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Supplementary Information for

ABL kinase inhibition promotes lung regeneration through expansion of an SCGB1A1+ SPC+ cell population following bacterial pneumonia

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Materials and Methods

Bacteria. *S. aureus* (*Ssp*. *aureus*, No. 25923; American Type Culture Collection) was grown as previously described (1). Dilutions of 5 X 10^8 CFU were used for mouse experiments, and dilutions of 1 X 10^8 CFU were used for cell culture experiments. *S. pneumoniae* (serotype 19, No. 49619; American Type Culture Collection) was grown as previously described (2). Dilutions of 6 X 10^5 CFU were used for mouse experiments.

Cell Culture. Primary human bronchial epithelial cells were isolated as previously described (3) and passage 1 cells were derived from human lungs unsuitable for transplantation from non-smoker organ donors without pre-existing lung disease under protocol #03-1396 approved by the University of North Carolina at Chapel Hill Biomedical Institutional Review Board. Informed consent was obtained from authorized representatives of all organ donors. 30,000 cells were plated into each well of 6.5mm polyester inserts containing 0.4µm pores (Sigma-CLS3470) coated with Type IV human placenta collagen (Sigma-C7521). 100µl of ALI medium was added to the insert and 600µl of ALI medium was added to the well at the time of plating. At Day 3, ALI medium from the insert was removed while that in the well was changed daily for 28 days. At Day 28, the inserts containing the cells were removed from their wells, washed with PBS, and incubated at 37ºC for 30 minutes with 1 X 10^8 CFU *S. aureus*. Cells were then washed three times with PBS and returned to wells containing 600µl of ALI medium to regrow. Cells were harvested at multiple time points up to five days after injury for protein or RNA extraction. All cultures were maintained at 37ºC in humidified air containing 5% CO_2.

Immunoblotting. Cells were lysed in radioimmunoprecipitation assay (RIPA) buffer with protease and phosphatase inhibitors, and cell debris was removed by microcentrifugation. Protein was quantified, and equal amounts of protein was separated by SDS-polyacrylamide gel electrophoresis (BioRad-1610183) and transferred onto 0.2µm pore nitrocellulose membranes. Membranes were probed with antibodies to ABL1 (BD-554148), ABL2 (Santa Cruz-sc134268), and α-tubulin (Millipore-05829) overnight at 4ºC, thoroughly washed, and then incubated with secondary HRP-tagged antibodies for one hour at room temperature. Blots were incubated using chemiluminescent reagents (ThermoFisher-34580) and developed using x-ray film (GE-45001).

Real-time RT-qPCR. RNA was isolated from cells using an RNA isolation kit (GE-25050071), and complementary DNA was synthesized using oligo(dT) primers and Moloney murine leukemia virus reverse transcriptase (Invitrogen). Real-time PCR was performed using iQ SYBR Green Supermix (BioRad-1708882). The primers used were as follows: human *ABL1*, GGCTGTGAGTACCTTGCTGC (forward) and GGCGCTCATCTTCATTCAGGC (reverse); human *ABL2*, AGTTTAGCACCAGGGTTCATCAG (forward) and CTTCCTATCCCTGGTGAAGCAT (reverse); human *GAPDH*, GGCTCTCCAGAACATCATCCCTGC (forward) and GGGTGTCGCTGTTGAAGTCAGAGG (reverse); mouse *Gapdh* AGGTCGGTGTGAACGGATTTG (forward) and

TGTAGACCATGTAGTTGAGGTCA (reverse); mouse *Sftpc* AACGCCTTCTCATCGTGGT (forward) and TAGATATAGTAGAGTGGTAGCT (reverse); mouse *ETV5* CCCGGATGCACTCTTCTCTATG (forward) and TCGGATTCTGCCTTCAGGAA (reverse); mouse *Lamp3* TGGAGCATATTTGACCATCTCA (forward) and CAAAGGCCTGAAGGTGGATA (reverse); mouse *Sftpa* CTGTCCCAAGGAATCCAGAG (forward) and CCGTCTGAGTAGCGGAAGTC (reverse). Analysis was performed using a BioRad CFX384 real-time machine and CFX Manager software. PCR assays were performed in duplicate. The expression of each gene was normalized to that of *GAPDH* (human) or *Gapdh* (mouse).

Mice. *CC10 (Scgb1a1)-CreERT*; *Rosa26R-CAG-farnesylated GFP (Rosa26-fGFP)* and *SPC (Sftpc)-CreERT2; Rosa26-tdTomato* mice were kindly provided by Dr. Mark Onaitis and generated by Dr. Brigid Hogan at Duke University and have been previously described (4, 5). These mice were crossed with *Abl1*$^{flox/flox}$ mice (6) into a C57BL/6 genetic background. Sox2^{tmHoch}/J mice (referred to as SOX2-eGFP mice in the text) were purchased from the Jackson Laboratory. *Gt(Rosa)26Sor*$^{tm9(EGFP/Rpl10z)Amc}$*/J* (referred to as *L10-eGFP* in the text) mice were purchased from the Jackson Laboratory and were crossed to *CC10-CreERT; Abl1*$^{flox/flox}$ mice into a C57BL/6 genetic background for the TRAP experiments. To induce expression of Cre-recombinase for both TRAP experiments and lineage tracing experiments, 8- to 20-week-old male and female mice were injected intraperitoneally four times every other day with 0.25mg/g body weight Tamoxifen (Sigma-T5648) in corn oil (Spectrum-CO136). Exposure to *S. aureus* was initiated 15 days after the last dose of Tamoxifen. Alternatively, mice were inoculated with purified Adenovirus5-CC10-Cre virus obtained from the University of Iowa Viral Vector Core Facility and generated by Dr. Anton Berns (Netherlands Cancer Institute). 10µl of stock virus solution was mixed in 30µl of Minimum Essential Medium and delivered intranasally twice, three days apart, three weeks prior to induction of *S. aureus* pneumonia. Mice were anesthetized using 0.3mg xylazine and 2.5mg/kg ketamine intraperitoneally prior to intranasal inoculation with a 50µl dilution of 5 X 10^8 *S. aureus*. The mice were monitored daily for weight loss and signs of respiratory distress and euthanized in an isofluorane chamber at days 0, 1, 2, and 3 after inoculation. All experiments were performed under the Duke University IACUC approved protocols: A098-16-04 and A130-16-06. Male and female mice at different ages (8 to 20 weeks old) were evaluated for differential response to drug (Abl kinase inhibitors and tamoxifen) and/or injury, and no significant effects of age and gender were observed.

