

Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- ☐ ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☐ ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ 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.
- ☒ ☐ A description of all covariates tested
- ☐ ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☐ ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☐ ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ ☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ ☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☒ ☐ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection

Images stained with H&E, Masson's Trichrome, Toluidine blue, and immunohistochemistry (IHC-DAB) and immunofluorescence (IF) were acquired with the Zeiss AxioScan.Z1 slide scanner, the Olympus VS-120 slide scanner, and the Leica Widefield inverted epifluorescence microscope equipped with a Q-Imaging MicroPublisher 5.0 RTC camera, Halogen and Mercury Arc Illumination, and Perkin Elmer Volocity software (Quorum Technologies, Puslinch, ON, Canada). Plan-Apochromat objectives were used (HCX PL APO, 40x/1.25-0.75, oil), in addition to a Fluotar objective (HC PL FLUOTAR, 10x/0.30, Ph1).

Images of immunofluorescence-stained cultured cells were acquired with the Zeiss Axio Observer 7 inverted confocal microscope equipped with a LSM 800 scan head and ZEN software (Zeiss, Oberkochen, Germany). Plan-Apochromat (PApo) objectives were (Zeiss, 20x, PApo 20x/0.8, 10x, PApo, 10x/0.45, and 63x, NA 1.4, Oil-DIC).

Live phase-contrast images were acquired with an Axio Imager upright microscope equipped with an AxioCam HRm camera, Apotome 2 structured illumination and ZEN software (Zeiss, Oberkochen, Germany; 40x/1.0 water-Immersion objective).

For SHG imaging of highly aligned collagen in implant capsule, images were acquired with a Nikon A1R HD MP+Multiphoton Imaging System (CF175 Apochromat 25x/1.10 NA, 2.0 mm WD, water) equipped with Nikon Halogen Illumination and NIS-elements AR software.

AFM measurements were acquired using AFM NanoWizard 4 and analysed using JPK Data Processing software (JPK, Berlin, Germany).

Luciferase activity was determined by light production from a luciferin substrate (Promega) using Centro LB960 Microplate Luminometer (Berthold Technologies).

Flow-cytometry samples were acquired using a Sony SA3800 spectral cell analyser, and analysed using FlowJo software (BD, 2019).

Western blot data were detected with the LI-COR system (Odyssey, LI-COR Biosciences).

Data analysis

Data and statistical analyses were performed using GraphPad Prism 9.

Image analysis was performed using Fiji (Image J). A Fiji customized macro was used to analyse the recruitment of active $\beta 1$ integrin to focal adhesions, and is available for download from GitHub (<https://github.com/NinaNoskovicova/Noskovicova-N.-et-al.-2021-NBE>).

Image processing was done using Adobe Photoshop CS4 (Adobe System, San Jose, CA).

Flow-cytometry data were analysed using FlowJo software (BD, 2019).

AFM data were analysed using JPK Data Processing software (JPK, Berlin, Germany).

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 and reviewers. 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 main data supporting the results in this study are available within the paper and its Supplementary Information. The data used to make the figures are available from figshare with the identifier <https://doi.org/10.6084/m9.figshare.14319758>. The raw and analysed datasets generated during the study are too large to be publicly shared, yet they are available for research purposes from the corresponding author on reasonable request.

Field-specific reporting

Please select the one below that is the best 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 the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Statistical tests were performed as indicated in Methods and in the figure legends, to assure appropriate sample sizes.
Data exclusions	No data were excluded, except from experiments that failed for obvious technical reasons.
Replication	Experiments have been repeated several times by the same or different experimenters, with reproducible outcomes.
Randomization	Positions of soft and stiff silicone implants were randomly allocated and shifted in different animals on the dorsum of the animals. The osmotic pump was allocated to the left subcutaneous pocket, and silicone implants to the right subcutaneous pockets, on the dorsum of the animals.
Blinding	The investigators were not blinded to group allocation during data collection/and or analysis.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

Immunohistochemistry (histology, IHC-DAB staining):

α -SMA (ms IgG1, 1:100, 611012, BDTL), β 1 integrin (ms IgG1, 1:100, MAB1965, Chemicon), α -SMA (rb IgG, 1:100, ab5694, Abcam), TGF- β 1 (rb IgG, 1:200, sc-146, Santa Cruz), pSmad3 (s423/425) (rb IgG, 1:20, CS9520s, Cell Signaling), MRTF-A (rb IgG, 1:50, sc-32909, Santa Cruz)

anti-m or anti-rb secondary horseradish peroxidase-conjugated antibodies (Envision+HRP System Labelled Polymer anti-m IgG RTU, Dako or goat-anti rb IgG, HRP polymer, ab214880, Abcam).

