SUPPLEMENTARY METHODS

Human Samples

Deidentified frozen lung tissue from the patients diagnosed with IPF on the basis of appropriate clinical-radiographic features and usual interstitial pneumonia on histopathologic examination or normal tissues were obtained from the National Institutes of Health Lung Tissue Research Consortium. Demographics of the study population are provided in Table S4. The Institutional Review Board at the University of Vermont certified that the study did not constitute human subjects research.

The Lung Genomics Research Consortium (LGRC) cohort was used to determine gene expression. Data from individuals with IPF and controls were used for this analysis. The gene expression data are available from the GEO database (http://www.ncbi.nlm.nih.gov/geo/) under the accession GSE47460. R software (2.12.2) was used for data analysis. Gene expression in lung tissue was available for 160 individuals with IPF and 132 controls from the LGRC cohort; demographic and physiological characteristics are presented in Supplementary Table S5. Lung function data (%DLCO) were available for 145 individuals with IPF and 92 controls from LGRC cohort.

Analysis of bulk RNA Seq gene expression data (GSE150910) was done in R software using the package “limma” (1). The FVC and %DLCO correlations with the gene expression were calculated using Pearson correlation. The significance of association was calculated using Fisher's asymptotic test. All the plots (figures S1B-D; S2D-L; S5D-F) were generated using the ggplot2 library in R.

Inducible club cell-specific *Pdia3* ablation

Age-matched male and female mice were used. Doxycycline-inducible-club cell (*Scgb1a1*) specific *Pdia3* knockout mice, referred to as ΔEpi-*Pdia3* (genotype *Scgb1a1-rtTA/TetOP-Cre/Pdia3*$^{loxp/loxp}$) were generated by breeding *Scgb1a1-rtTA*, *TetOP-Cre* mice with mice carrying the *Pdia3*$^{loxp/loxp}$ alleles (2, 3). Littermates containing either *Scgb1a1-rtTA/TetOP-Cre* or *Scgb1a1-rtTA/Pdia3*$^{loxp/loxp}$ and fed doxycycline-containing food (6 g/kg; Purina Diet Tech, St Louis, Mo) were used as control mice (*Ctr* mice). All mice were in C57BL6/NJ background. Mice were maintained on doxycycline-containing food from day 14 post BLM instillation until completion of the experiment as reported earlier (2).

Administration of LOC14

BLM instilled C57BL/6NJ male mice were treated therapeutically by oropharyngeal route at three different concentrations of LOC14 (Tocris, Cat. No. 5606; 0.015mg/kg, 0.15mg/kg and 1.5mg/kg weight of mice) from day 14 onward for five times at alternate day. On day 24, mice were harvested, and BALF and lungs were collected for analysis.

Blocking SPP1

To examine the role of Osteopontin in bleomycin-induced lung fibrosis, bleomycin challenged mice were further treated with anti-Osteopontin antibody (R&D systems, AF808; 3μg and 30μg) or isotype-specific IgG (R&D systems, AB-108-C; 3μg and 30μg) by intraperitoneal route using the same regimen as LOC14 treatment, i.e., bleomycin instillation at day zero followed by five times treatment from day 14 at alternate day

followed by harvest at day 24. After the experiments, BALF and lungs were collected for analysis.

Immunoprecipitation

Lung tissues were lysed in buffer containing 20mM Tris·HCl (pH 7.5), 150mM NaCl, 0.5% Nonidet P-40, 10% glycerol, and 1% protease inhibitor cocktail (Sigma-Aldrich, P8340) (v/v), 1% phosphatase inhibitor cocktails 1 and 2 (Sigma-Aldrich, P5726, P0044) (v/v). Insoluble proteins were pelleted via high centrifugation. PDIA3 was immunoprecipitated using anti-PDIA3 antibody (Enzo LifeSciences, ADI-SPA-585-F). Lung lysates from (PBS (n=3), BLM_14d (n=3), BLM_24d (n=3) and the IgG control BLM24d (n=1)) are mixed with PDIA3 antibody or IgG isotype control. PDIA3-bound proteins are immunoprecipitated using recombinant G agarose beads (Invitrogen,15920010). Samples were then suspended in loading buffer with dithiothrietol (DTT) and resolved by SDS-PAGE.