Inhibitors. GNF5 (N-(2-Hydroxyethyl)-3-(6-(4-(trifluoromethoxy)phenylamino) pyrimidin-4-yl)benzamide) was synthesized at the Duke University's Small Molecule Synthesis Facility, and validated by LC-MS and 1H-NMR/FT-IR spectra and with cell-based assays that confirm potencies and cell signaling inhibitory activities. For *in vivo* experiments, GNF5 was prepared in a suspension with 0.5% methylcellulose and 0.5% Tween-80 at a concentration of 10mg/mL, and mice were treated with either 20mg/kg, 40mg/kg, or 100mg/kg *b.i.d.* via oral gavage. Nilotinib was synthesized at the Duke University's Small Molecule Synthesis Facility, and validated by LC-MS and 1H-NMR/FT-IR spectra. For *in vivo* experiments, nilotinib was prepared in a suspension with

0.5% methylcellulose and 0.5% Tween-80 at a concentration of 10mg/mL, and mice were treated with 100mg/kg once daily via oral gavage.

Bronchoalveolar lavage preparation and assays. Bronchoalveolar lavage (BAL) fluid was collected immediately after euthanasia three days after exposure to *S. aureus* as previously described (1). Bilateral BAL was performed using two 1ml aliquots of sterile PBS with approximately 75-80% retrieval per mouse. 50µl cellular BAL fluid was stained with trypan blue, and the total cell count (not including red blood cells) was manually obtained using a Neubauer hemocytometer. The remaining BAL fluid was centrifuged to remove cellular debris, and the total protein concentration was quantified. CFU loads were measured by plating 50µL of isolated BAL fluid or homogenized lung sample into 10-cm cell culture plates with trypticase soy agar (VWR-90005-052) overnight. Biomarker analysis was performed as directed using the Essential Th1/Th2 Cytokine 6-Plex Mouse ProcartaPlex Kit (Thermo Fisher EPX060-20831-901).

Preparation of lung tissue sections. Mice were euthanized at days 0, 1, 3, 7, and 30 following exposure to *S. aureus*. The aorta was dissected to reduce intravascular blood volume, and the lungs were exposed through an incision across the diaphragm and the bottom half of the sternum. The trachea was exposed and cannulated with a sterile 22-gauge Abbocath-T catheter to inflation fix the mouse lungs. Fixation with 4% paraformaldehyde solution in PBS was performed for 15 minutes at room temperature by suspending fixation solution in an apparatus 40cm above the mice. The entire mediastinum including the trachea, lungs, and heart were then carefully excised and immediately placed in 4% paraformaldehyde for 4 hours on a rotator at 4^{o}C. The left lungs were paraffin embedded at the Duke University Immunohistopathology Core Facility and cut to 5µm thick sections. The right lungs were sucrose protected, frozen in Optimal Cutting Temperature (OCT) compound at -80^{o}C, and cut into 5µm thick sections.

Hematoxylin and eosin staining and quantification. Tissue sections were deparaffinized, rehydrated, and incubated with hematoxylin staining reagent for 10 minutes followed by treatment of acid alcohol, Scott's water, and an eosin secondary counter-stain for 1 minute each. Slides were cleared by xylene, mounted with mounting medium, and analyzed on a Zeiss Axio Imager upright microscope using a 10x objective. Entire left lung coronal sections at approximately the same depth were obtained for each mouse under each experimental condition. Lung sections were imaged and stitched together using the Zeiss Zen software to produce whole left lung images. A baseline measure of cell density was determined using the Histogram function of FIJI software in the group of uninfected mice. Percent infiltration for each mouse exposed to *S. aureus* was measured as the percent decrease in free air space (measured as the decrease in number of pixels with lighter shading using the Histogram function). A one-way ANOVA followed by a post-hoc Tukey test was performed to evaluate the differences in alveolar space infiltration between each group. No image adjustments were applied to H&E images prior to quantification.

Immunofluorescence. Left lung tissue sections were deparaffinized, rehydrated, and either heat inactivated (BioCare Medical Decloaking Chamber) or treated with 0.05% trypsin for five minutes. Right lung tissue sections were thawed at room temperature for 15 minutes. Both deparaffinized and frozen sections were then washed in PBS and blocked in 3% goat serum in PBS with 0.05% Tween-20 for one hour. Sections were incubated with primary antibodies in blocking solution overnight at 4ºC in a humidified chamber at concentrations indicated below. Sections were then washed with PBS followed by incubation with the appropriate secondary antibody in blocking solution for one hour at room temperature. Sections were then washed with PBS, incubated with the nuclear stain, Hoechst33342, and washed again with PBS before mounting using aqueous mounting media (Dako-S3025).

Quantification of Immunofluorescence Experiments. All cell counts were evaluated for entire left lung sections using a 10x objective on the Zeiss AxioImager microscope with Zen software at the Duke Light Microscope Core Facility. Cell counts were validated, and representative high-resolution images were taken using 40x and 100x objectives on the Leica SP8 confocal microscope. Stitched images were quantified using the Analyze Particle feature in Fiji software to determine total cell counts across the entire lung for each mouse (>100,000 cells counted per section). Alveolar size (area) was used as a quantitative measure of alveolar damage, and particle analysis was performed on RAGE-stained sections to determine average alveolar size over the entire lung. No image adjustments were applied to 10x objective stitched images prior to quantification. For the representative high-resolution images shown, linear scale adjustments were applied to GFP, CC10, Ki67, SPC, and RAGE antibody stains.

Antibodies. Antibodies for immunofluorescence experiments included: Anti-SPC (Millipore-AB3786) at a 1:1000 dilution, anti-GFP (Aves Labs-GFP-1020) at a 1:1000 dilution, anti-CCSP (SCGB1A1; CC10) (Millipore-07623) at a 1:500 dilution, anti-RAGE (R&D-MAB1179), and anti-Ki67 (Abcam-ab16667) at a 1:500 dilution. Antibodies for Western blot analysis included: ABL1 (BD-554148), ABL2 (Santa Cruz-sc134268), and α-tubulin (Millipore-05829). Secondary antibodies with fluorescent labels were purchased from ThermoFisher (anti-mouse and anti-rabbit Alexa Fluors 488, 561, and 647) and used at 1:1000 dilutions. Secondary antibodies with HRP tags were purchased from Jackson Laboratory and used at 1:2000 dilutions.

FACS Sorting / Analysis. Mice were euthanized 24 and 72 hours after *S. aureus* infection, and lungs were immediately harvested, cut into small pieces with scissors, and digested for 30 minutes at 37ºC using 3mL per lung of DMEM-F12 medium containing the enzymes: Type I collagenase (450U/mL), elastase (4U/mL), dispase (5U/mL), DNase I (0.33U/mL). Enzymes were neutralized in DMEM-F12 medium with 10% fetal bovine serum. Cells were then centrifuged, resuspended, and filtered through 70µm and 30µm cell strainers. Red blood cells were lysed using a lysis buffer (ThermoFisher-00433357). Cells were resuspended in DMEM-F12 medium in 2% bovine serum albumin and treated with propidium iodide prior to FACS sorting using a BD-DiVa system at the Duke Flow Cytometry Core Facility. RNA was collected from isolated GFP-labeled cells using an RNA isolation kit (GE-25050071), and samples were prepared for real-time RT-qPCR as

described above. For FACS analysis, following resuspension in DMEM-F12 in 2% BSA, cells were incubated for 5 minutes with an FcγRIII block (BD-53141), washed with DMEM-F12 in 2% BSA, and incubated with the appropriate antibodies: FITC anti-mouse CD45 (BioLegend-147709), PE anti-mouse Ly6G (BioLegend12-5931-81), and FITC anti-mouse F4/80 (BioLegend-53-4801-82), FITC CD3 (BioLegend-555274). Cells were washed twice with DMEM-F12 in 2% BSA and analyzed using the BD Fortessa X-20 at the Duke Flow Cytometry core facility. Data analysis was performed on FlowJo V10. Edu incorporation was assessed as directed using a Click-iT Edu Pacific Blue Flow Cytometry Assay Kit (Thermo Fisher C10418).

