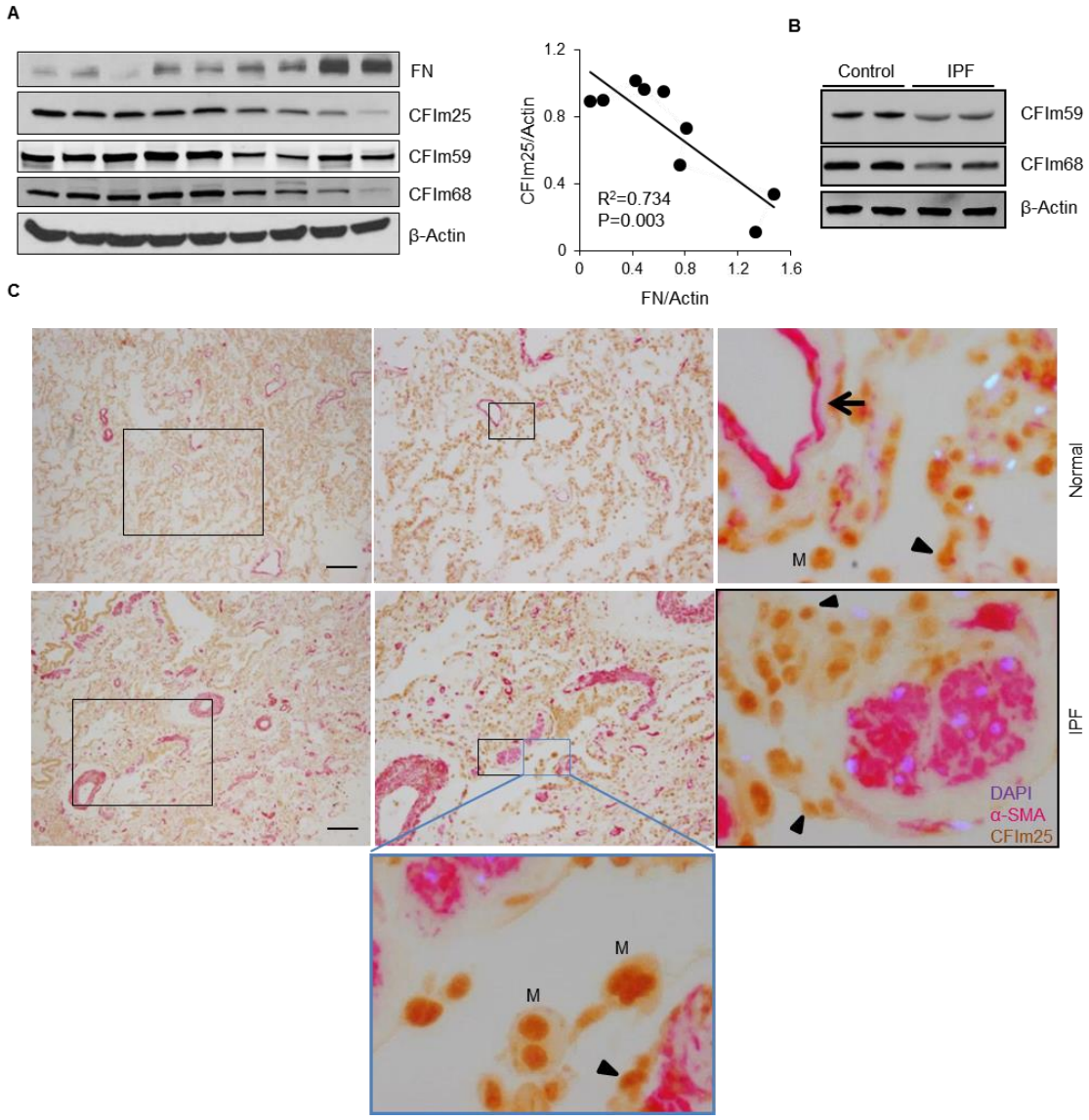
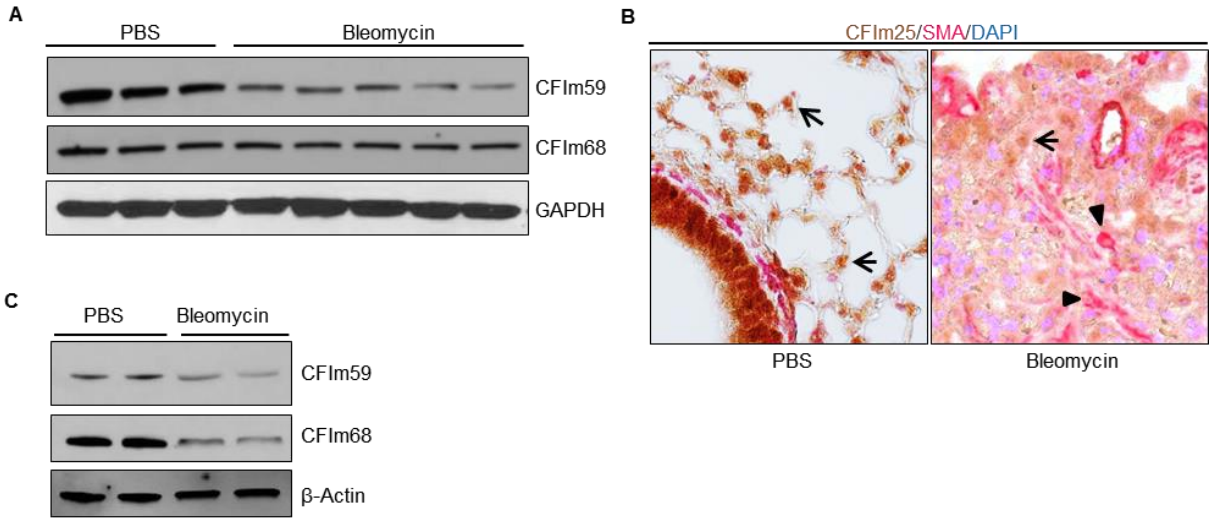
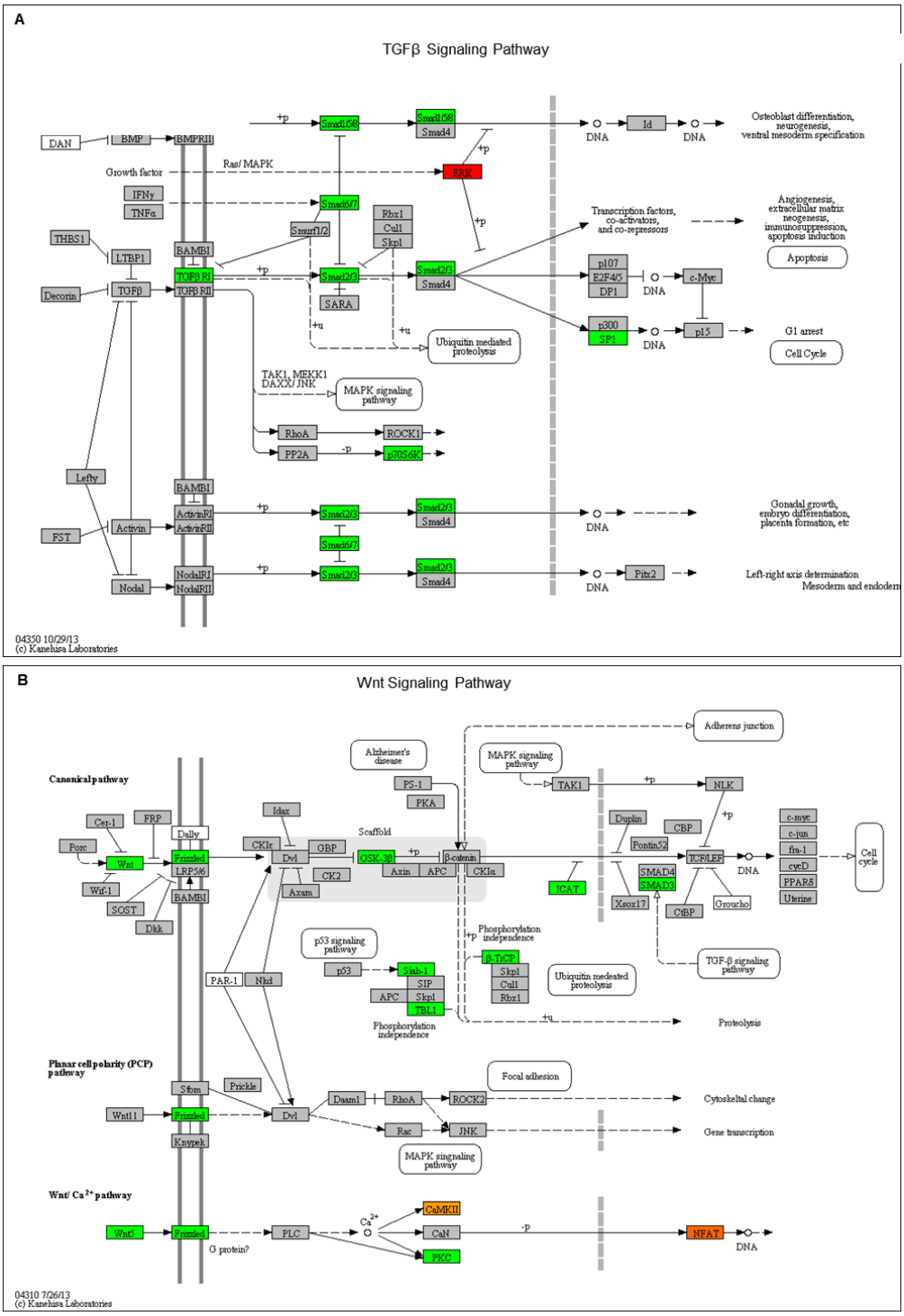