Western blot and densitometry analysis.

Right lung lobes were flash-frozen, pulverized and lysed in buffer containing 20mM Tris·HCl (pH 7.5), 150mM NaCl, 0.5% Nonidet P-40, 10% glycerol, and 1% protease inhibitor cocktail (Sigma-Aldrich, P8340) (v/v), 1% phosphatase inhibitor cocktails 1 and 2 (Sigma-Aldrich, P5726, P0044) (v/v). Insoluble proteins were pelleted via high centrifugation. Following protein quantitation of the supernatant using DC Protein Assay (Bio-Rad, 5000116) (4), samples were resuspended in loading buffer with dithiothrietol and resolved by SDS-PAGE and electrophoretically blotted onto Immun-Blot PVDF

membrane, and membranes were probed using a standard immunoblotting protocol. Western blots were performed using antibodies (Abs) directed against PDIA3 (LSBio; LS-B9768), SCGB1A1 (Santa Cruz Biotechnology; sc-390313), β actin (Sigma; A5441), GAPDH (BioLegend; 919501) and Osteopontin (R&D systems; AF808). The quantification of protein expression was performed by densitometry using ImageJ software (NIH, https://imagej.nih.gov/ij/). Details of the antibodies used for western blots can be found in table S6.

Measurement of lung hydroxyproline.

Lung collagen in mice were quantified by measurements of hydroxyproline levels in the upper right lobe. The upper right lobe was used to sample lung collagen levels throughout this study. Lobe was homogenized with a handheld homogenizer followed by hydrolysis in an equal volume of 6 N HCl for 18 h at 110°C. After hydrolysis lung samples were neutralized with NaOH. Following neutralization hydroxyproline assay was performed with the samples as previously described (5, 6).

RNA extraction and qRT-PCR.

Total RNA was extracted from lungs using Qiazol Lysis Reagent (Qiagen) and purified using the RNeasy kit (Qiagen). One microgram of RNA was reverse transcribed to cDNA (Promega) and qRT-PCR was performed for quantitative assessment of gene expression using SYBR green PCR Master Mix (Bio-Rad) as performed earlier in our lab (7). Expression values were normalized to the geometric mean of 3 housekeeping genes (*Gapdh*, *Pp1*, and *Rp2*) using the ΔΔCT method. Primers used are listed in table S7.

Histology and lung fixation.

After euthanization left lobe of lungs was fixed with 4% paraformaldehyde (FIBROSISA) overnight, embedded in paraffin and cut into 5 µm sections and affixed to glass microscope slides for staining with Masson's trichrome or immunostaining. Lungs sections were prepared by deparaffinizing with xylene and rehydrating through a series of ethanols. Fibrotic remodeling was assessed in mouse lung sections by Masson's trichrome staining (8). Slides stained with trichrome were imaged using an Aperio VERSA 8 Scanner Scope (Microscopy imaging Center, UVM).

For Immunostaining study antigen retrieval was done by heating slides for 20 min at 95 °C in sodium citrate buffer with 0.05% TWEEN-20 then rinsed in dH2O. For Immunofluorescence studies sections were then blocked for 1 h in 1% BSA in PBS, followed by incubation using the following primary antibodies: PDIA3 (LSBio, LS-B9768), at 1:300 and SCGB1A1 (Santa Cruz Biotechnology, sc-390313), at 1:300; pro-SPC (Seven Hills Bioreagents, WRAB-9337), at 1:200 and human SCGB1A1 (Abnova, H00007356-MO1) at 1:200 overnight at 4 °C. Slides were then washed 3×5 min in PBS and incubated with species-specific Alexafluor-488– or Alexafluor-647–conjugated secondary antibodies, and counterstained with DAPI in PBS at 1:4000 for nuclear localization (7, 9). Sections were imaged using a Nikon A1R Confocal laser-scanning microscope. Images were captured at 20x and/or 40x magnification. The image files were converted to Tiff format. Brightness and contrast were adjusted equally in all images.