TRAP Experiments. Homozygous *L10a-eGFP* mice were crossed with *CC10-CreERT; Abl1*$^{fl/fl}$ mice. Only mice heterozygous for *L10a-eGFP* were used for experiments. Pulldown of RNA from GFP-labeled ribosomes was performed as previously described (7). Briefly, anti-eGFP antibody (19C8 clone from Antibody & Bioresource Core Facility, MSKCC) was coupled to beads using the Invitrogen Dynameads Antibody Coupling Kit using 10µg purified antibody/mg beads for three days at 4ºC on a rotator. Beads were washed three times in 0.15M KCl and resuspended in 0.15M KCl with 30mM DHPC. Lung tissue was harvested from mice three days after infection with *S. aureus* and dissociated for five seconds at the lowest setting of a tissue homogenizer (OmniKit Homogenizing Kit) in homogenization buffer (20mM HEPES-JOH, 150mM KCl, 4mM $MgCl_2$, protease inhibitors, 0.5mM DTT, RNase inhibitor, 100µg/ml cycloheximide). Lysate was centrifuged, and the supernatant was incubated in 1% Ipegal CA-630 and 30mM DHPC on ice for five minutes. The mixture was centrifuged and incubated with the prepared beads for one hour at 4ºC on a rotator. Beads were washed five times with 0.35M KCl and eluted with water. RNA isolation and real-time RT-qPCR was performed as described above.

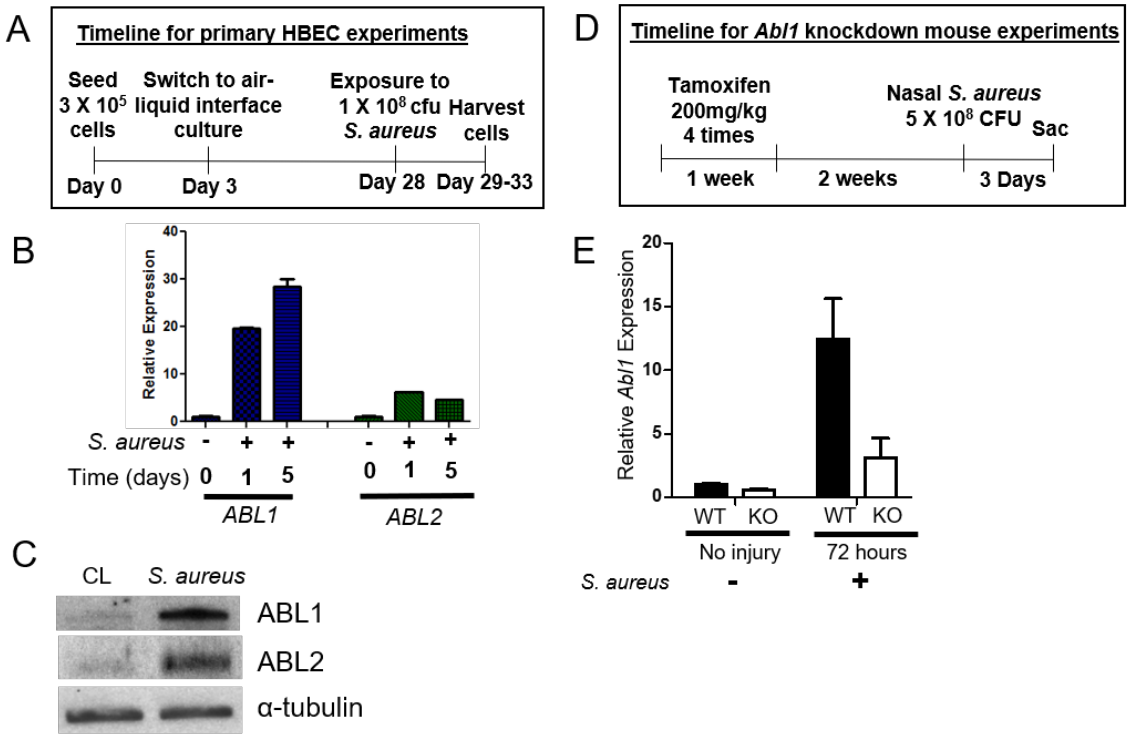

Fig. S1. Abl kinases are upregulated in primary human lung bronchial epithelial cells (HBECs) and GFP-labeled cells from *CC10 (Scgb1a1)-CreERT; Rosa26-fGFP; Abl1 WT* mice following exposure to *S. aureus.* **(A)** Timeline of air-liquid interface cultures: Primary HBECs are seeded on polyester inserts in a transwell chamber. Media from the top chamber is removed once the cells are confluent to promote differentiation of basal cells to luminal cells. Cells are exposed to *S. aureus* at day 28 once they have fully differentiated into a pseudostratified layer of ciliated, secretory, and basal cells and are then harvested one, two, and five days after injury. **(B)** mRNA expression of ABL kinases, predominantly *ABL1*, increases by 20 to 30-fold following exposure to *S. aureus*. n = 3 patients, each run in triplicate. **(C)** Immunoblotting with ABL1 and ABL2 specific antibodies shows an increase in ABL1 and ABL2 protein expression 24 hours after exposure to *S. aureus*. **(D)** Timeline of mouse experiment: Two weeks prior to nasal insufflation of 5 X 10^8 CFU *S. aureus*, mice were treated with tamoxifen to induce excision of $Abl1^{fl/fl}$ in *CC10 (Scgb1a1)-CreERT* mice. **(E)** Analysis of isolated GFP-labeled cells from mice showed that *Abl1* mRNA expression increases by >10-fold in GFP-labeled cells 72 hours after exposure to *S. aureus* and is decreased in $Abl1^{fl/fl}$ mice compared to wild-type control mice (n=4-8 animals per group; each sample run in triplicate). Graphs represent means with S.E.M.