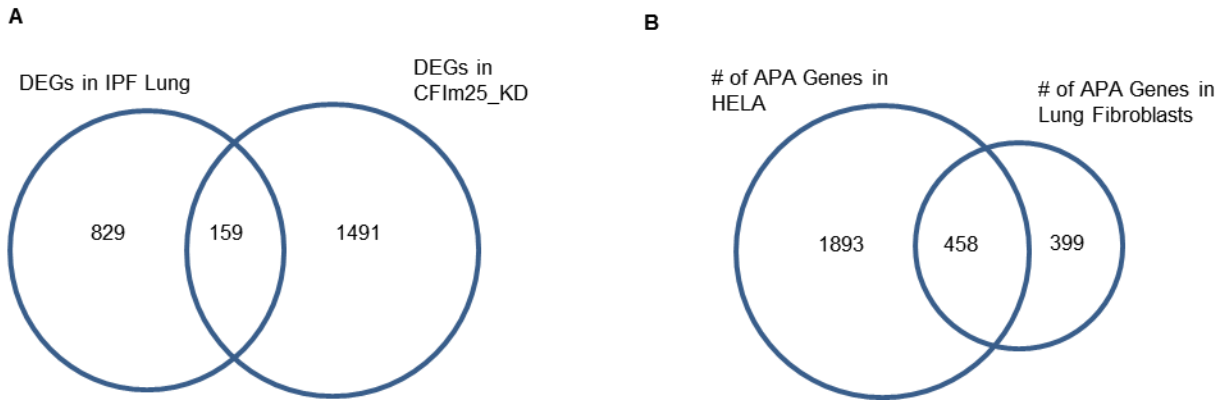
Supplemental Figure 1. CFIm components are down-regulated in IPF lungs. (A) Left panel: Protein levels of CFIm25, CFIm59, CFIm68 and FN were examined in IPF lungs with different degrees of pulmonary fibrosis. Right Panel: Linear regression and Pearson's correlation showing negatively correlated densitometry of CFIm25 and fibronectin (FN). R^2=0.734, P-value = 0.003. (B) Western blot showing CFIm59 and CFIm68 protein expression from primary fibroblast lines derived from normal or IPF lungs. (C) Dual-Immunohistochemistry indicated CFIm25 (Brown) and α-SMA (Red) expression in Normal and IPF lungs. Scale bar=200μm. M: macrophage. Arrow: Smooth muscle cells. Arrow head: epithelial cells.



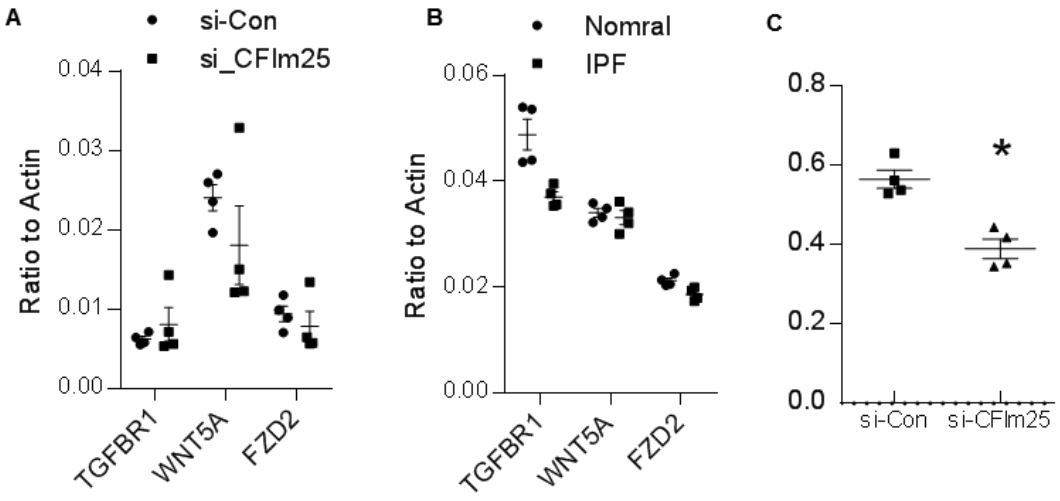
Supplemental Figure 2. CFIm components are down-regulated in an animal model with pulmonary fibrosis. (A) Western blot analysis of the protein expression of CFIm59 and CFIm68 in whole lung lysates at day 33 after PBS or bleomycin administration. (B) Immunohistochemistry was carried out to determine CFIm25 (brown) and α-SMA (pink) localization in lungs from mice exposed to PBS or bleomycin for 33 days. Arrow: CFIm25 positive cells. Arrow head: α-SMA positive but CFIm25 negative cells. Scale bar=100 μm. (C) Western blot was used to determine CFIm59, CFIm68 and β-actin protein levels in primary fibroblasts isolated from day 33 PBS or bleomycin-injected mouse lungs.



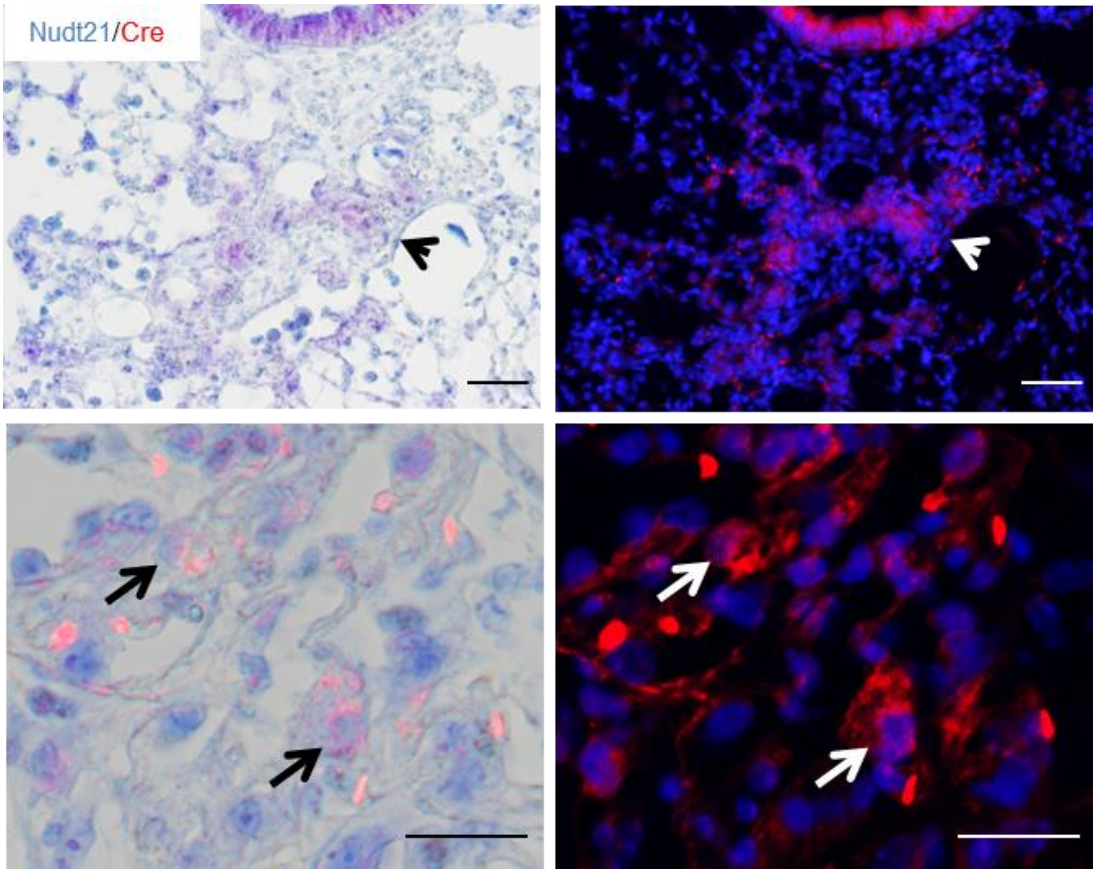
Supplemental Figure 3. Components in TGFβ and Wnt pathways have 3'UTR shortening after CFIm25 knockdown. KEGG pathway shows genes having 3'UTR shortening (green) or lengthening (red) in TGFβ (A) and Wnt pathways (B) in CFIm25 knockdown CCD8-Lu cells compared to controls. Data are from RNA-Seq.



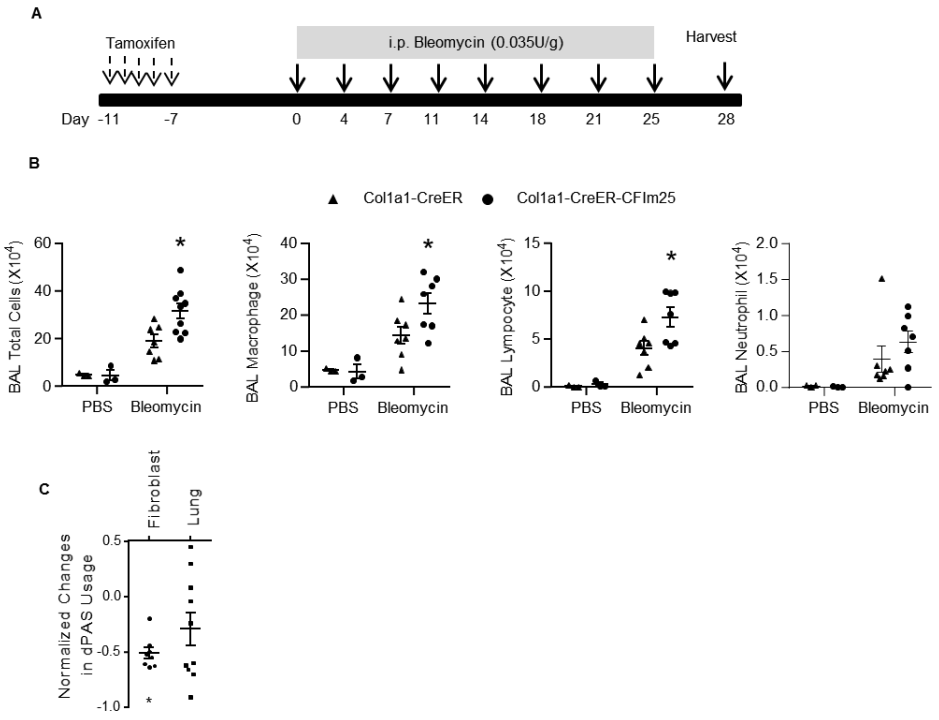
Supplemental Figure 4. Common genes between IPF gene signature and CFIm25 KD. (A) The differentially expressed genes (DEGs) identified in CFIm25 knockdown fibroblasts were compared with the known IPF gene list. (B) The APA genes caused by CFIm25 knockdown were compared between HELA cells and lung fibroblasts.