For immunohistochemistry after antigen retrieval tissue sections were blocked and processed further using Vector® Red Substrate Kit, Alkaline Phosphatase (AP) SK-5100

kit. The protocol was followed as suggested in the kit (10, 11). The antibody used for SCGB1A1 (Santa Cruz Biotechnology; sc-390313) at 1:200 and PDIA3 (LSBio, LS-B9768), at 1:150.

Bronchoalveolar lavage (BAL) cell count and differential staining

Bronchoalveolar lavage fluid (BALF) was collected by lavaging lungs with 1.0 mL of sterile PBS. Cells were isolated by centrifugation, and total cell counts were determined using a Guava easyCyte HT cytometer (Millipore) and analyzed using Flowjo (version 10.4.2, Ashland, OR: Becton, Dickinson and Company). Differential cell counts were obtained via cytospins using Hema3 stained (Fisher Scientific) total cells, on a minimum of 300 cells/animal, or using a Guava easyCyte HT cytometer with a protocol adapted from van Rijt *et al* (12). Briefly, isolated cells were incubated with TruStain fcX (BioLegend 101320) to reduce background staining, then incubated in a mix containing 3µL CD3 PerCP/Cy5.5 (BioLegend 100218), 3µL B220 PerCP/Cy5.5 (BioLegend 103236), 2µL CD11c APC (BioLegend 117310), 2µL I-A/I-E FITC (BioLegend 107616), and 1µL CCR3 PE (BioLegend 144506) per sample. Cells were identified based on forward and side scatter characteristics and differential staining for macrophages (CD11c+), lymphocytes (CD11c-, CD3/B220+), eosinophils (CD11c-, CD3/B220-, CCR3+) and neutrophils (CD11c-, CD3/B220-, CCR3-). Data was analyzed using Flowjo. Validity was tested against differential counts based on cytospins.

ELISA.

We used ELISA to measure concentrations of Osteopontin proteins in BALF and lung

tissue. For tissue ELISA right lung lobes were flash frozen, pulverized, and lysed in buffer containing 20mM Tris·HCl (pH 8.0), 150mM NaCl, 0.5% Nonidet P-40, 10% glycerol. Samples were normalized to total lung protein and assayed for Osteopontin proteins by ELISA (R&D Systems; DY441 for mouse and R&D Systems; DY1433 for human) according to manufacturer's instructions.

Mass Spectrometry

Sample preparation and trypsin digestion: Immunoprecipitates (PBS (n=3), BLM_14d (n=3), BLM_24d (n=3) and the IgG control BLM_24d (n=1)) were run briefly onto the SDS-PAGE (1/3 of the whole length of the gel), which was then stained with silver. For each lane (sample), the gel regions containing the antibody heavy and light chains (labeled as "IgG") and the separated proteins were excised separately (labeled as "IP"). This allows the high abundant IgG and proteins with similar molecular weight and the relatively low abundant proteins in the other gel regions to be analyzed by separate mass spectrometry runs to increase the proteome coverage. The gel pieces were minced to 1 mm^3 cubes, combined, destained and subjected to disulfide reduction and alkylation, and trypsin digestion protocols, as described previously.

Liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based protein identification: The tryptic peptides resuspended in 2.5% CH_3CN and 2.5% formic acid (FA) in water were analyzed on the Q-Exactive Plus mass spectrometer coupled to an EASY-nLC 1200 (Thermo Fisher Scientific). Samples were loaded onto a 100 µm x 350mm capillary column packed with UChrom C18 (1.8 µm particle size, 120 Å, Cat. No:

PN-80001; Nanolcms, CA) at a flow rate of 300 nl min^{-1}. The column end was laser pulled to a ~3 µm orifice and packed with minimal amounts of 5um Magic C18AQ before packing with the 1.8 um particle size chromatographic materials. Peptides of immunoprecipitated proteins were separated by a gradient of 0-35% CH_3CN/0.1% FA over 150 min, 35-80% CH_3CN/0.1% FA in 1 min and then 80% CH_3CN/0.1% FA for 8 min, followed by an immediate return to 0% CH_3CN/0.1% FA and a hold at 0% CH_3CN/0.1% FA. Peptides originating from heavy and light chains of IgG were separated by a gradient of 0-35% CH_3CN/0.1% FA over 60 min, 35-80% CH_3CN/0.1% FA in 1 min and then 80% CH_3CN/0.1% FA for 8 min, followed by an immediate return to 0% CH_3CN/0.1% FA and a hold at 0% CH_3CN/0.1% FA. Samples were randomized in run order and peptide standards (bovine serum albumin) were run between samples. Mass spectrometry data was acquired in a data-dependent "Top 10" acquisition mode with lock mass function activated (*m/z* 371.1012; use lock masses: best; lock mass injection: full MS), in which a survey scan from *m/z* 350-1600 at 70, 000 resolution (AGC target $1e^6$; max IT 100 ms; profile mode) was followed by 10 higher-energy collisional dissociation (HCD) tandem mass spectrometry (MS/MS) scans on the most abundant ions at 17,500 resolution (loop count = 10; AGC target $5e^4$; max IT 100 ms; centroid mode). MS/MS scans were acquired with an isolation width of 1.6 *m/z* and a normalized collisional energy of 26%. Dynamic exclusion was enabled (peptide match: preferred; exclude isotopes: on; underfill ratio: 1%; exclusion duration: 15 sec). Minimum AGC target = 5 e2.

Database searches: Raw files (.RAW) were analyzed using the Proteome Discoverer 2.4 (Thermo Fisher Scientific), with the two raw files ("IgG" and "IP") from each sample

imported as “fractions”. Product ion spectra were searched using the SEQUEST with the “Basic” Processing and Consensus workflows against a Uniprot *Mus musculus* protein database (UP000000589; downloaded Mar 3rd, 2020; 63,628 entries). Search Parameters were as follows: Full trypsin enzymatic activity; Mass tolerance at 10 ppm and 0.02 Da for precursor ions and fragment ions, respectively; dynamic modification on methionine (oxidation: +15.995 Da), and static modification on cysteines (carbamidomethylation: +57.021 Da). Percolator was included in the workflow to limit the false discovery rate to less than 1%. The resulting msf result files were incorporated into Q+S 4.11 (Proteome Software, OR) as mudPIT with “prefiltered mode” (Precalculated probability from Percolator was used) and Protein Cluster Analysis. FDR at protein and peptide levels at 1% and “Min number of peptides” = 2 were selected to achieve a 0.4% Protein Decoy FDR and 0.04% Peptide (PSM) Decoy FDR in the filtered dataset.

Statistical Analysis of the mass spectrometry data: The total spectral counts were statistically evaluated between “Control”, “BLM_14d” and “BLM_24d” with respect to specific protein isoforms/clustering. Statistical tools in Scaffold Quantitative Analysis Mode were used for pairwise comparisons (two-tailed t-test for BLM24d vs. PBS and BLM14d vs. PBS), and for the three-group comparison (ANOVA for BLM24d vs. BLM14d vs. PBS) with the following settings: No normalization was used; Min. Value = 0.5 (All spectral counts of 0 were replaced with a value of 0.5); and total spectra as quantitative method. “Spectral Counting Reports” were exported from Scaffold with “Show lower scoring peptides and <5% Probabilities” deactivated, and “Hide Decoy” selected. The total spectral counts of all proteins (including protein cluster members) and the