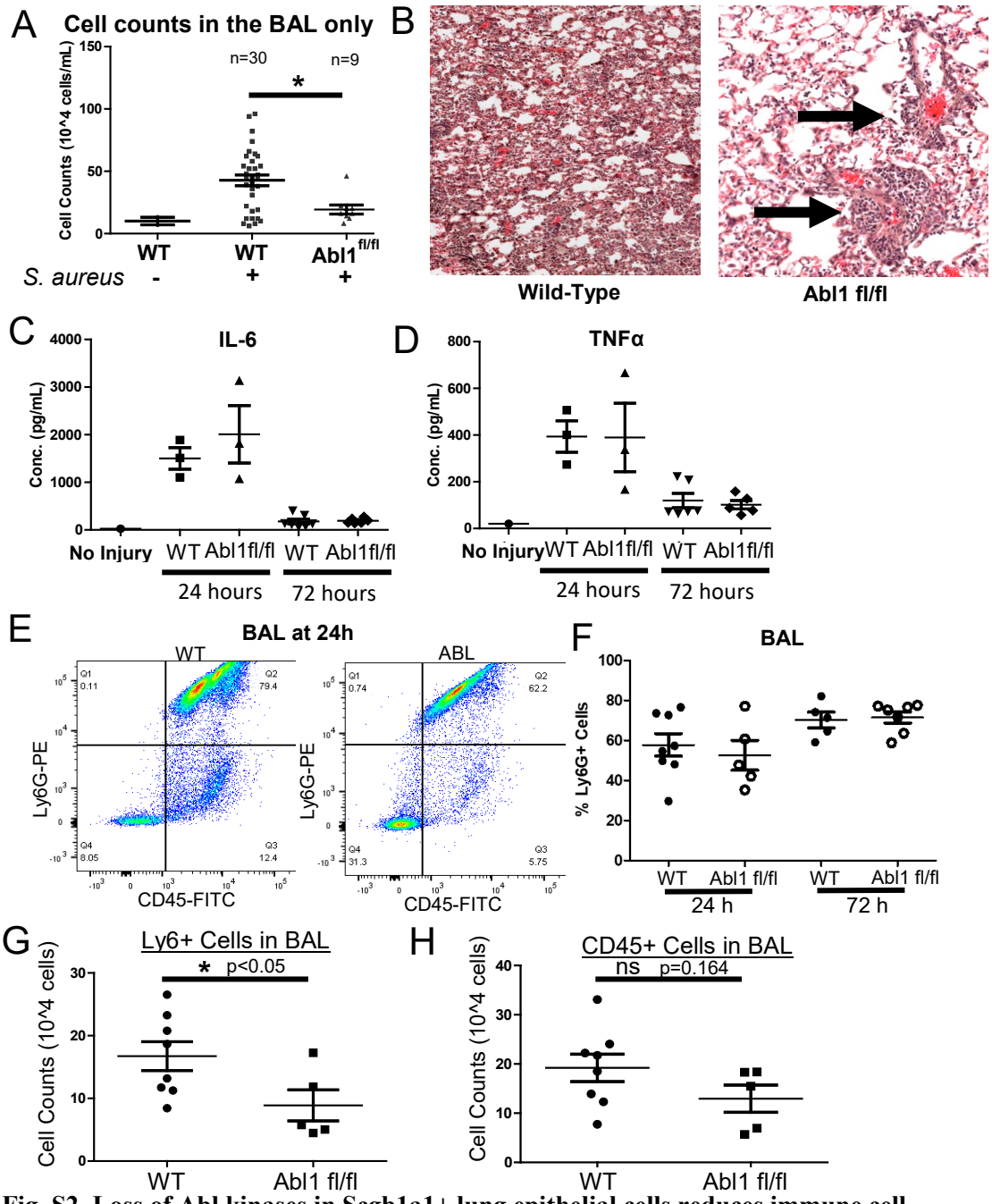

Fig. S2. Loss of Abl kinases in Scgb1a1+ lung epithelial cells reduces immune cell infiltration in the alveoli without affecting immune cell influx in the lung parenchyma following *S. aureus* induced lung injury. (A) 72 hours after exposure to *S. aureus*, *CC10 (Scgb1a1)-CreER; Abl1$^{fl/fl}$* mice demonstrate a dramatic reduction in leukocyte counts in the BAL fluid compared to wild-type mice. **(B)** H&E sections showing neutrophilic influx in the lungs of both wild-type and knockout mice (arrows) three days after exposure to *S. aureus,* but infiltration of immune cells into the alveolar space was reduced in knockout mice compared to wild-type mice. **(C-D)** BAL fluid in wild-type and control mice 24 and 72 hours after injury showed no significant change in cytokine production levels. **(E-H)** FACS analysis of cells from BAL fluid 24 hours after injury showed decreases in neutrophil (G) and total immune cell (H) populations without changing the proportion of neutrophil cells in the BAL fluid in knockout mice compared to wild type mice.

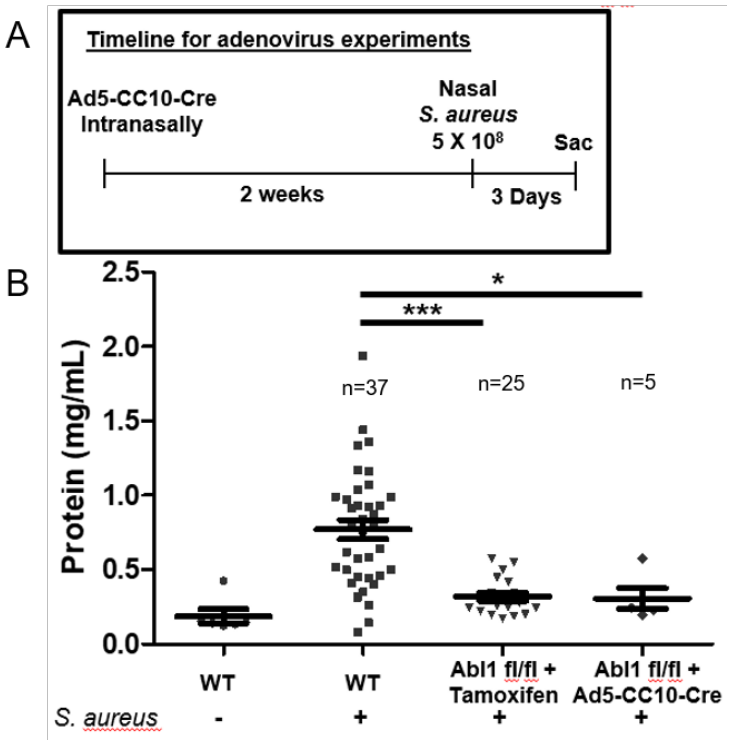

Fig. S3. Tamoxifen and adenoviral mediated excision of *Abl1*$^{fl/fl}$ mice results in reduced lung injury compared to wild-type mice 72 hours following nasal insufflation of *S. aureus*. (A) Timeline of experimental protocol: Two weeks prior to nasal insufflation of 5 X 10^8 PFU *S. aureus*, *Abl1*$^{fl/fl}$ mice were administered intranasal *Adenovirus5-CC10-Cre* virus to induce excision of *Abl1* in CC10 (Scgb1a1)-expressing cells. **(B)** Bronchioalveolar lavage showing decreased protein accumulation in the airspace in Abl1 knockout mice (induced by either tamoxifen delivery in *CC10-CreERT2* mice or *Ad5-CC10-Cre* virus) compared to wild-type mice.

