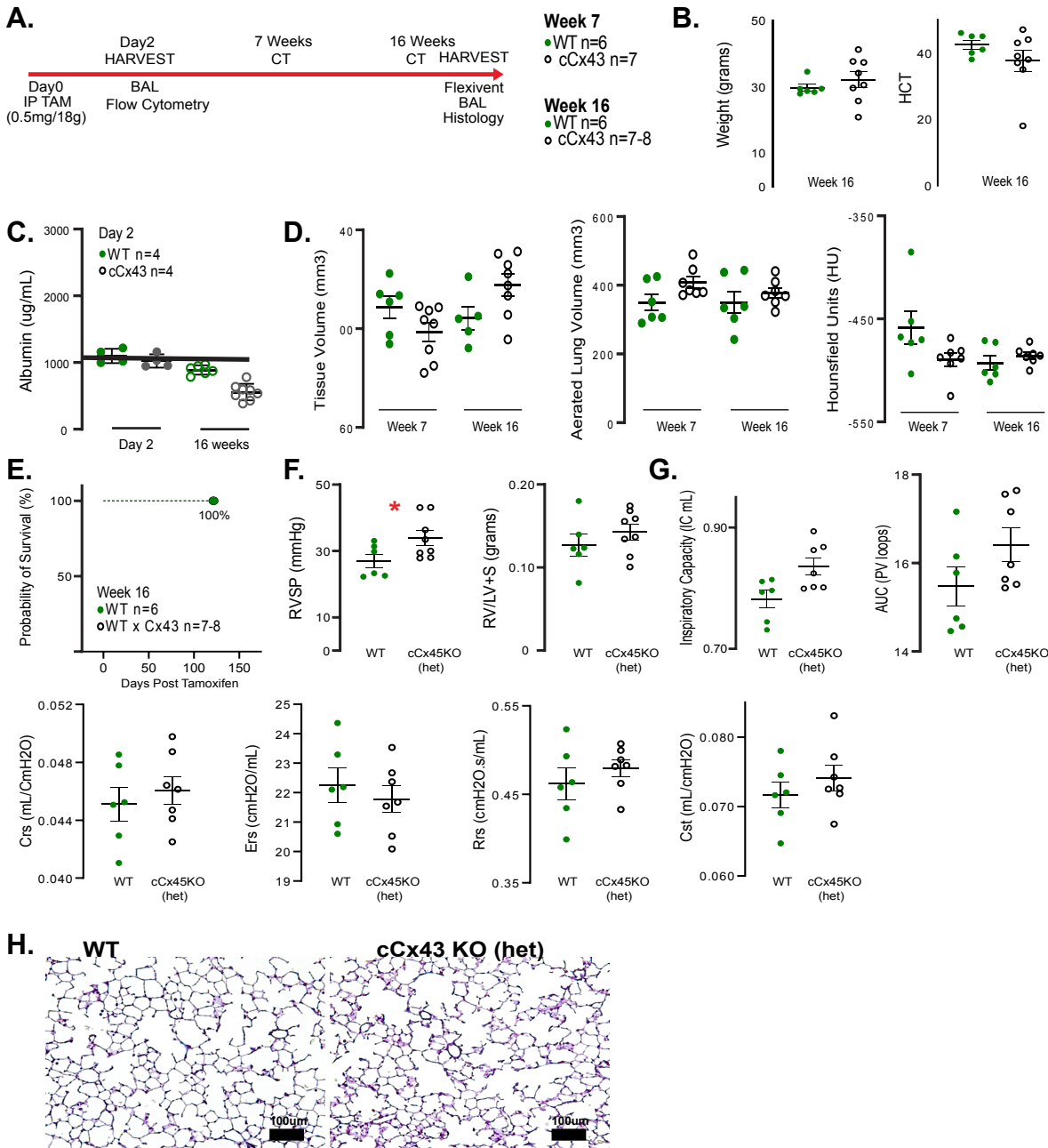


F. DTA PBS Vehicle D14

G. DTA Bleomycin D14



SUPPLEMENTAL FIGURE 3. The adaptive epithelial response to fibrotic injury resolves over time similar to WT. Mice were induced with a single low dose tamoxifen, 2 weeks later vehicle or bleomycin was instilled o.p. and mice harvested on day-14, 1 month and 3 month time points for analysis. **A.** Representative stitched images of cCx43KO mouse lung tissue sections. Scale =1000µm. n per group and key. **B.** Mouse weight and Fulton's index at time of harvest. **C.** MicroCT endpoints. **D.** Airway physiological measurements taken using a Flexivent. **E.** Vascular leak quantitated by albumin present in the BAL. Nonparametric one way Anova was used to define significance, *p<0.05, ** p<0.01, *** p<0.001. **F&G.** ABCG2CreERT2x fISTOP DTA mice were mice harvested on day-14 post PBS vehicle or bleomycin injury and trichrome staining performed. Scale =100µm.



SUPPLEMENTAL FIGURE 4. Heterozygous knockout of Cx43 in ABCG2 EPC does not significantly change the baseline phenotype and function of mouse lungs while ABCG2-eGFP EPC are decreased. **A.** Schematic of the experimental design, n per group and key. **B.** Mouse weight and hematocrit (HCT) at time of harvest. **C.** Vascular leak quantitated by albumin present in the BAL. **D.** MicroCT endpoints. **E.** Mean survival of mice at harvest. **F.** Right ventricular systolic pressure (RVSP) was increased in the cCx43KO mice in the absence of right ventricular hypertrophy (RV/LV+S). **G.** Airway physiological measurements taken using a Flexivent. Nonparametric one way Anova or unpaired Welch's t-test was used to define significance, *p<0.05, ** p<0.01, *** p<0.001. **H.** H&E stained paraffin tissue sections from agarose inflated mouse lungs at harvest. Scale = 100µm.

Supplemental Table 1. Reagent List

Antibody	Vendor	Catalog #	Dilution
B-Actin	Cell Signaling Technology	4970	1:1000
Goat Anti-Rabbit IgG HRP-Conjugate, Species Adsorbed	Millipore Sigma	AP187p	1:10,000
Horse Anti-Mouse IgG HRP-Linked	Cell Signaling Technology	7076	1:1000
Connexin 43	Cell Signaling Technology	3512S	1:1000 (WB) 1:50 (IF)
SOX2	R&D Systems	AF2018	1:200
Rabbit Anti-Goat IgG HRP Conjugated	Millipore Sigma	AP106P	1:10,000
Human <i>GJA1</i>	Thermo Fisher Scientific	4331182 Hs00748445_s1	
Human GAPDH	Thermo Fisher Scientific	4331182 Hs02786624_g1	
GFP	Antibodies Inc.	GFP-1010	1:500 (IF)
<i>Lycopersicon esculentum</i> tomato Lectin (LEL)-Dylight649	Vector Laboratories Inc.	DL-1178-1	100ug/mouse
Taqman RNA-to-Ct 1-Step Kit	Thermo Fisher Scientific	4392938	
RNeasy Mini Kit	Qiagen	74104	
TaqMan Fast Advanced Cells-To-CT Kit	Invitrogen	A35374	
RIPA Buffer	Cell Signaling Technology	9806S	
Halt protease and phosphatase inhibitors	Thermo Fisher Scientific	78444	
Pierce BCA Protein Assay Kit	Thermo Fisher Scientific	23227	
1.5mm thick NuPAGE 4-12% Bis-Tris gels	Thermo Fisher Scientific	NP0335BOX	
Clarity Western ECL Substrate	BioRad	170-5060	
Laemmli Sample Buffer	BioRad	1610747	