corresponding statistical analyses exported from Scaffold as “Spectrum Counting Reports” are included in Supplementary Tables S1, S2 and S3. Spectral counts of protein clusters (exported from “Current View” with “0”s replaced with “0.5”) were used to construct the heat maps and volcano plots for simplicity. One of the cluster members was selected to represent the cluster and the associated spectral counts were derived from the peptides of all the members (see Supplementary Tables for the spectral counts and p-values for all members/isoforms within clusters). Fold changes (log_2 ratio of the average number of peptides of the proteins between two groups) and p values ($-log_{10}$) were imported into Graph Pad Prism 8 (GraphPad Software Inc., CA) for constructing volcano plots. Heat maps were generated by first scaling the total spectral counts in individual samples so that all the counts in all samples summed up to the number of samples *100 (this allows the fold change of proteins of varying abundances be represented on the same color intensity scale) and then importing the scaled values into Graph Pad Prism 8 (Dobule gradient; Baseline value set as 100). The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE (13) partner repository with the dataset identifier PXD021715 and 10.6019/PXD021715".

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Supplementary Figures Legends

Figure S1. Various PDIs along with UPR markers are up regulated in IPF patients. (A) *PDIA3* mRNA levels in Control (n=132) and IPF (n=160) patients (*PDIA3* is marked in red). (B) Box plots displaying the distribution (five-point summary) of expression levels of *PDIA3* gene in healthy controls and IPF. Each point in the plot represents a sample and the lower and upper hinges correspond to the first and third quartiles (the 25th and 75th percentiles) of each distribution. The upper whisker extends from the hinge to the largest value no further than 1.5 * IQR and the lower whisker extends from the hinge to the smallest value at most 1.5 * IQR of the hinge, where IQR or the inter-quartile range is distance between the first and third quartiles. Points beyond the end of the whiskers are potential outlier samples in each case. (C-E) *PDIA3* mRNA expression and correlation with % DLCO and FVC in IPF and controls. The FVC/DLCO measurements are on the y-axis and mRNA expression levels on the x-axis. Each circle/point represents a patient sample within the study and the blue-colored points are healthy controls while the red-colored points represent IPF samples. The FVC and %DLCO correlations with the gene expression were calculated using Pearson correlation. The significance of association was calculated using Fisher's asymptotic test. All the plots were generated using the ggplot2 library in R. (F-H) mRNA levels of UPR markers *HSPA5*, *HSP90B1*, and *XBP1* in Control (n=132) and IPF (n=160) patients. Unpaired two-tailed non-parametric Mann-Whitney *t* test. Error bars represent ±STDEV.

Figure S2. UPR markers and club cell markers in fibrotic mice and IPF. (A and B) measurement of *Hspa5* and *Xbp1s* (spliced form) in BLM or PBS challenged mice

harvested at various time points. *p<0.05 as compared to PBS group and #p<0.05 as compared to 4 day-BLM group by ANOVA, error bars represent ±SEM (n=5-9 mice/group). (C) IHC staining (red) for PDIA3 and SCGB1A1 in serial (5μm) sections of the lungs, the arrow indicates PDIA3 and SCGB1A1 staining in the same cells (arrows). Secondary antibody staining on fibrotic mouse lungs is used as a negative control. Scale bar 400μm. (D-F) Club cell markers in control and IPF lungs. Box plots displaying the distribution (five-point summary) of expression levels of club cell markers in healthy controls and IPF. Each point in the plot represents a sample and the lower and upper hinges correspond to the first and third quartiles (the 25th and 75th percentiles) of each distribution. The upper whisker extends from the hinge to the largest value no further than 1.5 * IQR and the lower whisker extends from the hinge to the smallest value at most 1.5 * IQR of the hinge, where IQR or the inter-quartile range is distance between the first and third quartiles. Points beyond the end of the whiskers are potential outlier samples in each case. (G-L) Correlation of club cell markers with % DLCO and FVC in IPF and controls. The FVC/DLCO measurements are on the y-axis and mRNA expression levels on the x-axis. Each circle/point represents a patient sample within the study and the blue-colored points are healthy controls while the red-colored points represent IPF samples. The FVC and %DLCO correlations with the gene expression were calculated using Pearson correlation. The significance of association was calculated using Fisher's asymptotic test. All the plots were generated using the ggplot2 library in R.