Immunofluorescence staining:

α -SMA (ms IgG2a, 1:100, α -SM1, a kind gift from Dr. Giulio Gabbiani, University of Geneva, Switzerland), collagen I (rb IgG, 1:100, 600-401-103-05, Rockland), fibronectin (rb IgG, 1:500, F3648, Sigma), CD68 (ms IgG1, 1:100, ab31630, Abcam), integrin β 1 (CD29, clone 9EG7, rat IgG2a, 1:100, 550531, BD Pharmingen), vinculin (rb IgG, 1:100, 700062, ThermoFisher Scientific), α v integrin (CD51, clone 21, ms IgG1, 1:50, 611012, BD Bioscience), CD68 (rb IgG, 1:100, ab125212, Abcam), vitronectin (rb IgG, 1:100, ab235987, Abcam), LTBP-1 (rb IgG, 1:100, ab39, a kind gift of Dr. C.-H. Heldin, University of Uppsala, Sweden), pMLC2 (pMLC, Ser19) (m IgG1, 1:250, 36755, Cell Signaling), pSmad3 (rb IgG, 1:50, 9520, Cell Signaling), MRTF-A (rb IgG, 1:50, 14760S, Cell Signaling).

Isotype-specific secondary antibodies Alexa647-conjugated goat anti-m IgG2a (1:100, A-21241, Molecular Probes, LifeTechnologies Inc.), Alexa488-conjugated goat anti-rb IgG (1:100, A-11034, Invitrogen), goat anti-rat-IgG Alexa Fluor 488 (1:100, A-11006, Invitrogen), goat anti-rb-IgG Alexa Fluor 647 (1:100, A-21246, Invitrogen), goat anti-mIgG1 TRITC (1:100, 1070-03, Southern Biotechnology). Phalloidin-Alexa 568 (1:100, A-12379, Invitrogen) was used to stain F-actin. DAPI dihydrochloride (1:50, D9542, Sigma-Aldrich) was used to visualize nuclei

Western blot:

α -SMA (m IgG2a, 1:500, α -SM1), vimentin (rb IgG, 1:100, D21H3, 5741, Cell Signaling), N-cadherin (m IgG1, 1:500, clone 32, 610920, BD), lamin B1 (rb IgG, 1:500, ab16048, Abcam), human LAP (goat IgG, 1:500, AF-246-NA, R&D Systems), and anti-FLAG (m IgG1, clone M2, 1:1000, F1804, Sigma-Aldrich).

fluorescently labelled anti-m 680 nm (1:10,000, LIC-926-68020, Mandel Scientific), anti-goat 800 nm (1:10,000, LIC-926-32214), and anti-rb 800 nm (1:10,000, LIC-926-32211, Mandel Scientific) IRDye secondary antibodies

Flow cytometry:

anti-m CD16/32 (Trustain FCX, 101320, Biolegend), fixable viability dye eFluor 506, F4/80-BV421 (rat IgG2b, κ , clone BM8, 123131, BioLegend), CD45-PE/Cy7 (rat IgG2b, κ , clone 30-F11, 103114, BioLegend), CD11b-AF594 (rat IgG2b, κ , clone M1/70, 101254, BioLegend), Ly6C-FITC (rat IgM κ , clone AL-21, 553104, BD Biosciences), CD206-APC (rat IgG2b, κ , clone C068C2, 141708, BioLegend), CD161-PerCP/Cy5.5 (m IgG2a, κ , clone PK136, 1143640, Sony), CD3-PerCP/Cy5.5 (Hamster IgG, clone 145-2C11, 1101640, Sony), Ly6G-PerCP/Cy5.5 (rat IgG2b, κ , clone 1AB, 1238080, Sony), CD40-PE/Cy5 (rat IgG2b, κ , clone 3/23, 124618, BioLegend), Integrin β 1 (CD29) – AF700 (Armenian Hamster IgG, clone HM β 1-1, 102218, BioLegend), Integrin α (CD51)-PE (rat IgG2b, κ , clone RMV-7, 104105 BioLegend)

Validation

All antibodies have been validated in-house, in addition to what is provided by the manufacturer. Validation includes use of the antibody on cell types that are negative for the epitope, secondary antibody only controls, and IgG controls.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)

Hi5 and Sf9 insect cells for production of human recombinant LAP protein.