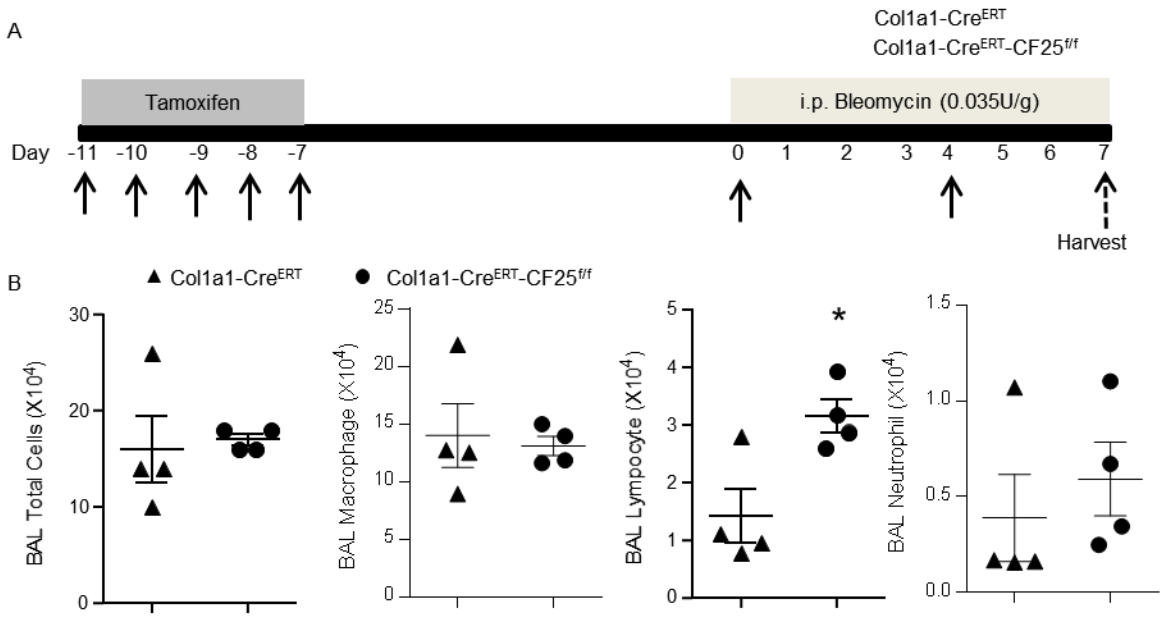
Supplemental Figure 5. Transcript expression of CFIm25 targets and fibroblasts proliferation. Realtime PCR was carried out to determine the transcript expression of CFIm25 targets (TGFBR1, FZD2 and WNT5A) in (A) CFIm25 knockdown CCD8-Lu fibroblasts and (B) primary normal or IPF lung fibroblasts. (C) Fibroblast proliferation was analyzed using the WST-1 reagents (Sigma-Aldrich). n=3 biological replications* duplicated. * P< 0.05 student t-test vs si-Con.



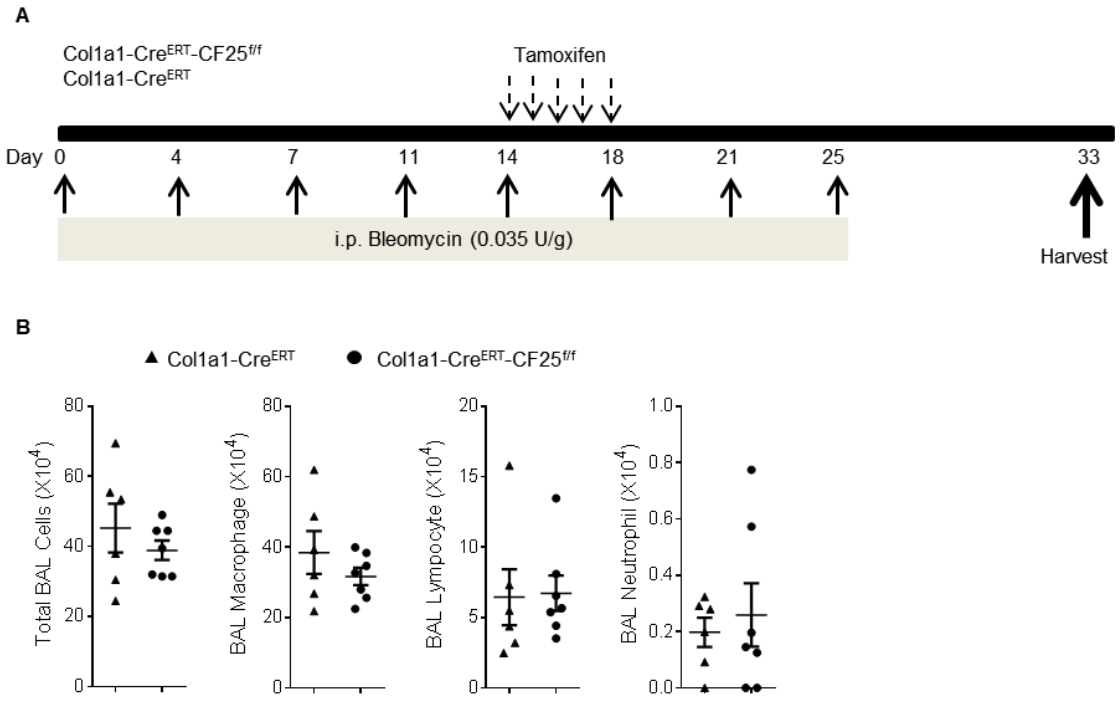
Supplemental Figure 6. CFIm25 and Cre co-staining in mouse lungs. Dual Immunostaining was carried out to localize the expression of CFIm25 (blue) and Cre (red) in Col1a1-creER-CFIm25$^{f/f}$ mice injected with i.p. bleomycin. Arrow points to Cre positive cells. Scale bar=100 μm.



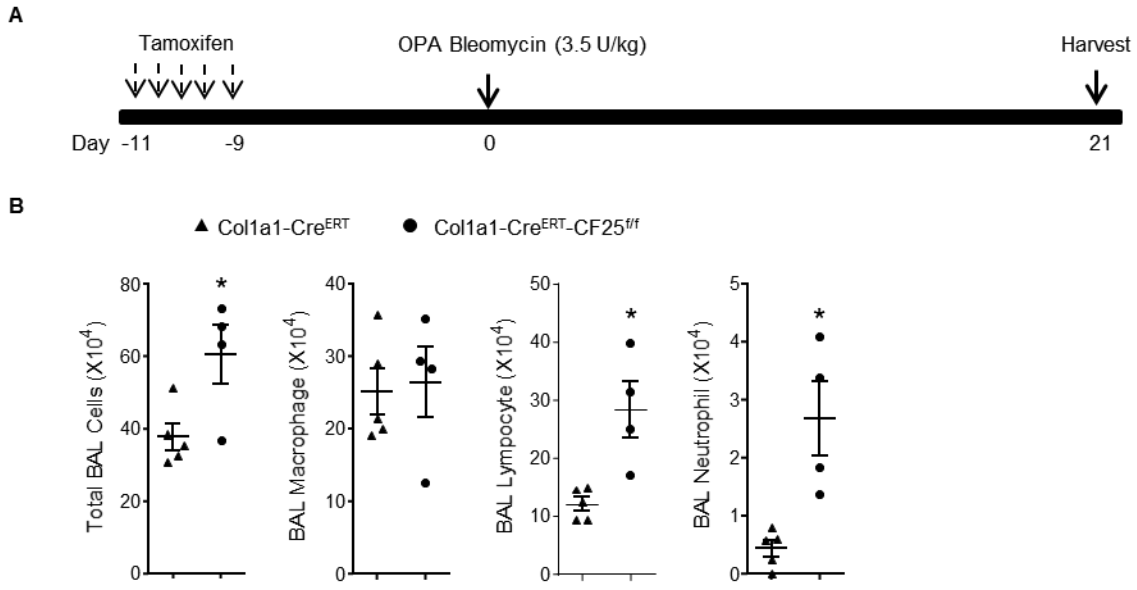
Supplemental Figure 7. Inflammatory profile of CFIm25 conditional knockout mice treated with repeated i.p. bleomycin. (A) Diagram showing the experimental procedure. 4-6 week old Col1a1-CreER-CFIm25$^{f/f}$ mice and age and sex matched littermate controls were i.p. administrated with 75 mg/kg tamoxifen daily for 5 days to induce cre activation. A week after the last tamoxifen injection, mice were injected with reparative PBS or 0.035u/g bleomycin via i.p. twice a week for 4 weeks. Lungs were collected 28 days after the first bleomycin injection for analysis. (B) The total cell number as well as the number of macrophages, lymphocytes and neutrophils in the bronchial alveolar lavage fluid (BAL) was counted. n>4 biological replications.* P<0.05 one way ANOVA followed by Bonferroni's multiple comparisons test vs Col1a1-CreER treated with bleomycin. (C) The dPAS usage of Col1a1 was analyzed by realtime PCR to show its 3'UTR shortening in primary fibroblasts isolated from the lungs of non-bleomycin injected Col1a1-CreER-CFIm25$^{f/f}$ mice or the lungs of the Col1a1-CreER-CFIm25$^{f/f}$ mice treated with bleomycin. Data were normalized to corresponding Col1a1-creER fibroblasts or lungs. n>5 biological replications. * P<0.05 one sample t-test vs 0.



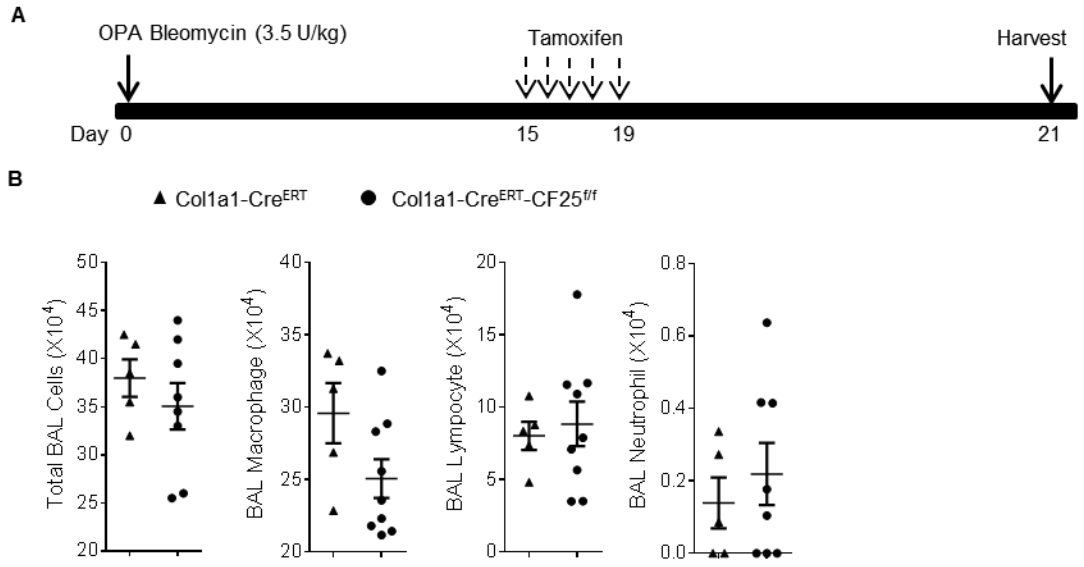
Supplemental Figure 8. Inflammatory profile of CFIm25 conditional knockout mice treated with repeated i.p. bleomycin for 7 days. (A) Diagram showing the experimental design. 4-6 week old Col1a1-CreER-CFIm25$^{f/f}$ mice and matched controls were i.p. administrated with tamoxifen daily for 5 days to induce cre activation. A week after the last tamoxifen injection, mice were injected with reparative PBS or 0.035u/g bleomycin via i.p. twice a week. BAL was collected 7 days after the first bleomycin injection for analysis. (B) The total cell number as well as the number of macrophages, lymphocytes and neutrophils in BAL was counted. n>5 biological replications. * P<0.05 nonpaired t-test with equal variance vs Col1a1-CreER control.



