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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section). n/a Confirmed

	\boxtimes	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	\boxtimes	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
	\square	A description of all covariates tested
	\square	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	\boxtimes	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
	\boxtimes	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> values as exact values whenever suitable.
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\ge		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes		Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
	\boxtimes	Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on statistics for biologists may be useful.

Software and code

Policy information ab	pout <u>availability of computer code</u>
Data collection	No software was used to collect data.
Data analysis	Seurat v2.2 was used to process single cell data. STAR software v2.4.2a and DESeq2 v1.14.0 were used for bulk RNAseq. SingleR v1.0 was used to annotate the samples and is available at https://github.com/dviraran/SingleR. All figures and tables were generated using R, and the code for generating the figures is available at: https://github.com/dviraran/SingleR/manuscript_figures/. FlowJo v10.5.3 was used to analyze flow cytometry data. ImageJ 1.51 and ImageScope v12.3.3 were used for image analysis.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the findings of this study are available from the corresponding author upon request. RNAseq data have been deposited in the GEO depository under accession numbers GSE111664, GSE111690, and GSE114005 and at ArrayExpress under accession number E-MTAB-7142.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences Behavioural & social sciences

For a reference copy of the document with all sections, see <u>nature.com/authors/policies/ReportingSummary-flat.pdf</u>

Life sciences

Study design

All studies must dis	close on these points even when the disclosure is negative.
Sample size	Sample sizes were based on statistical analyses that established significant differences between groups in previous studies.
Data exclusions	Data were not excluded from the analysis.
Replication	All findings were mutiply replicated to confirm reproducibility as indicated in the text. All attempts at replication were successful.
Randomization	Groups were allocated randomly for in vitro assays and for mouse models of fibrosis. Human samples for analysis were selected randomly.
Blinding	Investigators were blinded with respect to group allocation for all assays including measurement of lung collagen and image analysis for quantitation of gap closure and cell number in photomicrographs.

Materials & experimental systems

Policy information about availability of materials



Antibodies

Antibodies used

SiglecF- APC (eBioscience, cat#50-1702-82, clone 1RNM44N, lot 4285690, dilution 1:100), MHCII-APC-Cy7 (eBioscience, cat#47-5321-82, clone M5/114.15.2, lot 4310394, dilution 1:100), CD11c-PE (BD Biosciences, cat#557401, clone HL3, lot 7012770, dilution 1:100), SiglecF (R&D Systems, cat#AF1706, lot KPA011707A, dilution 1:100), Mertk (R&D Systems, cat#AF591, lot DGS05, dilution 1:100), PDGFRbeta (eBioscience, cat#14-1402-82, clone APB5, lot 4322162, dilution 1:100), CD68 (Abcam, clone KP1, cat#ab955, lot GR3192728, dilution 1:100), MafB (Sigma, cat#HPA005653, lot 6117647, dilution 1:100), Alexa fluorophore secondary antibodies (Invitrogen and Abcam), PDGF-AA (Millipore, 07-1436, lot 3100458, dilution 1:100 or 0.05 microgram/mL), Rabbit 1gG isotype control (Abcam, cat#ab199376, lot GR3195151-2, 0.05microgram/mL), PDGFRalpha (R&D Systems, cat#AF1062, lot HMQ0217091, dilution 1:100). Secondary antibodies, all Donkey used at dilution 1:200: anti-goat 555 (Invitrogen, cat#A21432, lot 1249013), anti-goat 647 (Invitrogen, cat#A21447, lot 1977345), anti-rabbit 555 (Abcam, cat#ab150062, lot GR297073-1), anti-rabbit 647 (Abcam, cat#ab150063, lot GR-289647-4), anti-rat 555 (Abcam, cat#ab150154, lot GR2901144-1), anti-rat 647 (Abcam, cat#ab150155, lot GR303632-3).

Validation

All antibodies used were commercially available with accompanying validation information available at vendor websites.

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Eukaryotic cell lines

Policy information about <u>cell line</u>	<u>25</u>
Cell line source(s)	Flbroblasts 3T3 cells from ATCC.
Authentication	The cell line was used directly from the vendor. No further authentication was performed.
Mycoplasma contamination	Mycoplasma testing was not performed after purchase.
Commonly misidentified lines (See <u>ICLAC</u> register)	We did not use any commonly misidentified cell lines per the current ICLAC register.
Research animals	
Policy information about studies	involving animals; ARRIVE guidelines recommended for reporting animal research
Animals/animal-derived mater	ials Mouse, 129S1 and C57BL/6 ages 8-12 weeks of both sexes were used.
Human research participants	
Policy information about studies	involving human research participants
Population characteristics	Lung samples were acquired from patients with idiopathic pulmonary fibrosis (IPF) at the time of lung transplant or from control

and 1 with nintedanib. For unused donor controls, demographic data were not collected.

ranging in age from 49 to 67, 5 females and 1 male. At the time of transplant, one patient was on treatment with pirfenidone

Method-specific reporting

n/a Involved in the study

 ChIP-seq

 Flow cytometry

 Magnetic resonance imaging

Flow Cytometry

Plots

Confirm that:

The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

 \bigotimes All plots are contour plots with outliers or pseudocolor plots.

A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Mouse lungs were collagenase digested into single cell suspensions as described in Methods.
Instrument	BD FACSAria2 or SONY SH800 FACS
Software	FlowJo
Cell population abundance	Cell populations depicted in Supplementary Figure 5.
Gating strategy	Gating strategy depicted in Supplementary Figure 5.

X Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.