Primary bone-marrow-derived macrophages for in vitro studies.

Primary mouse fibroblasts explanted from subcutaneous tissue and fibronectin-knockout mouse embryonic fibroblasts (MEF FN-/-) for in vitro studies.

Authentication

Hi5 (BTI-TN-5B1-4) cells: originated from Trichoplusia ni, the cabbage looper.

Sf9 cells (CRL-1711™; ATCC): originated from Spodoptera frugiperda, fall armyworm.

Primary bone-marrow-derived macrophages: femur and tibia of C57BL/6 mice were dissected, and bone marrow was flushed using macrophage base medium (45% DMEM, 45% Ham's F12, 3% l-glutamine at 200 mM, 10% FBS, and 1% P/S) supplemented with M-CSF, followed by 5-days culture in the same medium (M0 macrophages). Mature macrophages were polarized by adding LPS to generate M1 macrophages or IL-4 to generate M2 macrophages for additional 3 days.

Primary mouse fibroblasts explanted from subcutaneous tissue: primary dermal fibroblasts.

Fibronectin-knockout mouse embryonic fibroblasts (MEF FN-/-) were developed together with R. Fässler (Max Planck Institute of Biochemistry, Munich, Germany). In brief, ES cells were isolated from embryonic day 14.5 FN floxed embryos, immortalized via retroviral transduction of SV-40 large T antigen, cloned, and treated with adenoviral Cre to delete the floxed FN alleles. The FN targeting vector spanned the region from the promoter to the second intron. For the floxed FN allele, loxP sites were confirmed within the 5'-untranslated region and within the first intron. Cre-mediated recombination at these two loxP sites removed the start codon, signal sequence, and the exon/intron border of exon 1 to generate the null allele (Sakai et al., 2001).

Mycoplasma contamination

Hi5, Sf9, primary bone-marrow-derived macrophages, primary mouse fibroblasts explanted from subcutaneous tissue and fibronectin-knockout mouse embryonic fibroblasts (MEF FN-/-) tested negative for mycoplasma contamination.

Commonly misidentified lines
(See [ICLAC](#) register)

No commonly misidentified cell lines were used.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	12–16-weeks-old wild-type C57BL/6 and transgenic C57BL/6 mice expressing GFP under control of the Col1α1(I) promoter; male and female mice.
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	The institutional veterinary authority approved all procedures in accordance with Canadian guidelines (animal protocol #20011739).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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	Tissue surrounding the implants was excised and immediately placed in tissue-digestion buffer containing 1.5 mg/ml collagenase A and 0.4 mg/ml deoxyribonuclease I (diluted in HBSS. Tissue was then placed at 37°C under agitation for 2 h. Digestion was terminated with PBS containing 2% FBS and 25 mM HEPES, and the digest was passed through a 70-µm mesh cell strainer followed by centrifugation at 1,500 rpm for 5 min at 4°C and resuspension of the pellet in red blood cell lysis buffer for 5 min at RT. Finally, the reaction was diluted three times with Hanks' balanced salt solution and centrifuged again. To assess tissue macrophage polarization states, the resulting cell pellet was resuspended in 2% serum PBS and labelled with fluorochrome-conjugated primary antibody mix. For flow cytometry of cultured bone-marrow-derived macrophages, cells were disassociated with accutase solution for 15 min, and resuspended in PBS containing 2% FBS and 25 mM Hepes, and labelled with fluorochrome-conjugated primary antibody mix. For flow cytometry analysis of samples from GFP mice, cell suspensions were produced as above, and the resulting cell pellet was resuspended in 2% serum PBS and labelled with fluorochrome-conjugated primary antibody mix. All cells were finally passed through a 35-µm strainer cap and samples were analysed using a Sony SA3800 spectral cell analyser and analysed using FlowJo software (BD, 2019).
Instrument	Sony SA3800 spectral cell analyser
Software	FlowJo TM software (v.10.7.1)
Cell population abundance	N/A
Gating strategy	For flow-cytometry analysis of samples from GFP mice: single cells -> live cells by viability stain negative cells -> GFP- and GFP+ cells. For flow-cytometry analysis of macrophages: single cells -> live cells viability stain negative cells -> CD11b pos f4/80 pos cells.

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