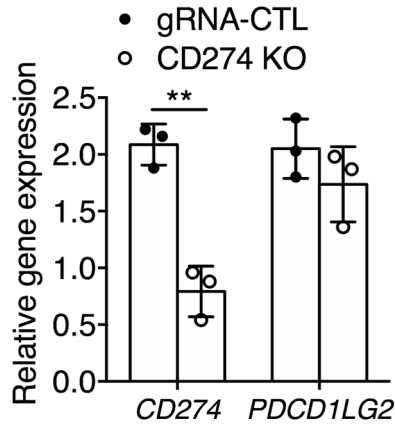
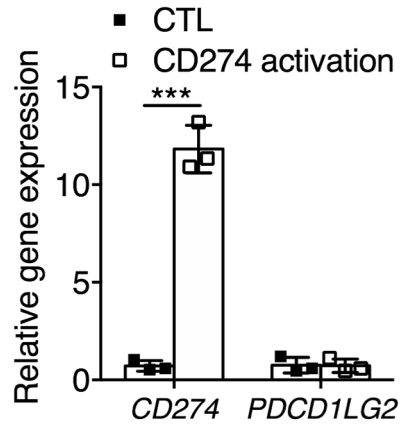
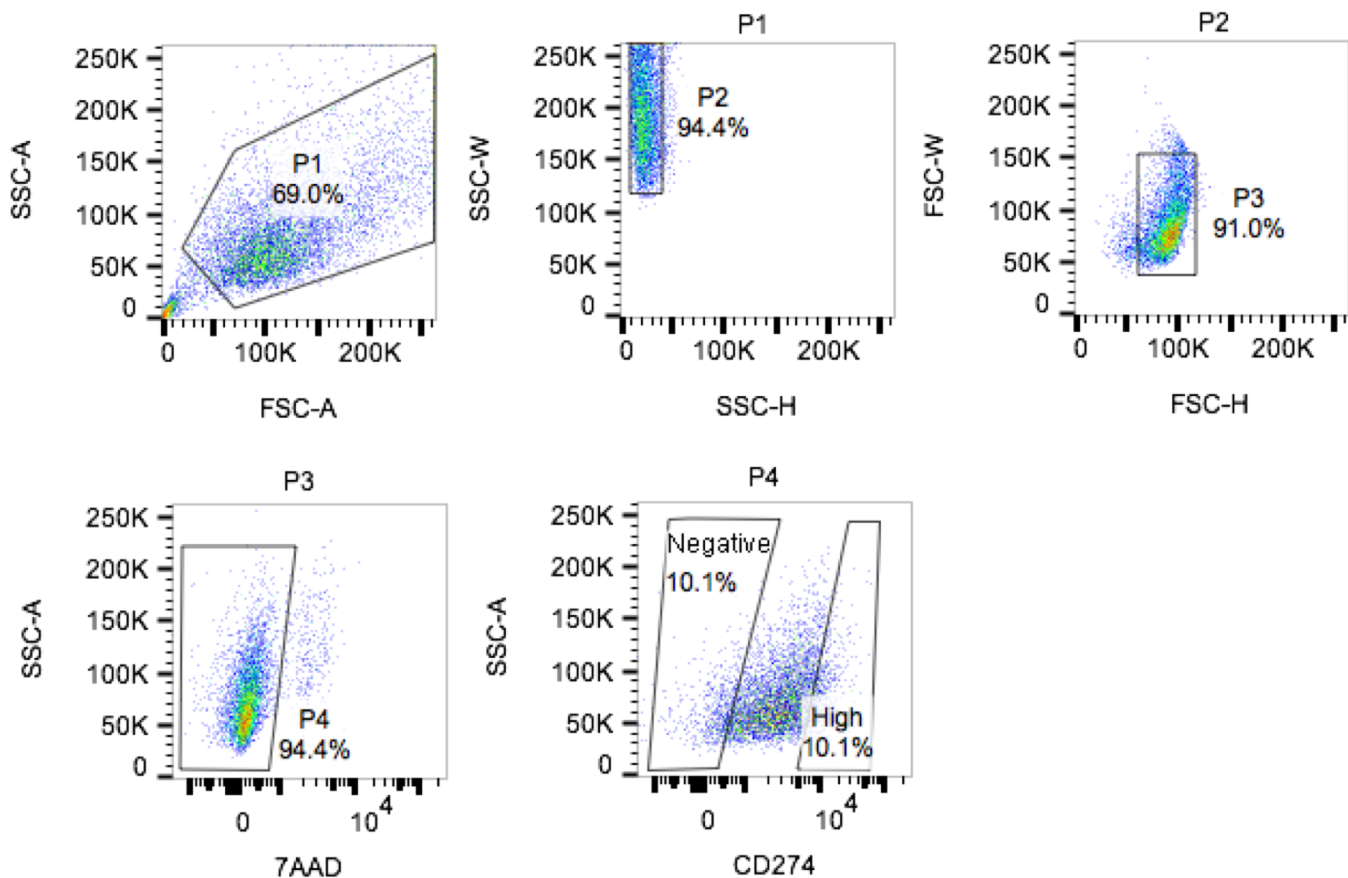