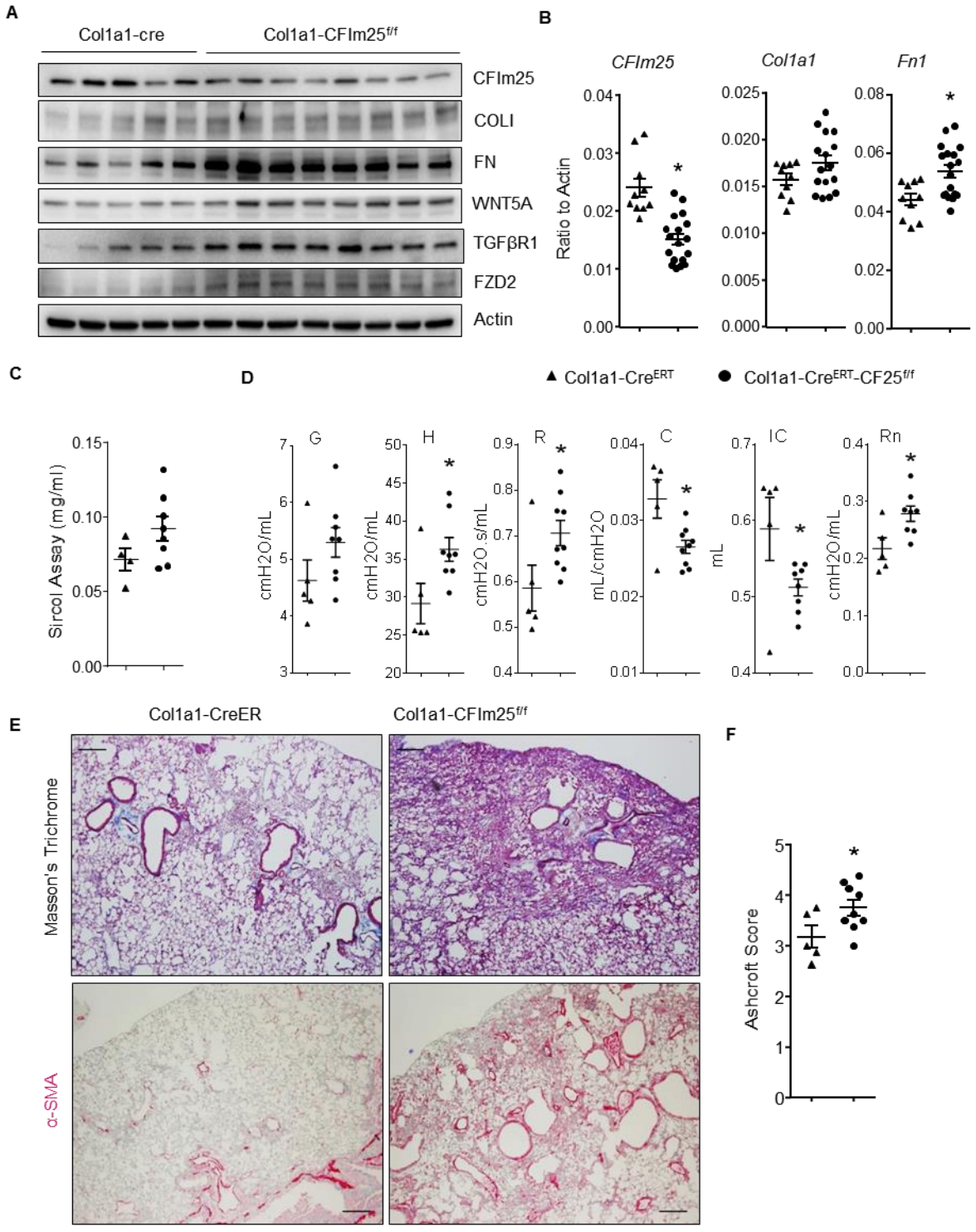
Supplemental Figure 9. Inflammation in Col1a1-CreER-CFIm25$^{f/f}$ mice with delayed cre activation. (A) Diagram showing the experimental design. 4-6 week old Col1a1-CreER-CFIm25$^{f/f}$ mice and age and sex matched littermate controls were i.p. administrated with PBS or bleomycin bi-weekly for 4 weeks. Starting on day 15 after the first bleomycin injection, mice were i.p. injected with tamoxifen daily for 5 days to induce cre recombination. Samples were collected on day 33 day after the first bleomycin injection for analysis. (B) The total cell number as well as macrophage, lymphocyte and neutrophil numbers in BAL were counted. n>8 biological replications.



Supplemental Figure 10. Col1a1-CreER-CFlm25$^{f/f}$ mice had more severe inflammation in response to single oropharyngeal (OPA) bleomycin injection. (A) Diagram showing the time line of experimental treatment. 4-6 week old Col1a1-CreER-CFlm25$^{f/f}$ mice and age and sex matched littermate controls were i.p. administrated with 75 mg/kg tamoxifen daily for 5 days to induce cre activation. After a week, mice were injected with PBS or bleomycin through OPA instillation. BALs were collected 21 days after bleomycin injection for analysis. (B) The total number of BAL cells, BAL macrophages, lymphocytes and neutrophils were counted. n>4 biology replications, * P<0.05 nonpaired t-test with equal variance vs Col1a1-CreER control.

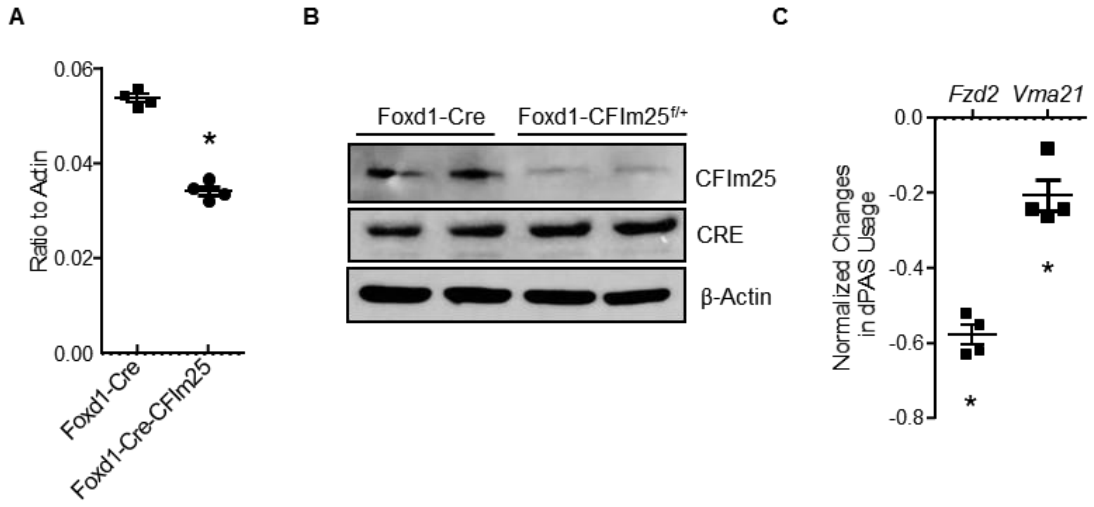


Supplemental Figure 11. Inflammatory profile in Col1a1-CreER-CFIm25$^{f/f}$ mice treated with oropharyngeal (OPA) and delayed Cre activation. (A) Diagram showing the experimental design. 4-6 week old Col1a1-CreER-CFIm25$^{f/f}$ mice and age and sex matched littermate controls were injected with PBS or bleomycin through OPA instillation. Starting on day 15, mice were i.p. administrated with 75 mg/kg tamoxifen daily for 5 days to induce cre activation. BAL was collected on day 21 for analysis. (B) The inflammatory profile of the BAL was analyzed. n>5 biological replications.

