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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>.

Stat	istica	l 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	a Confirmed			
	X Th	he $\underline{\text{exact sample size}}(n)$ for each experimental group/condition, given as a discrete number and unit of measurement		
	X AI	n indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly		
		he 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.		
\boxtimes	A	description of all covariates tested		
	X A	description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons		
	⊠ A	full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>ariation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)		
	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 <i>Give P values as exact values whenever suitable.</i>			
\boxtimes	Fc	or Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings		
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes			
	Es	stimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated		
	Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)			
Our web collection on <u>statistics for biologists</u> may be useful.				
Software and code				
Poli	cy infor	rmation about <u>availability of computer code</u>		
Da	ata coll	ection Las X		
Da	ata ana	llysis Graphpad prism 7.0d, ImageJ 1.50i		
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 <u>availability of data</u>

All manuscripts must include a <u>data availability statement</u>. 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

Biochemichal data and imaging data are available upon request.

Field-spe	cific reporting		
Please select the be	est fit for your research. If you are not sure, read the appropriate sections before making your selection.		
∑ Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences		
For a reference copy of t	he document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf		
Life scier	ices study design		
All studies must dis	close on these points even when the disclosure is negative.		
Sample size	minimum of 3 biological replicates		
Data exclusions	no data were excluded		
Replication	all attempts to replicate were succesful.		
Randomization	Random selection of sample from the population was performed		
Blinding	Blinding was performed		
Materials & experimental systems n/a Involved in the study Unique biological materials Antibodies Palaeontology Palaeontology Human research participants Methods n/a Involved in the study ChIP-seq Flow cytometry MRI-based neuroimaging			
Unique biolo	ogical materials		
,	about <u>availability of materials</u>		
Obtaining unique	materials Unique Material used are available from author.		
Antibodies			
Antibodies used	Goat anti-Human IgM-MU chain specific antibody (Sigma-Aldrich #10759-1MG), rabbit anti-CD18 antibody (Acris Antibodies GmbH, Germany, Cat. Number B0842-1), biotinylated goat anti-rabbit antibody (Dako Agilent Pathology Solution, USA), phosphorylated Akt serine 473 (Cell Signaling Technology, Cat. Number 4060), pan Akt antibody (Cell Signaling Technology), GAPDH antibody (Cell Signaling Technology).		
Validation	Were already validated in previous pubblications.		

Eukaryotic cell lines

Policy information about <u>cell lines</u>

Cell line source(s)

CLL cells (# Hs 505.T, ATCC® CRL-7306™), BMDMs were obtained from bone marrows isolated from femurs and tibias of C57Bl/6J mice, Neutrophils were obtained from bone marrow isolated from femurs and tibias of C57Bl/6J mice, PBMCs were isolated from blood, LL97a derived from a 48 years-old male (ATCC, Manassas, USA), CCD-16Lu obtained from a 35 years old male that died of astrocytoma —a disease unrelated to IPF - (ATCC), NHLF (#CC-2512; Lonza), DHLF-IPF (#CC-7231, Lonza, Switzerland).

Authentication	N/A
Mycoplasma contamination	Cells were negative for Mycoplasma and routinely tested.
Commonly misidentified lines (See <u>ICLAC</u> register)	N/A

Animals and other organisms

Policy information about <u>studies involving animals</u> ; <u>ARRIVE guidelines</u> recommended for reporting animal research				
Laboratory animals	C57BL/6J and Balb/c mice, males, 6-8 weeks.			
Wild animals	N/A			

Wild animals

N/A

Field-collected samples

N/A

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).

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 Cells were obtained from lymph nodes and spleen from naive C57BL/6. Then the cells were purified with CD4 T cell isolation Kit

and with CD25 biotin and microbeads anti-biotin. After, the cells were cultured for 72 hours in a 96-wells plate with anti-CD3/ CD28 coated (1 ug/ml), TGF-B (1 ng/ml) or Cl27C (1, 3, 10 or 30 uM). After 72 hours, the cells were harvested and stained with PBS (2% Bovine serum fetal) and anti-CD4 BV450 and fixable viability dye APC-Cy7 for 10 minutes. Then, the cells were fixed and permeabilized with intracellular fixation and permeabilization buffer set (eBioscience). At permeabilization process, anti-FoxP3 APC was used. After the staining, the cells were acquired with FACS VERSE machine and analyzed by FlowJo X software.

Instrument FACS VERSE

Software FACSDiva for data acquisition and FlowJo X for post-acquisition analyzes.

Cell population abundance 50.000 events

Gating strategy Doublets were excluded by FSC-H and FSC-A gating (G1) and cell debris were excluded by SSC-A and FSC-A gating (G2) for all flow

cytometry analysis. Proportion of viable cells was obtained by staining with fixable viability dye APC-Cy7.

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