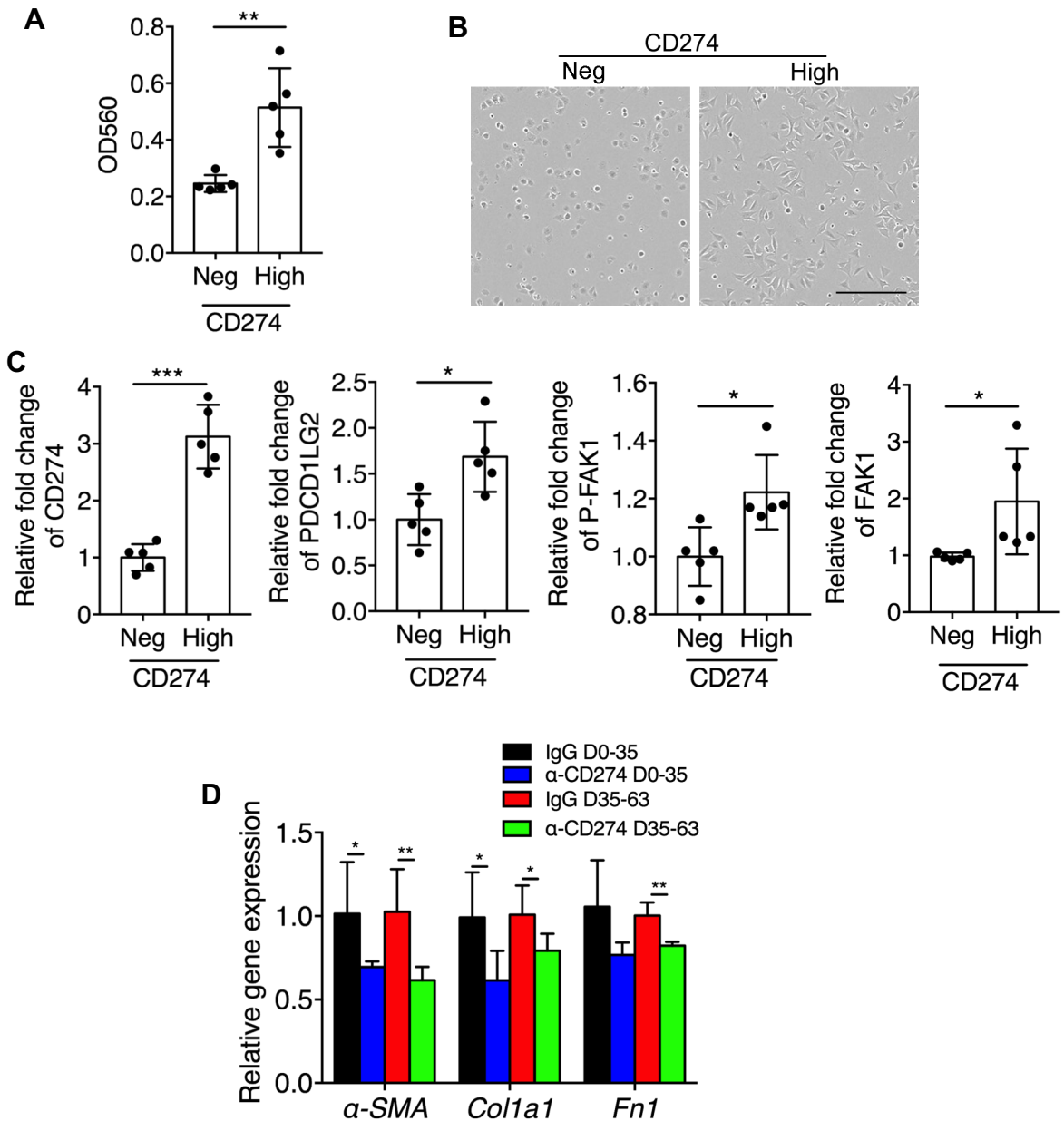
Supplementary Figure 1. (A) Western blot analyses of CD274, p-FAK1, FAK1 and GAPDH in healthy and IPF lung fibroblasts. GAPDH served as equal loading control. (B) Flow cytometry analysis of CD274 expression in CD31- CD45- EPCAM- mesenchymal cells. (C) Immuno-co-staining of CD274 and PDGFR β , Endomucin, CD8 α or α -SMA. Scale bar: 50 μ m.