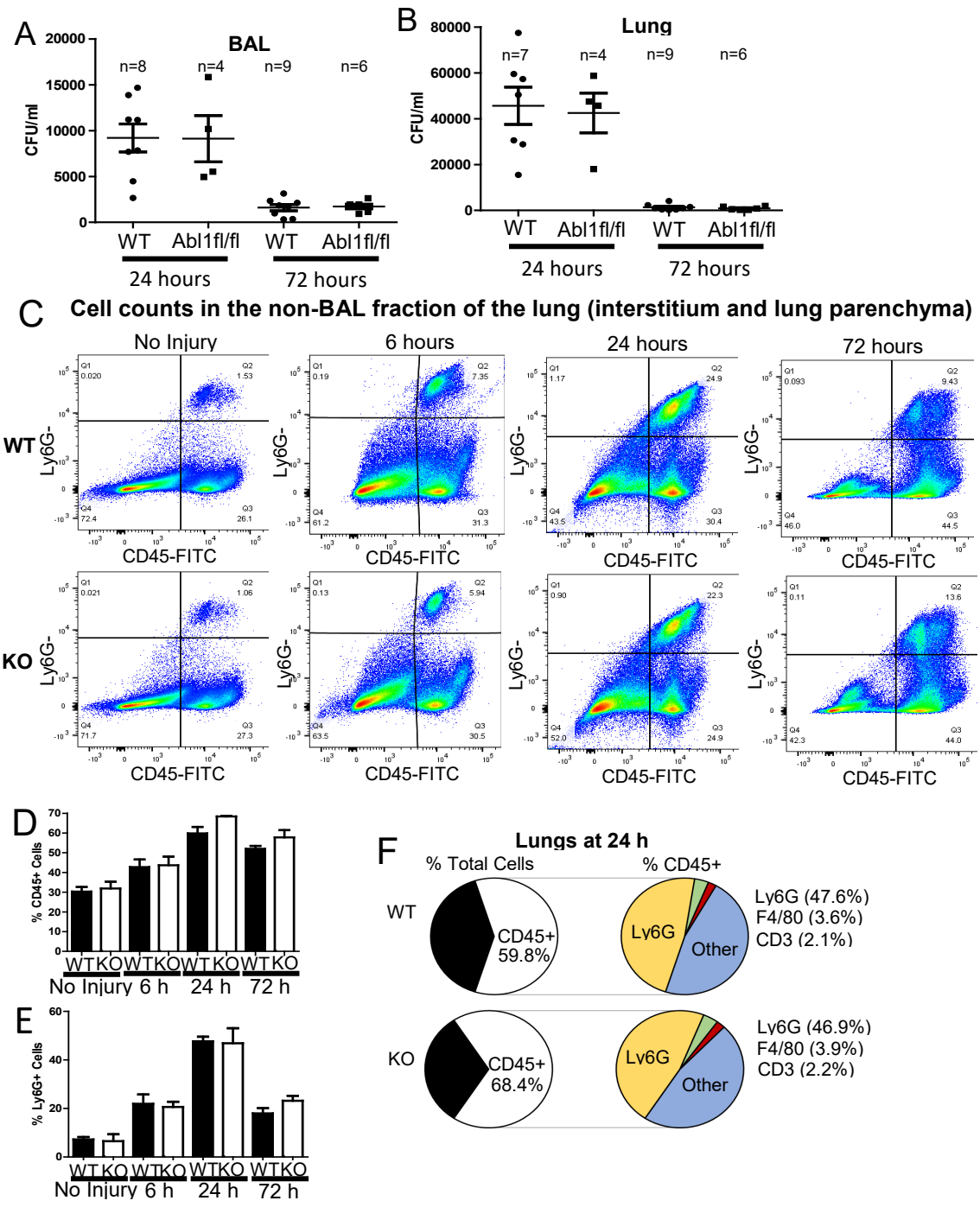

Figure S4. Loss of *Abl1* in Scgb1a1+ lung epithelial cells does not confer differential susceptibility to *S. aureus* infection or immune cell response in the lung parenchyma compared to wild-type mice. (A-B) BAL fluid (A) and non-BAL whole lung cell isolation (B) showed no significant difference in *S. aureus* CFU counts 24 h and 72 h after injury in wild-type versus knockout mice. **(C-F)** FACS analysis (C) and quantification (D-E) of the non-BAL lung cell populations (interstitial and parenchymal cells) without injury and 6 h, 24 h, and 72 h after injury showed no significant changes in neutrophils (Ly6G+), macrophages (F4/80+), and T-cells (CD3+) in wild-type versus knockout mice as shown in the pie-chart (F).