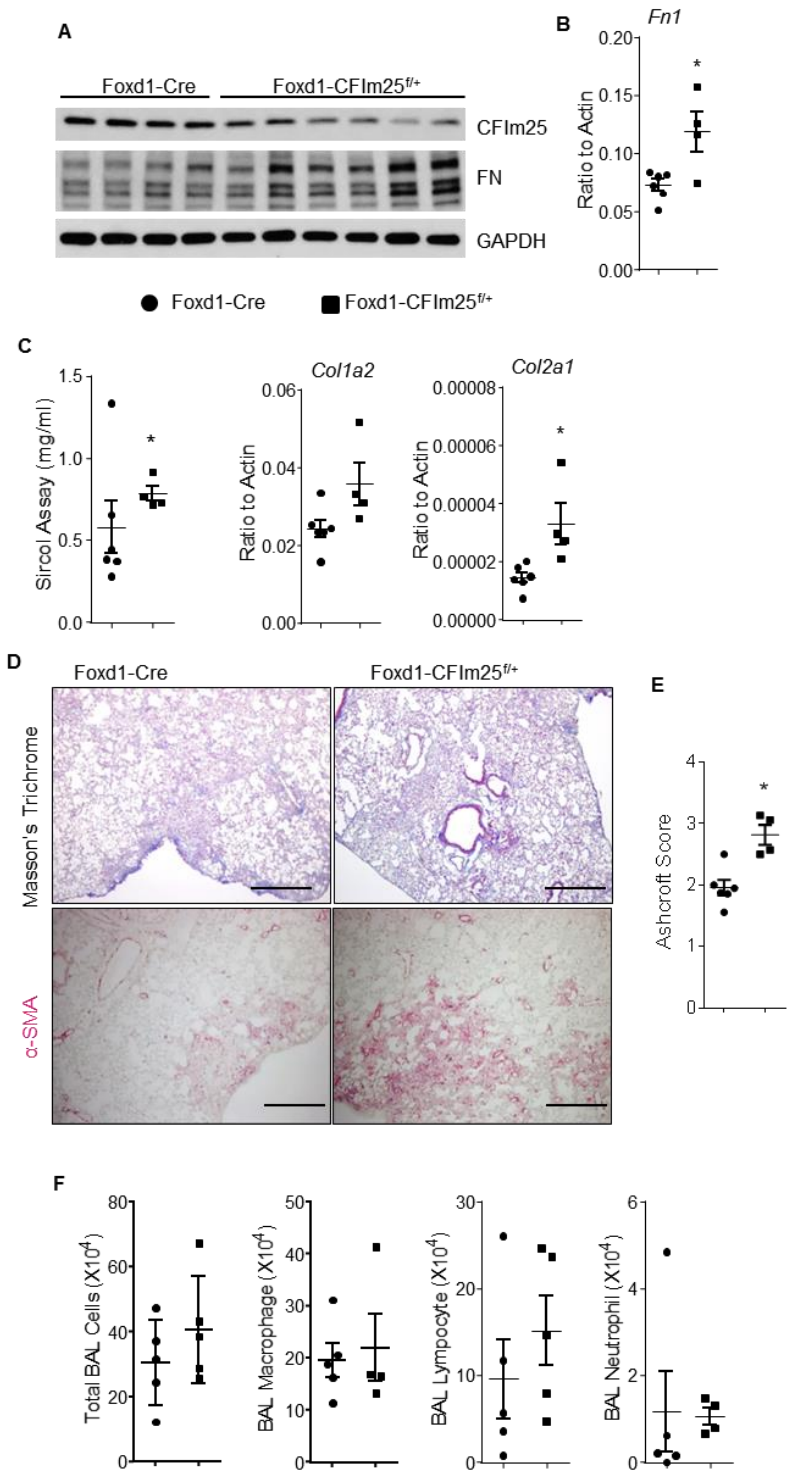


Supplemental Figure 12. CFIm25 depletion in later fibrotic stage exaggerated OPA bleomycin-induced pulmonary fibrosis. 4-6 week old Col1a1-CreER-CFIm25$^{f/f}$ mice and age and sex matched littermate controls were injected with PBS or bleomycin through OPA instillation.

Starting on day 15, mice were i.p. administrated with 75 mg/kg tamoxifen daily for 5 days to induce cre activation. BAL was collected on day 25 for analysis. (A) Western blot showing the expression of CFIm25, fibrotic makers COLI and FN, and CFIm25 targets WNT5A, TGFBR1 and FZD2 expression in whole lung lysates. (B) Realtime PCR was performed to determine the transcript levels of *CFIm25*, *Col1a1* and *Fn1* in the lungs of Col1a1-CreER-CFIm25$^{f/f}$ and control mice treated with bleomycin. (C) Sircol assay was carried out to determine soluble collagen levels in BAL. (D) Lung functional assay was performed using the flexiVent system to determine the levels of tissue damping (G), tissue elastase (H), resistance (R), compliance (C), inspiratory capacity (IC) and Newtonian resistance (Rn). (F) Masson's trichrome and α-SMA staining show the collagen deposition and myofibroblasts differentiation. Scale bar= 200 μm. (G) The pulmonary fibrosis of Masson's trichrome stained slides was quantified by blind Ashcroft Assay. * $P<0.05$ nonpaired t-test with equal variance, n>5 biological replications.

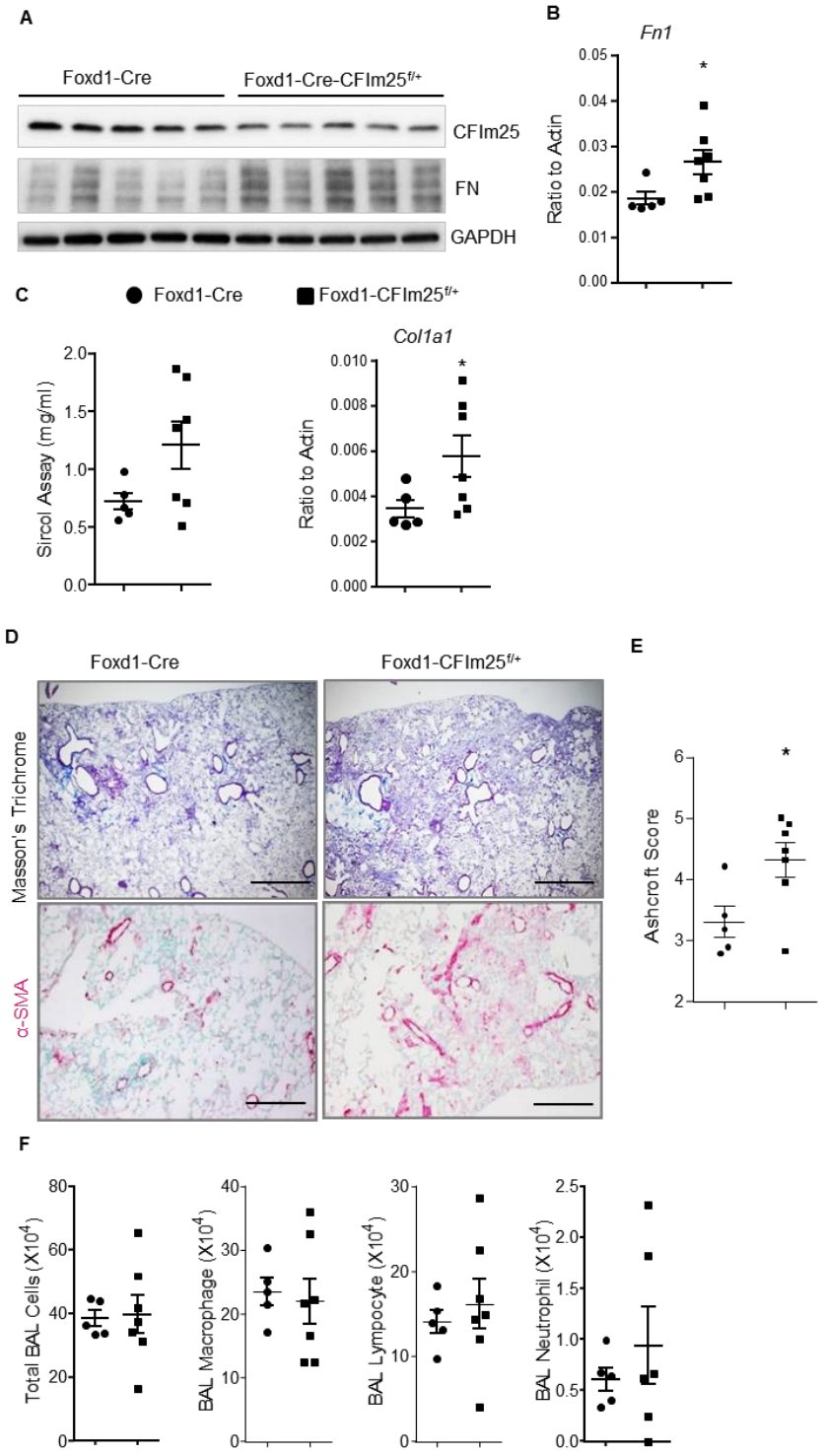


Supplemental Figure 13. CFIm25 expression is decreased in fibroblasts isolated from Foxd1-Cre-CF25$^{f/+}$ mice. Fibroblasts were isolated from age and sex matched Foxd1-cre or Foxd1-Cre-CFIm25$^{f/+}$ mice. (A) Real-time PCR was carried out to determine CFIm25 transcript levels. n=3 biological replications. * P<0.05 nonpaired student t-test with equal variance. (B) Western blot was performed to show CFIm25 and Cre expression. (C) Real-time PCR was performed to check the dPAS usage of FZD2 and Vma21 in primary fibroblasts. Results are shown as $\log_2$(fold changes of Foxd1-Cre-CFIm25$^{f/+}$ to Foxd1-cre) + standard error. n=3 biological replications. * P<0.05 one sample t-test vs 0.



Supplemental Figure 14. i.p. bleomycin-induced pulmonary fibrosis is exaggerated in Foxd1-Cre-CFIm25$^{f/+}$ Mice. 4-6 week old Foxd1-Cre-CFIm25$^{f/+}$ mice and age and sex matched littermate controls were i.p. administrated with bleomycin bi-weekly for 4 weeks. Lungs were

collected on day 28 after the first bleomycin injection for analysis. (A) Western blot shows CFIm25 and FN expression in the lungs of control and Foxd1-CFIm25$^{f/+}$ mice. (B) The transcript levels of FN were determined by realtime PCR. (C) Collagen levels were determined by Sircol assay (left panel), and realtime PCR was carried out to show Col1a2 and Col2a1 expression. Pulmonary fibrosis was analyzed using Masson's trichrome and α-SMA staining (D), and Ashcroft assay (E). (F) The BAL inflammatory profile was determined using the differential assay. *P<0.05 nonpaired t-test with equal variance, n>4 biological replications. Scale bar=500μm.



Supplemental Figure 15. Pulmonary fibrosis induced by bleomycin via intratracheal instillation is exaggerated in Foxd1-Cre-CFIm25$^{f/+}$ mice. 4-6 week old Foxd1-Cre-CFIm25$^{f/+}$ mice and age and sex matched littermate controls were administrated with 2.5u/kg bleomycin

through intratracheal instillation. Lungs were collected on day 28 for analysis. (A) Western blot shows CFIm25 and FN expression in the lungs of control and Foxd1-CFIm25$^{f/+}$ mice. Pulmonary fibrosis was analyzed using realtime PCR for FN (B), sircol assay (C, left panel), Real-time PCR for Col2a1 (C, right panel), Masson's trichrome and α-SMA staining (D), and Ashcroft assay (E). (F) The total inflammatory cells as well as the number of macrophages, lymphocytes and neutrophils in BAL were counted. *P<0.05 nonpaired t-test with equal variance, n>5 biological replications. Scale bar=500μm.