A**B**

Supplementary Figure 2. KO and activation of CD274 in IPF lung fibroblasts. Gene expression of CD274, PDCD1LG2 in IPF lung fibroblasts after CD274 KO (A) or activation (B) by qRT-PCR. Data are mean \pm sem (n = 3 per group). ** $P < 0.01$, *** $P < 0.001$ by Two-way ANOVA.



Supplementary Figure 3. Fluorescence-activated cell sorting of CD274^{High} and CD274^{neg} fibroblasts. 7-aminoactinomycin D (7AAD) was used to exclude of nonviable cells.



Supplementary Figure 4. Cell adhesion assay of CD274^{Neg} and CD274^{High} IPF lung fibroblasts and expression of fibrotic markers in the lungs of the mice received IgG and α -CD274 after CD274^{High} fibroblasts injection: (A) Col IV-mediated Cell Adhesion. CD274^{High} and CD274^{neg} cells were harvested by flow sorting. Then these cells were allowed to attach to Col IV coated 48-well plate for 1 hr at 100,000 cells/well in serum free medium. Adherent cells were stained with and quantified at OD 560nm after extraction. (B) Representative image of CD274^{High} and CD274^{Neg} cells after 1hr culture on Col IV coated plate. Scale bar: 300 μ m. (C) Quantification of p-FAK1, FAK1, CD274 and PDCD1LG2 protein expression level in CD274 negative and high lung fibroblasts. D) Relative expression of α -SMA, *Col1a1* and *Fn1* by RT-PCR. Throughout, data are mean \pm sem (n = 5 per group). * P<0.05, ** P<0.01 by student's t test.