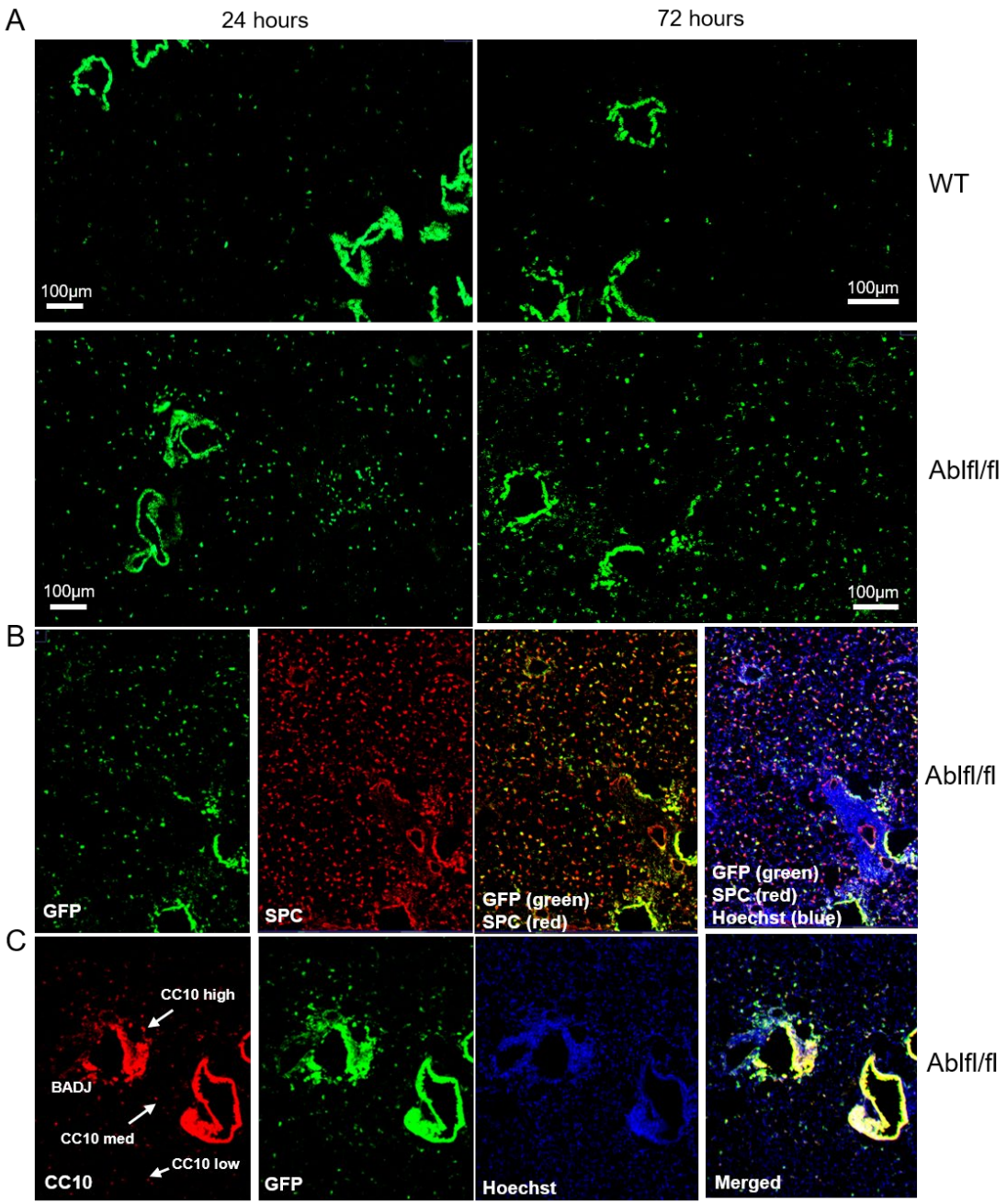

Fig S5. Loss of *Abl1* promotes expansion of Scgb1a1+ SPC+ cell population in mouse lungs following injury. (A) Whole left lungs from wild-type and $Abl1^{fl/fl}$ mice were sectioned and stained with a GFP antibody 24 or 72 hours following nasal insufflation of *S. aureus*. Zoomed in subsets provided for visualization of GFP+ (*Scgb1a1* driver) cells in the alveolar space. **(B)** Co-staining with SPC and GFP antibodies shows a dramatic expansion of GFP+ (*Scgb1a1* driver) SPC+ cells throughout the alveolar space following injury. **(C)** Staining with an antibody for CC10 (Scgb1a1) shows high expression of CC10 in cells in close proximity to the BADJ with progressively lower expression further away from the BADJ.

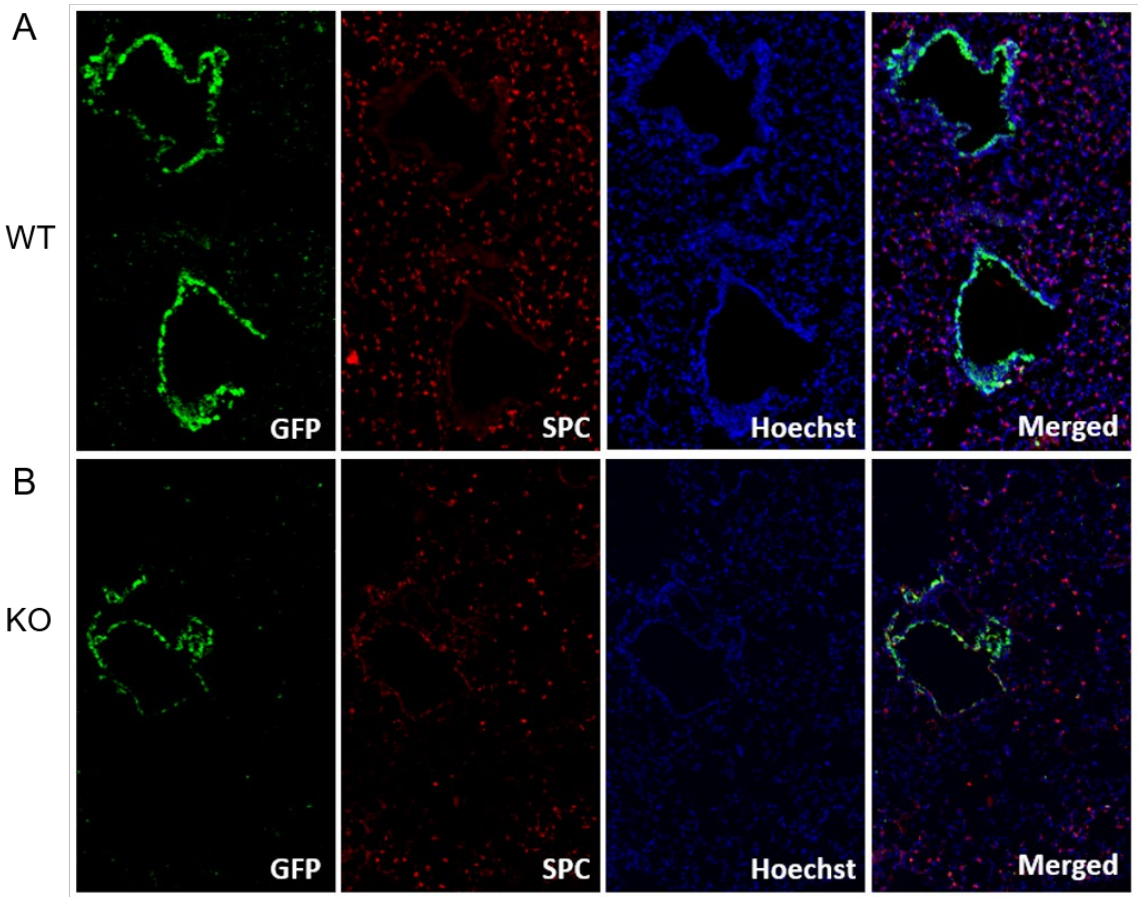

Fig S6. No significant change in double-positive GFP+ (*Scgb1a1* driver) SPC+ cell populations in the alveolar space in uninfected wild-type and *Abl1* knockout mice. *CC10-CreERT; Rosa26-fGFP; Abl1*^{wt} **(A)** and *Abl1*$^{fl/fl}$ **(B)** mice were given four doses of tamoxifen. After four months, lungs were harvested, and lung sections were probed with antibodies for GFP and SPC. There was no significant difference in the observed double-positive GFP+ SPC+ cell population in the alveolar space in these uninfected mice. Scale bar = 60µm.