Supplemental Table 1. APA genes in CFIm25 knockdown fibroblasts.

Gene Symbol	CFIm25KD vs Control PDUI
LPP	-0.805
ATP11C	-0.775
ELMOD2	-0.75
SLC7A11	-0.71
GXYLT1	-0.705
GPN3	-0.7
SLC12A2	-0.7
DCAF7	-0.69
NCBP2	-0.675
TMOD2	-0.67
BCAT1	-0.66
ANP32E	-0.635
TMEM53	-0.625
NUDT12	-0.605
BNIP3	-0.585
IGF2BP1	-0.585
ITCH	-0.575
C17orf76-AS1	-0.57
NUDT13	-0.57
VMA21	-0.565
KLHDC5	-0.56
GRPEL2	-0.555
IL6	-0.55
SNX4	-0.55
TRAPPC2	-0.55
ADAM12	-0.545
LIMCH1	-0.545
TBC1D12	-0.545
ADAMTS6	-0.535
JAZF1	-0.535
SETD6	-0.535
CYLD	-0.53
AGTPBP1	-0.525
CHST11	-0.525

Gene Symbol	CFIm25KD vs Control PDUI
RPL28	-0.32
SGCD	-0.32
SORT1	-0.32
WDFY2	-0.32
ASIC1	-0.315
C11orf75	-0.315
C5orf24	-0.315
C9orf78	-0.315
CD46	-0.315
CUL5	-0.315
FKTN	-0.315
FZD6	-0.315
KAT6A	-0.315
MSH3	-0.315
RCE1	-0.315
SNPH	-0.315
TMEM241	-0.315
ZWINT	-0.315
AKAP11	-0.31
ARHGAP18	-0.31
CD109	-0.31
COQ10A	-0.31
CPEB2	-0.31
GPATCH3	-0.31
GPRC5B	-0.31
HP1BP3	-0.31
INO80	-0.31
JMJD4	-0.31
KIAA1143	-0.31
MAP2	-0.31
SCAF4	-0.31
SIKE1	-0.31
TTC8	-0.31
ZNF608	-0.31

Gene Symbol	CFIm25KD vs Control PDUI
USP7	-0.225
WWC2	-0.225
ZNF295	-0.225
C8orf42	-0.22
CETN3	-0.22
DAB2	-0.22
EIF2S3	-0.22
ESYT2	-0.22
KIAA0494	-0.22
LOC100505876	-0.22
NAPG	-0.22
NDFIP2	-0.22
PTEN	-0.22
TMEM56-RWDD3	-0.22
XPO5	-0.22
ASXL1	-0.215
DICER1	-0.215
GJC1	-0.215
GK	-0.215
LONRF1	-0.215
LPCAT4	-0.215
MKI67IP	-0.215
MTSS1	-0.215
OAZ1	-0.215
SLC31A1	-0.215
TMEM48	-0.215
TRIP11	-0.215
UBE2J1	-0.215
UBE4B	-0.215
ZRANB1	-0.215
C16orf87	-0.21
CBWD2	-0.21
CDH2	-0.21
CEP104	-0.21

NFATC2IP	-0.525	BAG5	-0.305	CHMP4B	-0.21
CHST7	-0.52	CNOT4	-0.305	DNAJC25	-0.21
OSBPL8	-0.52	CRTC2	-0.305	DNM2	-0.21
SMAD5	-0.52	DHFR	-0.305	GATAD2A	-0.21
EDEM1	-0.51	FMN1	-0.305	GNG2	-0.21
PAPD4	-0.51	KIAA0182	-0.305	GPT2	-0.21
RFC5	-0.51	PHF15	-0.305	HADH	-0.21
PTAR1	-0.505	PROSER1	-0.305	HNRNPA0	-0.21
WRN	-0.505	TBCC	-0.305	MDM4	-0.21
SYT11	-0.5	USP42	-0.305	MIER1	-0.21
VPS36	-0.5	BTBD9	-0.3	SFXN1	-0.21
XPO4	-0.5	C1orf55	-0.3	UBIAD1	-0.21
DENND3	-0.495	CSTF3	-0.3	UCK2	-0.21
TMEM59	-0.495	GOLM1	-0.3	YBEY	-0.21
ACSS3	-0.49	LDLRAD3	-0.3	AES	-0.205
KLF12	-0.49	PAK2	-0.3	ATXN2	-0.205
SYPL1	-0.49	RUNX1	-0.3	C15orf40	-0.205
TBRG1	-0.485	SEC24A	-0.3	CDC42BPA	-0.205
FAM91A1	-0.48	TFEB	-0.3	CEP57L1	-0.205
IDH3A	-0.475	TMEM87B	-0.3	CSNK1G3	-0.205
PLA2G4A	-0.475	WDR77	-0.3	DOK1	-0.205
LARGE	-0.47	WDR92	-0.3	HSDL2	-0.205
TEAD4	-0.47	ZBTB41	-0.3	KIAA0586	-0.205
TMEM186	-0.47	ZNF688	-0.3	NOL8	-0.205
AASDHPPT	-0.465	ANGPTL2	-0.295	PRKAR1A	-0.205
C7orf41	-0.465	BCKDHB	-0.295	RPL34	-0.205
ETNK1	-0.465	C6orf228	-0.295	SMAD3	-0.205
SPAG16	-0.465	DPH3	-0.295	TMEM123	-0.205
DNM1L	-0.46	DYNC1LI1	-0.295	ASNSD1	-0.2
EIF2C4	-0.46	EIF4G3	-0.295	ATF2	-0.2
WDR89	-0.46	GPR155	-0.295	CCBE1	-0.2
ARSK	-0.455	LETM1	-0.295	COL5A2	-0.2
EGLN1	-0.455	MYO5A	-0.295	GRB10	-0.2
MIS12	-0.455	OXR1	-0.295	PARD3	-0.2
C1GALT1C1	-0.45	PCMT1	-0.295	PP7080	-0.2
C1orf159	-0.45	RPIA	-0.295	SH3BP2	-0.2
DCP2	-0.45	SBF2	-0.295	SIK3	-0.2
CEP70	-0.445	STX12	-0.295	SNX5	-0.2
DLG3	-0.445	TIA1	-0.295	SYF2	-0.2

FGF14	-0.445	ZBTB44	-0.295	TLE3	-0.2
FLNB	-0.445	ZBTB45	-0.295	TMEM230	-0.2
LOC439994	-0.445	CNOT3	-0.29	TSPAN6	-0.2
TNRC6B	-0.445	GEMIN2	-0.29	VAMP4	-0.2
CCL28	-0.44	GTF2H2B	-0.29	VCPIP1	-0.2
PELI2	-0.44	LOC440944	-0.29	YIPF6	-0.2
SMC5	-0.44	MRPS18A	-0.29	ABHD13	-0.195
WDR25	-0.44	NEURL4	-0.29	ACER3	-0.195
FBRSL1	-0.435	RCAN2	-0.29	AP1G1	-0.195
G2E3	-0.435	RTN2	-0.29	BNIP3L	-0.195
PLXNA1	-0.435	TAF12	-0.29	CCDC90B	-0.195
SPOPL	-0.43	ZNF507	-0.29	CREM	-0.195
STON1	-0.43	ABCA6	-0.285	CTNNBIP1	-0.195
C18orf25	-0.425	ATL3	-0.285	HDGFRP3	-0.195
DCAF17	-0.425	ATP6V1G2	-0.285	IMPACT	-0.195
DYRK2	-0.425	BAALC	-0.285	ISCA1	-0.195
ISCU	-0.425	C1D	-0.285	KCTD10	-0.195
LRRC49	-0.425	CPNE3	-0.285	MAP3K13	-0.195
NUP107	-0.425	DSEL	-0.285	MECP2	-0.195
ABL2	-0.42	INSIG1	-0.285	TPT1-AS1	-0.195
C3orf23	-0.42	MSI2	-0.285	WDR7	-0.195
DEPDC5	-0.42	PDE4DIP	-0.285	AKT3	-0.19
IFNAR1	-0.42	PTP4A2	-0.285	C12orf65	-0.19
MAGI1	-0.42	PTRH2	-0.285	CAST	-0.19
SLC35B4	-0.42	SARS2	-0.285	CEBPG	-0.19
TNKS	-0.42	YME1L1	-0.285	HLTF	-0.19
NEDD4	-0.415	ZBTB1	-0.285	KLHL5	-0.19
OSBPL3	-0.415	APPBP2	-0.28	MAPKAP1	-0.19
RAB3B	-0.415	C20orf20	-0.28	MFSD8	-0.19
SLC23A2	-0.415	CBFB	-0.28	MLLT3	-0.19
CDC42SE2	-0.41	CD164	-0.28	RBPMS	-0.19
CERS6	-0.41	DNAJC3	-0.28	SCD	-0.19
IMMP2L	-0.41	FAM208A	-0.28	SERP1	-0.19
RGN	-0.41	MAPRE2	-0.28	SH3GLB1	-0.19
MPHOSPH9	-0.405	PEX19	-0.28	SLC25A37	-0.19
MSRA	-0.405	PHC3	-0.28	STAM2	-0.19
NRF1	-0.405	RASSF4	-0.28	STRN	-0.19
SPCS3	-0.405	SRR	-0.28	TRIM27	-0.19
USP47	-0.405	UST	-0.28	ZNF576	-0.19