Figure S3. PDIA3 levels after Dox treatment in mouse lung and expression of various *PDIA*s with LOC14 treatment. (A-B) Representative images from confocal

microscopy stained for SCGB1A1 (green), PDIA3 (red), and nucleus (blue) and quantitation of SCGB1A1 and PDIA3 staining in PBS challenged *ctr* and *ΔEpi-Pdia3* mice lungs. Unpaired t-test, (n=4 mice/group); error bars ±SEM. (C-I) Analysis of mRNAs for various *PDIA*s and ER stress markers (*Hspa5* & *Xbp1*) in the lungs challenged with BLM or PBS and treated with DMSO or LOC14. Outlier removed in *Pdia3* BLM + DMSO (n=1) *p<0.05 as compared to PBS group and #p<0.05 as compared to BLM+DMSO group by ANOVA, error bars represent ±SEM (n=5-7 mice/group).

Figure S4. Inflammatory cells and ALT measurement in LOC14 treated mice. (A-E) Measurement of various inflammatory cells in the BALF by flow cytometry. Outliers removed in Total cells PBS+L14 0.15mg/kg (n=1), BLM+L14 0.015mg/kg (n=3), BLM+L14 0.15mg/kg (n=3) and BLM+L14 1.5mg/kg (n=2); Macrophages PBS+L14 0.15mg/kg (n=1), BLM+L14 0.015mg/kg (n=2), BLM+L14 0.15mg/kg (n=2) and BLM+L14 1.5mg/kg (n=1); Neutrophils PBS+L14 0.15mg/kg (n=2), BLM (n=2), BLM+L14 0.015mg/kg (n=2), BLM+L14 0.15mg/kg (n=1) and BLM+L14 1.5mg/kg (n=1); Eosinophils PBS+L14 0.15mg/kg (n=1), BLM (n=1), BLM+L14 0.015mg/kg (n=1), BLM+L14 0.15mg/kg (n=4) and BLM+L14 1.5mg/kg (n=1); Lymphocytes PBS+L14 0.15mg/kg (n=1), BLM (n=1), BLM+L14 0.015mg/kg (n=2), BLM+L14 0.15mg/kg (n=1) and BLM+L14 1.5mg/kg (n=1). (F) Measurement of liver Alanine Aminotransferase (ALT) in the serum. *p<0.05 as compared to PBS group and #p<0.05 as compared to BLM+DMSO group by ANOVA, error bars represent ±SEM (n=5-9 mice/group).