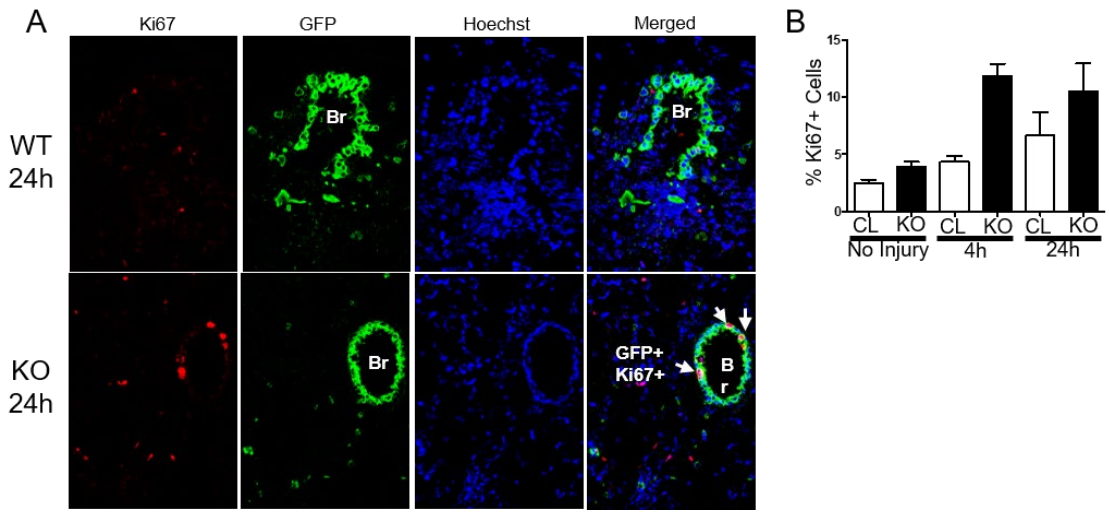

Fig S7. Loss of *Abl1* promotes proliferation of GFP+ (*Scgb1a1* driver) cells in bronchioles 4 hours and 24 hours following injury. (A) Immunofluorescence staining revealed an increased expression of the proliferation marker, Ki67, 24 hours following injury in the bronchioles (Br) of $Abl1^{fl/fl}$ mice compared to $Abl1^{wt}$ mice. **(B)** Quantification of the fraction of GFP+ cells that were also Ki67+ in $Abl1^{wt}$ and $Abl1^{fl/fl}$ mice without injury and 4 hours and 24 hours after delivery of *S. aureus* showing an increase in GFP+ Ki67+ cells in knockout mice compared to wild-type mice (n=5-8 mice per group).

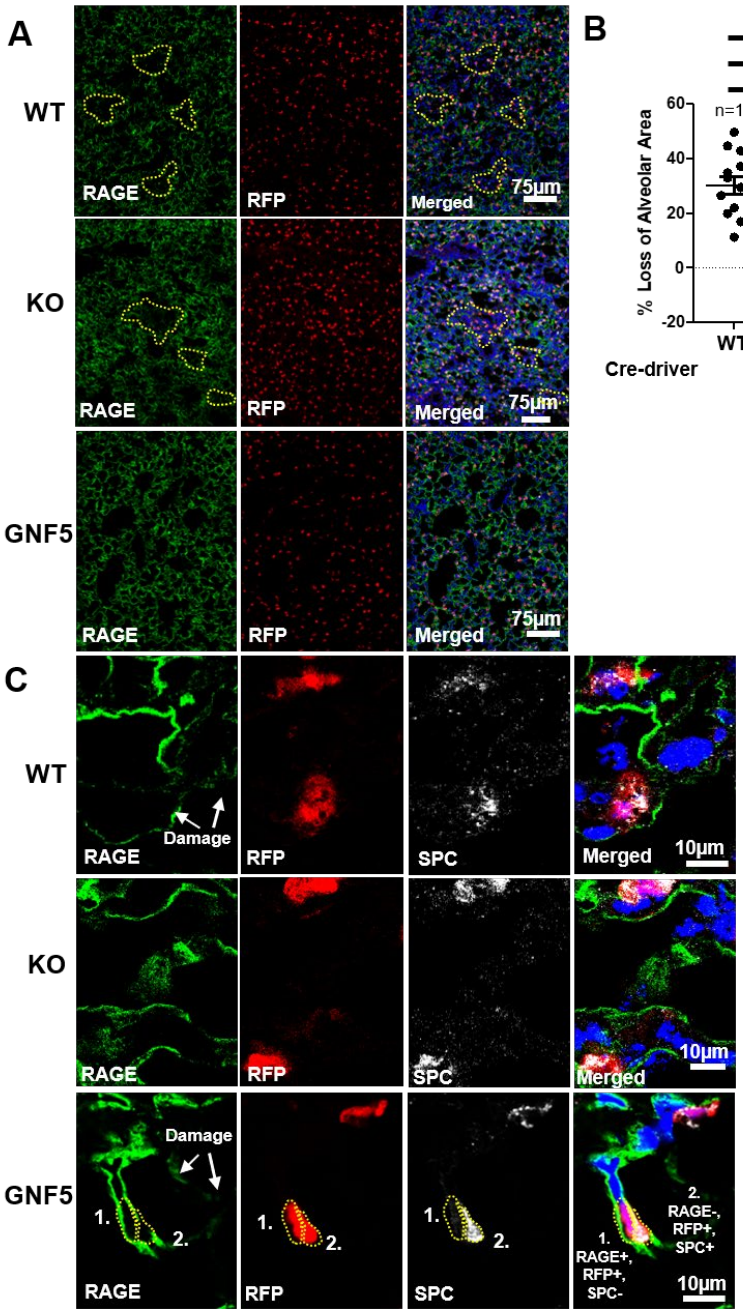

Fig S8. Pharmacological (global) inhibition of Abl kinases but not conditional loss of *Abl1* in SPC+ cells leads to increased regeneration of Type I alveolar epithelial cells after injury. (A) 3 days after exposure to *S. aureus*, increased damage (dotted lines) to the alveolar epithelium was observed in *SPC-CreERT2; Rosa26-tdTomato; Abl*^{wt} and *Abl1*$^{fl/fl}$ mice compared to *SPC-CreERT2; Rosa26-tdTomato* mice treated with the Abl kinase inhibitor, GNF5. **(B)** Quantification showing reduced damage (as measured by loss of alveolar area/volume compared to uninfected mice) in GNF5-treated mice compared to *Abl1*^{wt} or *Abl1*$^{fl/fl}$ mice 3 days after injury. **(C)** In untreated, wild-type and knockout mice, no RAGE+ cells were observed that were also tdTomato+ (stained by RFP). By contrast, RAGE+, tdTomato+, SPC- cells (Cell 1) derived from RAGE-, tdTomato+, SPC+ cells (Cell 2) were observed at areas of damage in *SPC-CreERT2; Rosa26-tdTomato* mice treated with GNF5 three days following exposure to *S. aureus.*