ZNF138	-0.405	ANKS3	-0.275	ADH1B	-0.185
C14orf79	-0.4	CASP6	-0.275	CLUAP1	-0.185
HNRNPUL2	-0.4	DCUN1D1	-0.275	DPY19L4	-0.185
KRT8	-0.4	GFPT1	-0.275	GATAD2B	-0.185
MUTED	-0.4	HMGN3	-0.275	IRF2BP2	-0.185
RASAL2	-0.4	INO80C	-0.275	KDM1B	-0.185
SLC9A7	-0.4	MRPL35	-0.275	KHSRP	-0.185
UBR3	-0.4	SGSM3	-0.275	LOC100128252	-0.185
ZEB1-AS1	-0.4	SLC30A7	-0.275	RALA	-0.185
ZNF862	-0.4	TGIF2	-0.275	REEP5	-0.185
CPNE7	-0.395	TMEM41A	-0.275	SRSF10	-0.185
FAM173B	-0.395	ZNF697	-0.275	TMBIM6	-0.185
LAMC1	-0.395	AKIRIN2	-0.27	TMEM136	-0.185
PDHB	-0.395	CHD3	-0.27	TRAF3IP1	-0.185
PIR-FIGF	-0.395	GABPB2	-0.27	VGLL3	-0.185
RTKN	-0.395	HSD17B7	-0.27	ZNF652	-0.185
TMEM50B	-0.395	KANSL1L	-0.27	ABHD5	-0.18
EIF2C2	-0.39	KIAA0564	-0.27	CDS2	-0.18
JHDM1D	-0.39	L3MBTL3	-0.27	CIAO1	-0.18
MBLAC2	-0.39	MORC3	-0.27	EWSR1	-0.18
TGFBR1	-0.39	PDE12	-0.27	HSPBP1	-0.18
TMCC1	-0.39	RAB11FIP1	-0.27	MAP4K4	-0.18
UBR1	-0.39	RWDD2A	-0.27	ME1	-0.18
C20orf24	-0.385	SIAH1	-0.27	MRPL42	-0.18
MTMR11	-0.385	SOCS6	-0.27	NBN	-0.18
PBX1	-0.385	SPTLC2	-0.27	NDRG3	-0.18
ADAMTSL1	-0.38	ATP10A	-0.265	PRKD3	-0.18
CCDC91	-0.38	BTRC	-0.265	RBM39	-0.18
CHD6	-0.38	CREBRF	-0.265	STX7	-0.18
HIPK1	-0.38	CYB5R2	-0.265	STXBP5	-0.18
ITSN1	-0.38	FAM114A2	-0.265	SUPT3H	-0.18
MED6	-0.38	IPO7	-0.265	ZNF592	-0.18
PTBP3	-0.38	MEX3B	-0.265	ATG13	-0.175
QSER1	-0.38	RAB4A	-0.265	MPZL1	-0.175
CEP68	-0.375	TAF1D	-0.265	NAV2	-0.175
EIF2C3	-0.375	CAV2	-0.26	NCOA3	-0.175
FKBP14	-0.375	CPEB1	-0.26	SP1	-0.175
HMGCR	-0.375	CTHRC1	-0.26	STXBP6	-0.175
IGHMBP2	-0.375	ENPP1	-0.26	UBL3	-0.175

JAK2	-0.375
MAP2K7	-0.375
NPAS2	-0.375
PUS7	-0.375
SHC3	-0.375
ZNF480	-0.375
ARID5A	-0.37
C21orf91	-0.37
C22orf39	-0.37
CHCHD7	-0.37
FAM168B	-0.37
GTF2H2D	-0.37
LOC100506714	-0.37
RNF2	-0.37
VWA5A	-0.37
WNT5A	-0.37
ZNF207	-0.37
ABI2	-0.365
FGF1	-0.365
MGAT2	-0.365
MRS2	-0.365
SPINT2	-0.365
AHDC1	-0.36
ARHGAP32	-0.36
C20orf112	-0.36
ITGA1	-0.36
LRRC8C	-0.36
NEO1	-0.36
PMS1	-0.36
SETD8	-0.36
ABCC5	-0.355
DNAJC5	-0.355
FAM179B	-0.355
HACE1	-0.355
NIPSNAP3A	-0.355
NSD1	-0.355
PDK1	-0.355
SEPT6	-0.355
SLC25A22	-0.355

HS2ST1	-0.26
MIF4GD	-0.26
PAK1	-0.26
RCHY1	-0.26
RLIM	-0.26
RNASEH2A	-0.26
TIMM8A	-0.26
TMEM30A	-0.26
TMTC3	-0.26
ZNF211	-0.26
ZNF673	-0.26
ATL2	-0.255
BACE1	-0.255
BICD2	-0.255
CAB39L	-0.255
CEP112	-0.255
HIST1H2BC	-0.255
LOC100507463	-0.255
MGEA5	-0.255
MPPE1	-0.255
NFASC	-0.255
PBX3	-0.255
RGL1	-0.255
SLAIN2	-0.255
SLC35A2	-0.255
TIPRL	-0.255
TMF1	-0.255
TTC28-AS1	-0.255
VPS29	-0.255
ZC3H14	-0.255
ZFHX3	-0.255
ZNF846	-0.255
ALMS1	-0.25
DCAF5	-0.25
DCTN6	-0.25
KANSL2	-0.25
MEIS2	-0.25
MUT	-0.25
PRKCA	-0.25

UBQLN1	-0.175
UBR2	-0.175
WDR44	-0.175
WDR5	-0.175
ZFX	-0.175
ABCA8	-0.17
ARL4A	-0.17
CDH6	-0.17
CUL4B	-0.17
FAM126A	-0.17
GOT1	-0.17
GPR180	-0.17
KIAA0100	-0.17
MAN1C1	-0.17
PXMP4	-0.17
RABGEF1	-0.17
RBM12	-0.17
REEP3	-0.17
SCARB2	-0.17
SPATA2	-0.17
TMEM33	-0.17
TTC39C	-0.17
U2SURP	-0.17
ATP6V1G1	-0.165
CADM1	-0.165
CAMK2N1	-0.165
ENSA	-0.165
IMPAD1	-0.165
LNPEP	-0.165
NIPA2	-0.165
PIGK	-0.165
PLA2G12A	-0.165
SDC2	-0.165
SKIL	-0.165
SLC2A8	-0.165
SPRYD7	-0.165
STAU2	-0.165
TCF3	-0.165
BAHD1	-0.16

STX6	-0.355	RC3H2	-0.25	C19orf12	-0.16
SUPT4H1	-0.355	SNAI1	-0.25	CCDC47	-0.16
TRABD	-0.355	SPRED1	-0.25	COPS2	-0.16
VOPP1	-0.355	TANC1	-0.25	EEF1E1	-0.16
ZNF498	-0.355	TBX2	-0.25	GOLGB1	-0.16
ZRSR2	-0.355	TRERF1	-0.25	METTL2A	-0.16
ADAMTS5	-0.35	TRMT11	-0.25	MRI1	-0.16
CYB561D1	-0.35	UBASH3B	-0.25	MTERFD2	-0.16
GNB4	-0.35	ZCCHC11	-0.25	NAP1L1	-0.16
KLHL24	-0.35	ZFYVE1	-0.25	PCMTD1	-0.16
POLR1D	-0.35	ASB1	-0.245	PDS5A	-0.16
PPIL2	-0.35	C4orf46	-0.245	PGM2	-0.16
SNX30	-0.35	CHD9	-0.245	PPM1B	-0.16
UFM1	-0.35	CYP2U1	-0.245	PTPLAD2	-0.16
ZNF267	-0.35	FAM122B	-0.245	SEL1L	-0.16
ACADM	-0.345	HUS1	-0.245	STK10	-0.16
ACADSB	-0.345	MCPH1	-0.245	SYAP1	-0.16
AGPAT5	-0.345	MED13L	-0.245	USP32	-0.16
ATG4A	-0.345	MRE11A	-0.245	WDFY3	-0.16
C7orf42	-0.345	PCGF6	-0.245	WDR36	-0.16
C8orf83	-0.345	RORA	-0.245	YIPF4	-0.16
DHCR7	-0.345	RPRD1A	-0.245	ATG2B	-0.155
FAM50B	-0.345	RPS6KB1	-0.245	CYBRD1	-0.155
LMCD1	-0.345	SSBP3	-0.245	DCBLD1	-0.155
PODXL	-0.345	SYTL2	-0.245	ELP2	-0.155
PRPF38A	-0.345	TCFL5	-0.245	FAM103A1	-0.155
RNF44	-0.345	ADSS	-0.24	FAM82B	-0.155
SGTB	-0.345	C6orf89	-0.24	LOC401093	-0.155
TBL1XR1	-0.345	C7orf23	-0.24	PDCL3	-0.155
TBP	-0.345	CCRL1	-0.24	PRDX6	-0.155
ACAP2	-0.34	EP400	-0.24	PTPLA	-0.155
AP1AR	-0.34	HAUS6	-0.24	RTN3	-0.155
ARNTL2	-0.34	METTL8	-0.24	SCN9A	-0.155
CCDC77	-0.34	PHACTR2	-0.24	UBE2Q2	-0.155
CLASP1	-0.34	TMEM106B	-0.24	ZCCHC10	-0.155
CPSF2	-0.34	TPP2	-0.24	ZNF148	-0.155
GOLGA1	-0.34	ZHX3	-0.24	APH1B	-0.15
GSK3B	-0.34	ZNF74	-0.24	ARMC8	-0.15
IGF1R	-0.34	C12orf29	-0.235	C11orf73	-0.15

KITLG	-0.34	C5orf22	-0.235	CCDC72	-0.15
LPGAT1	-0.34	CDC73	-0.235	DOCK5	-0.15
MED28	-0.34	DNAJB6	-0.235	GUCY1B3	-0.15
MEF2C	-0.34	FOXF1	-0.235	MARCH6	-0.15
OSGIN1	-0.34	IREB2	-0.235	PIGN	-0.15
PFAS	-0.34	ISG20L2	-0.235	PTPN18	-0.15
RABEP1	-0.34	LRRFIP2	-0.235	TBC1D19	-0.15
SMAD6	-0.34	PMEPA1	-0.235	SUV420H1	0.15
VDR	-0.34	PRPF18	-0.235	SENP3-EIF4A1	0.17
XRN1	-0.34	PTGER2	-0.235	LOX	0.175
ZMYM4	-0.34	RNF141	-0.235	ITGB1BP1	0.18
ADAMTS8	-0.335	WIPF1	-0.235	THRA	0.18
ATXN1	-0.335	ZNF516	-0.235	LOC284385	0.195
NPR3	-0.335	ACP1	-0.23	TNFAIP6	0.225
PHKA1	-0.335	AGPS	-0.23	C16orf5	0.23
SAR1A	-0.335	AIMP1	-0.23	ANGEL1	0.235
SDHD	-0.335	APPL1	-0.23	DOHH	0.24
SMARCA1	-0.335	ARL8B	-0.23	USP33	0.25
SMN1	-0.335	BAZ2A	-0.23	FLCN	0.255
WWTR1	-0.335	BCORL1	-0.23	TRPM4	0.255
ZADH2	-0.335	CRYBB2P1	-0.23	PSG1	0.265
CMTM7	-0.33	DCUN1D4	-0.23	CAMK2D	0.275
GNB1	-0.33	DDHD2	-0.23	MBD1	0.275
IP6K2	-0.33	DNAJC18	-0.23	LACTB	0.28
KCTD1	-0.33	EIF2AK2	-0.23	PTPN4	0.28
NIN	-0.33	ERC1	-0.23	NMT2	0.29
PPP2R5A	-0.33	GOLT1B	-0.23	SLC11A2	0.29
SNRNP48	-0.33	HCFC2	-0.23	N4BP1	0.295
TMEM55A	-0.33	NUS1	-0.23	SEPT1	0.295
TNFRSF6B	-0.33	PAXIP1	-0.23	LOC100652739	0.305
ATP2C1	-0.325	PWWP2A	-0.23	WDYHV1	0.305
CRLF3	-0.325	SBDSP1	-0.23	CREB3L2	0.31
DEGS1	-0.325	SEH1L	-0.23	GTPBP3	0.31
EFNA4	-0.325	SNX13	-0.23	LOC652276	0.31
GTF2H2C	-0.325	TNPO1	-0.23	RAD51D	0.31
KANK1	-0.325	VHL	-0.23	C1orf27	0.32
LIN52	-0.325	ZNF780A	-0.23	PLEKHF1	0.32
MAN2A1	-0.325	BBIP1	-0.225	ARHGEF19	0.335
MAP3K2	-0.325	BMP2K	-0.225	NAPB	0.345