Figure S5. Analysis of PDIA3 interacting partners. (A) Heat map of interacting partners of PDIA3 in fibrotic mouse lung, analyzed 24-day post BLM challenge (n=3 samples/group, "C" immunoprecipitation using non-specific IgG used as a control). Identified proteins with a p value < 0.05 (two-tailed t-test: 14-day post BLM challenge vs. PBS) are represented. The number next to the gene symbol indicates the members in the cluster associated with that protein. The scale of the color intensity is arbitrary. (B) Volcano plot depicting the significance of interactions of PDIA3 post immunoprecipitation and mass spectrometry. Fold changes of 2 and p value at 0.05 (two-tailed t-test: 24-day post BLM challenge vs. PBS) are indicated by dotted lines on the x- and y-axis, respectively. (C) Silver stain of bands excised and analyzed by mass spectrometry. (D) Box plots displaying the distribution (five-point summary) of expression levels of *SPP1* gene in healthy controls and IPF. Each point in the plot represents a sample and the lower and upper hinges correspond to the first and third quartiles (the 25th and 75th percentiles) of each distribution. The upper whisker extends from the hinge to the largest value no further than 1.5 * IQR and the lower whisker extends from the hinge to the smallest value at most 1.5 * IQR of the hinge, where IQR or the inter-quartile range is distance between the first and third quartiles. Points beyond the end of the whiskers are potential outlier samples in each case. (E-F) *SPP1* expression and correlation of *SPP1* with % DLCO and FVC in IPF and controls. The FVC/DLCO measurements are on the y-axis and mRNA expression levels on the x-axis. Each circle/point represents a patient sample within the study and the blue-colored points are healthy controls while the red-colored points represent IPF samples. The FVC and %DLCO correlations with the gene expression were

calculated using Pearson correlation. The significance of association was calculated using Fisher's asymptotic test. All the plots were generated using the ggplot2 library in R.

Figure S6. Inflammatory cells measurement in SPP1 blocking antibody treated mice. (A) Measurement of total inflammatory cells in the BALF by flow cytometry. (B) Measurement of various types of inflammatory cells in the BALF by flow cytometry. *p<0.05 as compared to PBS+VC group by ANOVA, error bars represent ±SEM (n=10-16 mice/group).

Figure S7. Expression of *PDIA3* and *SPP1* in various cell types in control and IPF lungs. Bar plots showing the *PDIA3* (A and B) and *SPP1* (C and D) expression in different cell types in control and IPF lungs from two publicly available single cell RNA-seq datasets. The bar plots are downloaded from the IPF single cell atlas (https://p2med.shinyapps.io/IPFCellAtlas/)(14). Boxes highlight *PDIA3* or *SPP1* expression in club cells.

Figure S8. Expression of proSP-C, SCGB1A1 and PDIA3 in mouse model of fibrosis and/or IPF and normal lungs. (A and B) Representative images from confocal microscopy stained for proSP-C (green), PDIA3 (red), and nucleus (blue) and quantitation of proSP-C and PDIA3. Secondary antibody (without primary) staining on fibrotic mouse lungs is used as the negative control. n=3-4 mice/group; error bars ±SEM. Scale bar 50μm. (C and D) Representative images from confocal microscopy on IPF and normal lungs stained for proSP-C (green), PDIA3 (red), and nucleus (blue) and quantitation of proSP-C and PDIA3. Secondary antibody (without primary) staining on IPF lung is used

as the negative control. n=4-5 samples/group; error bars ±SEM. Scale bar 50μm. (E and F) Representative images of from confocal microscopy stained for SCGB1A1 (green), PDIA3 (red), and nucleus (blue) and quantitation of SCGB1A1 and PDIA3. Secondary antibody (without primary) staining on IPF lung is used as the negative control. n=4-5 samples/group; error bars ±SEM. Scale bar 50μm.

Supplementary Table S1. Proteins identified in IP and mass spectrometry-based proteomics in the BLM 24d, BLM 14d, and PBS challenged groups. (<1% FDR).

Supplementary Table S2. Protein identified with a differential abundance in BLM 14d vs. PBS challenged ($p < 0.05$, two-tailed t-test).

Supplementary Table S3. Protein identified with a differential abundance in BLM 24d vs. PBS challenged ($p < 0.05$, two-tailed t-test).

Supplementary Table S4: Patient demographic data between control and IPF patients in the 2014/2015 Cohorts from LTRC.

Supplementary Table S5: Patient demographic data of non-IPF and IPF patients from the Lung Genomics Research Consortium.

Supplementary Table S6: Antibodies used in this research study.

Supplementary Table S7: Primers sets to detect mouse mRNAs.