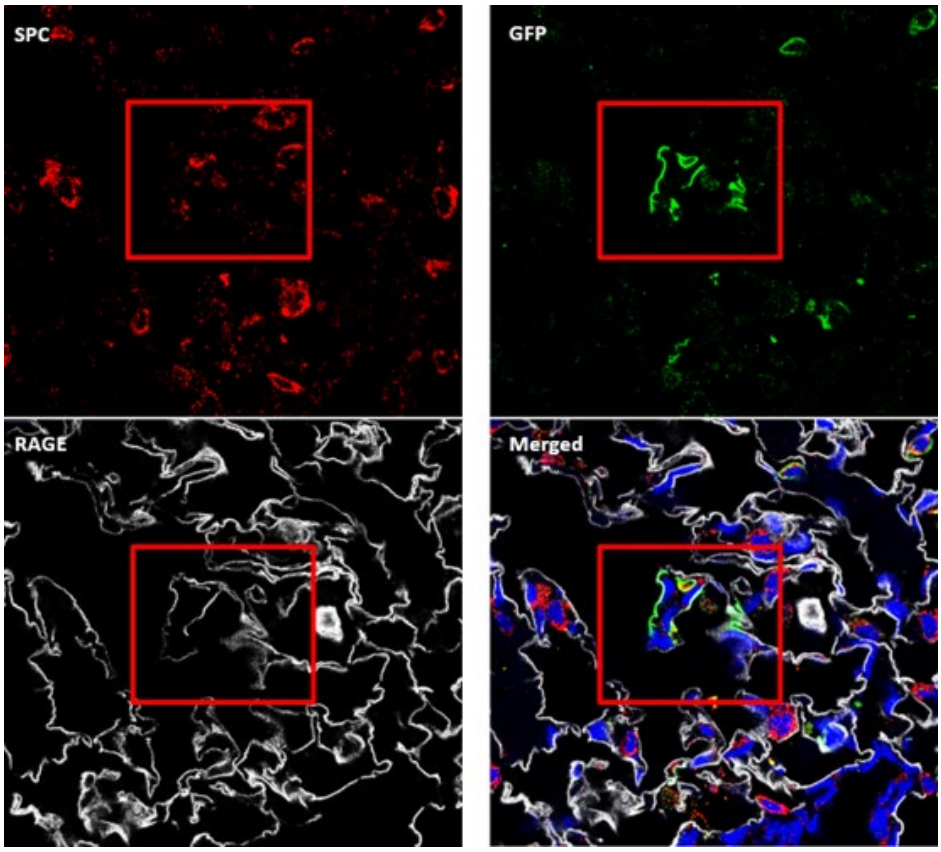

Fig S9. Lineage tracing of Scgb1a1-expressing cells in *CC10 (Scgb1a1)-CreERT2* mice using the *Rosa26-fGFP* reporter reveals the presence of small clusters of GFP+ RAGE+ cells at Day 30 following infection in wild-type mice. *CC10 (Scgb1a1)-CreERT2; ROSA26-fGFP* mice treated with tamoxifen two weeks prior to inducing lung injury were evaluated 30 days after injury for GFP+ populations in the lung. Staining for antibodies to GFP (*Scgb1a1* driver), SPC (Type II AEC marker), and RAGE (Type I AEC marker) revealed the presence of small clusters of GFP+ RAGE+ cells that were not observed at earlier time points.

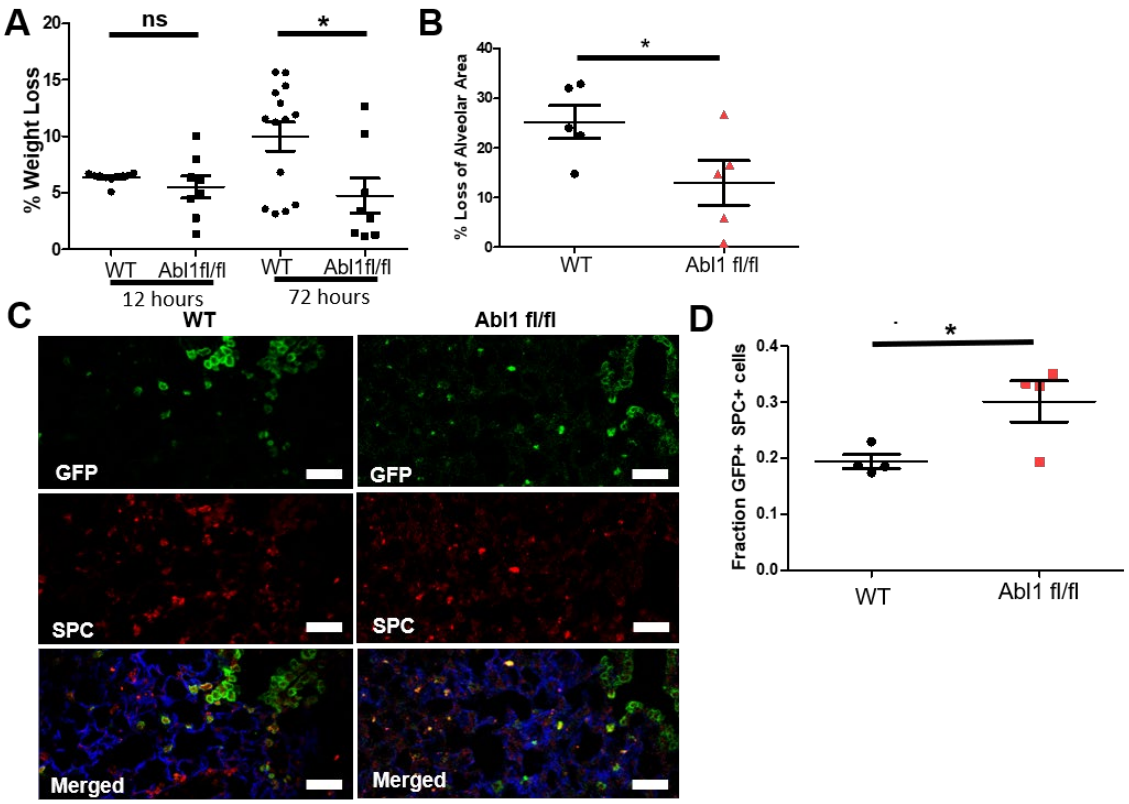

Fig S10. Conditional knockout of *Abl1* in *CC10 (Scgb1a1)-CreERT; Rosa26-fGFP* mice cells leads to expansion of double positive GFP+ SPC+ cells following exposure to *S. pneumoniae*. *CC10 (Scgb1a1)-CreERT2; Rosa26-fGFP* mice treated with tamoxifen two weeks prior to inducing lung injury. Mice were inoculated with $6X10^5$ CFU *Streptococcus pneumoniae* and evaluated at multiple time points after injury. **(A)** Knockout mice show reduced weight loss three days after injury compared to wild-type mice (n=8-14 mice per group). **(B)** Quantification of RAGE staining showed reduced alveolar damage (as measured by alveolar area/volume) in knockout mice compared to wild-type mice three days after infection with *S. pneumoniae* (n=5 mice per group). **(C-D)** A significant expansion of double positive GFP+ SPC+ cells was observed within 6 hours after injury in knockout mice compared to wild-type mice (n=4 mice per group). Scale bar = 50µm.

Movie S1. 30-second video corresponding to Fig. 1B shows that loss of *Abl1* in Scgb1a1+ cells leads to faster recovery compared to wild-type mice 24 hours after exposure to *S. aureus*.

Movie S2. 30-second video corresponding to Fig. 4B shows that treatment with the Abl kinase inhibitor, GNF5, promotes faster recovery of mice compared to vehicle control-treated mice 24 hours after exposure to *S. aureus*.

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