MED23	-0.325	CARD8	-0.225	TYW1B	0.35
MTA1	-0.325	CD44	-0.225	METTL18	0.355
PAFAH1B1	-0.325	CGGBP1	-0.225	WDR4	0.36
RALGAPB	-0.325	COX15	-0.225	NFATC1	0.365
SERPINB8	-0.325	CREB1	-0.225	PINX1	0.365
SYNJ2BP	-0.325	GSTM2	-0.225	PPP2R5B	0.365
ZCCHC9	-0.325	HIRA	-0.225	ECT2	0.37
ZNF785	-0.325	IER3IP1	-0.225	ABCC3	0.38
CCDC68	-0.32	KIF1B	-0.225	ZNF184	0.4
CCNY	-0.32	NSUN4	-0.225	EIF2B3	0.425
DUSP6	-0.32	NUFIP1	-0.225	TRIM52	0.43
EVI5	-0.32	PBRM1	-0.225	CLEC16A	0.45
FZD2	-0.32	PSMD12	-0.225	TXNDC16	0.46
LZTFL1	-0.32	RAB27A	-0.225	BCCIP	0.475
MAPRE1	-0.32	RNF170	-0.225	PMS2P5	0.485
MXD4	-0.32	RWDD4	-0.225	MAPK1	0.605
ODZ4	-0.32	TUSC2	-0.225	BCAP29	0.715
PKNOX1	-0.32	ULBP2	-0.225		

Supplemental Table 2. Top 20 miRNAs that lost their binding sites due to the APA events in CFIm25 knockdown fibroblasts.

miRNA	# of Sites Lost
miR-124-3p.1	131
miR-30-5p	120
miR-181-5p	103
miR-340-5p	95
miR-124-3p.2/506-3p	93
miR-15-5p/16-5p/195-5p/424-5p/497-5p	92
miR-101-3p.2	90
miR-23-3p	89
miR-200bc-3p/429	88
miR-9-5p	88
miR-144-3p	87
miR-182-5p	86
miR-19-3p	86
miR-27-3p	83
miR-101-3p.1	80
miR-17-5p/20-5p/93-5p/106-5p/519-3p	80
miR-128-3p	79
miR-130-3p/301-3p/454-3p	79
miR-29-3p	77
miR-141-3p/200a-3p	76

*MiRNAs in bold are known to play a role in fibroblast differentiation/proliferation or tissue fibrosis.

Supplemental Table 3. Common DEGs in CFIm25 knockdown fibroblasts and the known IPF gene signature.

Gene ID	Log2(si_CFIm25/si_Con)	Log2(IPF/Control)
ABCA3	-1.91926	-1.0209542
ACTG2	-2.35198	1.47459924
ADAMTS14	1.17731	2.63599873
ADAMTS6	1.64319	1.09538168
AFF2	2.27541	-1.1947328
AFF3	1.22945	-1.6453562
ALPK2	2.64008	1.3146374
ANKRD29	-1.13402	-1.1229262
ANLN	-3.34674	2.01294529
ANXA3	2.4787	-1.4035878
AOX1	1.71616	1.22872774
APCDD1	-2.16801	1.00114504
ARRB1	-1.59741	-1.0718066
ASB5	1.68517	1.94833333
ASIC1	1.74966	1.47220738
ASPM	-2.41917	1.47075064
BDNF	1.87847	-1.6816031
BEX1	2.62369	-1.4555025
BOC	1.56377	1.16645038
BUB1B	-2.99253	1.01141858
C10orf10	2.28966	-1.1814377
CACNA2D3	2.53359	-1.0336005
CCBE1	1.31356	-1.2546692
CCDC80	2.68252	1.57409033
CCNB2	-2.49919	1.13652672
CDC45	-3.24191	1.09321883
CDCA2	-2.09534	1.17296438
CDH2	1.86774	2.21768448
CDK1	-3.38669	1.0038486
CDKN3	-2.18027	1.23724555
CENPA	-3.1059	1.33587786
CENPE	-2.05038	1.06561069
CENPF	-2.79223	1.09331425
CENPK	-1.67765	1.35080789
CENPM	-2.11488	1.25062977
CEP55	-2.97455	1.58922392
CFB	1.07436	1.49012723
CFI	2.43825	1.38724555

CHI3L2	2.9285	-1.0806616
CHRM2	1.24087	-1.7261578
CKAP2L	-3.63755	1.29292621
CLCA2	3.48881	1.90713104
CLEC3B	2.15033	-1.1264822
CLGN	2.07775	1.07167939
CNTN3	1.55014	2.06971374
COL14A1	1.23523	2.32713104
COL15A1	1.86738	1.89344784
COL3A1	1.29708	2.58252545
CRABP2	3.05319	2.05078244
CTHRC1	1.64762	2.46924936
CXCL6	3.26212	2.11110687
CYP1B1	3.47292	1.91522265
DENND3	-1.3741	-1.286056
DEPDC1B	-2.49164	1.44528626
DLC1	1.10484	-1.0132761
DLGAP5	-3.93007	1.68340331
DLL4	-1.92364	-1.5814249
DNAH5	-1.19579	1.40537532
DPYSL4	-1.29454	1.15358779
E2F7	-1.074	1.14372774
EFCC1	-1.63527	-1.5712087
EFNB2	1.05585	-1.048187
ESCO2	-4.64924	1.49136132
ESM1	-3.43525	-1.9379262
EXO1	-1.79802	1.0353626
EYA2	1.58751	1.40381043
F2RL2	1.72482	1.82664758
FAM13C	1.07527	1.0528117
FAM150A	-2.19627	1.35189567
FAM167A	1.58491	-2.6040712
FBN2	1.70961	1.44793893
FKBP11	3.00571	1.55675573
FOS	1.0202	-1.4555153
FOXF1	-1.08136	-1.113944
FRAS1	3.62633	-1.0709987
GADD45B	1.74883	-1.5455725
GALNT15	4.13775	1.47670483
GREM1	2.73423	3.38742366
HMMR	-4.33037	1.43556616

HSD17B2	-4.14582	-1.7285814
HSD17B6	-2.24649	-1.4505344
IGDCC4	1.36209	2.33412214
IGF1	2.85768	2.18835242
IGFBP5	1.12243	1.36569338
IL13RA2	1.67894	4.19562977
IL6	2.42978	-2.1046501
IRS2	1.25219	-1.106215
ITGA7	1.06395	1.4365458
IVL	2.69804	1.46294529
JUNB	1.31393	-1.390986
KCTD16	3.02208	-1.2212659
KIAA0101	-2.56449	1.33110051
KIAA1462	-1.45268	-1.0541476
KIF20A	-3.12424	1.50719466
KLF2	-1.02441	-1.3188232
KLF4	1.02742	-1.6401399
KLF6	-1.02105	-1.2372519
KLHL13	-1.07562	1.30507634
KLHL4	2.76745	1.01649491
KNTC1	-1.00242	1.18386768
LMCD1	2.03881	-1.0479135
LRP4	-1.22664	-1.2818448
MDGA1	1.46777	-1.251902
MEDAG	1.4759	2.07821883
MELK	-1.43661	1.259243
MEX3A	-1.60588	1.03235369
MMP1	1.24466	5.25875318
MMP10	-3.90203	2.97176209
MMP11	-1.24676	2.23676845
NDRG4	-2.40982	-1.9253753
NLGN1	1.85829	1.11262087
NME5	-1.06357	1.18517176
NPR3	1.57756	-1.1933524
NUF2	-3.57133	1.25318702
OSR2	1.16886	1.32763995
PBK	-3.56782	1.25137405
PDGFD	2.83817	1.21368321
PHLDA2	-1.20783	1.06866412
PLK4	-2.55742	1.10657125
POLQ	-3.53327	1.05310433

PSAT1	2.75283	2.06625318
PTGS2	-1.4558	-1.2176781
RAB27B	1.65965	1.14827608
RGCC	-1.83785	-1.500229
S1PR1	1.11278	-1.0245102
SCG2	2.17708	1.19209924
SCG5	1.54755	2.99074427
SEMA3B	1.38483	-1.0817557
SERPINF1	1.45504	1.65510178
SFRP2	3.08421	3.2695229
SGCG	3.68212	-1.7925064
SIK1	1.56189	-1.3305662
SLC1A3	2.72257	1.09741094
SLC27A6	1.21923	-1.4960623
SLC39A8	1.90731	-1.0824936
SOCS3	1.96148	-1.5212659
SPAG4	1.87982	1.4253117
SPC25	-1.80218	1.01256997
SPP1	-1.78908	3.30293893
SSTR1	1.71087	-1.8697964
STC1	-1.55469	-1.4252545
STC2	1.86314	-1.5470356
STXBP6	1.1328	-1.9298346
SULF1	2.28765	1.46793893
TEK	1.42747	-1.1449809
TGFB3	1.68339	1.10923664
TMEM100	-1.02387	-1.748944
TMEM130	4.65364	-1.270528
TMEM26	1.25466	-1.065528
TOP2A	-3.15981	1.59639313
TSGA10	1.24526	1.29635496
TTK	-3.19864	1.69747455
TUBB2B	-2.20912	1.68152036
TUFT1	3.44077	-1.4920611
VCAN	2.69815	1.48886132
VNN2	1.60016	-1.0396501
WDR63	-1.25007	1.26304071
ZCCHC5	4.33955	1.22080153
ZNF469	1.54644	1.04293257