Supplementary Table 1: Top 50 up-regulated genes in invasive fibroblasts

	ID	geneName	logFC	Fold Change	PValue	FDR
1	ENSG00000240386	<i>LCE1F</i>	2.75223657	6.737608357	8.17E-30	7.11E-28
2	ENSG00000138623	<i>SEMA7A</i>	2.710360098	6.544849865	9.32E-101	3.19E-97
3	ENSG00000212724	<i>KRTAP2-3</i>	2.577089352	5.967345676	1.85E-36	2.79E-34
4	ENSG00000120217	<i>CD274</i>	2.566132578	5.922197393	9.58E-60	7.57E-57
5	ENSG00000213417	<i>KRTAP2-4</i>	2.342505916	5.071828336	9.46E-17	2.16E-15
6	ENSG00000180914	<i>OXTR</i>	2.336833403	5.051925637	4.17E-37	6.48E-35
7	ENSG00000078401	<i>EDN1</i>	2.334215058	5.042765221	7.88E-23	3.40E-21
8	ENSG00000214518	<i>KRTAP2-2</i>	2.180094259	4.53183162	9.24E-15	1.66E-13
9	ENSG00000187173	<i>LCE2A</i>	2.154248495	4.451367135	2.84E-17	6.99E-16
10	ENSG00000170961	<i>HAS2</i>	2.081307081	4.231904528	1.49E-50	6.64E-48
11	ENSG00000095752	<i>IL11</i>	2.07346639	4.208967559	1.94E-18	5.44E-17
12	ENSG00000113070	<i>HBEGF</i>	2.01446962	4.040320164	9.41E-40	1.86E-37
13	ENSG00000164283	<i>ESMI</i>	1.970071515	3.917875396	2.33E-48	8.55E-46
14	ENSG00000163273	<i>NPPC</i>	1.966400261	3.907918178	4.60E-28	3.35E-26
15	ENSG00000242550	<i>SERPINB10</i>	1.941935834	3.842208564	2.58E-33	3.24E-31
16	ENSG00000142871	<i>CYR61</i>	1.888455197	3.7023857	8.69E-30	7.50E-28
17	ENSG00000197632	<i>SERPINB2</i>	1.874314726	3.666274295	3.24E-27	2.18E-25
18	ENSG00000131016	<i>AKAP12</i>	1.821182941	3.533708271	5.18E-106	2.66E-102
19	ENSG00000106366	<i>SERPINE1</i>	1.81985067	3.530446538	1.46E-32	1.66E-30
20	ENSG00000139211	<i>AMIGO2</i>	1.698925951	3.246591681	2.64E-25	1.48E-23
21	ENSG00000134259	<i>NGF</i>	1.687485205	3.220947632	1.38E-22	5.77E-21
22	ENSG00000181751	<i>C5orf30</i>	1.660047093	3.160268404	3.31E-18	9.00E-17
23	ENSG00000118523	<i>CTGF</i>	1.648933175	3.136016553	3.48E-21	1.28E-19
24	ENSG00000140379	<i>BCL2A1</i>	1.598976094	3.029282436	6.70E-15	1.21E-13
25	ENSG00000127124	<i>HIVEP3</i>	1.591009915	3.012601637	1.95E-48	7.43E-46
26	ENSG00000128567	<i>PODXL</i>	1.583691253	2.99735768	4.79E-30	4.32E-28
27	ENSG00000132688	<i>NES</i>	1.507776322	2.843713892	2.87E-16	6.13E-15
28	ENSG00000169429	<i>CXCL8</i>	1.470696158	2.771556001	4.41E-08	3.00E-07
29	ENSG00000134775	<i>FHOD3</i>	1.450951596	2.733883178	5.11E-36	7.49E-34
30	ENSG00000113578	<i>FGF1</i>	1.449315153	2.730783903	2.07E-34	2.73E-32
31	ENSG00000135074	<i>ADAMI9</i>	1.423047766	2.681513963	2.26E-39	4.14E-37
32	ENSG00000243444	<i>PALM2</i>	1.421422775	2.678495319	1.10E-34	1.51E-32
33	ENSG00000103489	<i>XYLT1</i>	1.419491363	2.674911875	3.07E-25	1.71E-23
34	ENSG00000087494	<i>PTHLH</i>	1.418229352	2.672572995	1.31E-11	1.62E-10
35	ENSG00000122641	<i>INHBA</i>	1.417335032	2.670916791	1.56E-22	6.50E-21
36	ENSG00000169436	<i>COL22A1</i>	1.402470497	2.643538792	8.27E-22	3.23E-20
37	ENSG00000117525	<i>F3</i>	1.393307634	2.626802319	5.99E-53	3.42E-50
38	ENSG00000070404	<i>FSTL3</i>	1.367627631	2.580458861	1.06E-41	2.42E-39
39	ENSG00000090530	<i>LEPREL1</i>	1.36290476	2.572025169	2.04E-32	2.27E-30
40	ENSG00000154447	<i>SH3RF1</i>	1.361788135	2.570035228	1.02E-47	3.38E-45
41	ENSG00000176170	<i>SPHK1</i>	1.34425329	2.538987497	1.41E-16	3.13E-15
42	ENSG00000167772	<i>ANGPTL4</i>	1.332145878	2.517768919	3.80E-34	4.95E-32
43	ENSG00000151136	<i>BTBD11</i>	1.312979334	2.484540973	5.96E-38	9.87E-36
44	ENSG00000104722	<i>NEFM</i>	1.310949826	2.481048307	1.16E-21	4.45E-20
45	ENSG00000144583	42433	1.306771612	2.473873296	5.07E-17	1.21E-15
46	ENSG00000221852	<i>KRTAPI-5</i>	1.301583043	2.464992135	1.40E-06	7.12E-06
47	ENSG00000108854	<i>SMURF2</i>	1.288268896	2.442348199	1.05E-48	4.15E-46
48	ENSG00000197646	<i>PDCD1LG2</i>	1.281386289	2.430724336	3.79E-41	8.47E-39
49	ENSG00000170681	<i>MURC</i>	1.254144784	2.385257109	1.14E-19	3.61E-18
50	ENSG00000139174	<i>PRICKLE1</i>	1.227554205	2.341696663	5.35E-35	7.42E-33

Supplementary Table 2: Checkpoint gene expression

Gene expression	Stimulatory checkpoint molecules	Gene expression		Inhibitory checkpoint molecules
		non-invasive	invasive	
N/A	<i>CD27</i>	14.338	38.375	<i>CD274</i>
N/A	<i>CD28</i>	30.475	47.075	<i>PDCD1LG2</i>
N/A	<i>CD40</i>	56.593	86.603	<i>RGMB</i>
N/A	<i>IL2RB</i>	N/A		<i>PDCD1</i>
N/A	<i>TNFRSF9</i>	N/A		<i>ADORA2A</i>
N/A	<i>TNFRSF4</i>	No change		<i>CD276</i>
N/A	<i>TNFSF18</i>	N/A		<i>VTCN1</i>
N/A	<i>ICOS</i>	N/A		<i>BTLA</i>
		N/A		<i>CTLA-4</i>
N/A, not available.		N/A		<i>IDO1</i>
		N/A		<i>KIR3DL1</i>
		N/A		<i>LAG3</i>
		N/A		<i>HAVCR2</i>
		N/A		<i>C10orf54</i>

Supplementary Table 3. Patient sample information

Sample ID	Sex	Age	Donor Disease status	Passage of Fibroblasts for RNA-seq
IPF006-15	F	75	IPF	P3
IPF007-14	M	59	IPF	P4
IPF006-15	F	75	IPF	P6
IPF011-14	M	73	IPF	P4
IPF001-14	M	68	IPF	P4
IPF002-14	M	66	IPF	P5
IPF001-15	M	72	IPF	P5
IPF003-15	F	68	IPF	P4
IPF001-15	M	72	IPF	P3
CC009-15	M	71	Normal	P4
CC007-15	M	21	Normal	P4
CC008-15	F	50	Normal	P4
CC006-14	M	49	Normal	P5
CC003-14	M	17	Normal	P4
CC003-15	M	52	Normal	P4
CC004-14	M	66	Normal	P5
CC008-14	M	26	Normal	P5
CC002-14	M	23	Normal	P4