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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 our Editorial Policies and the Editorial Policy Checklist.

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	Nikon Elements software 5.11 (confocal microscopy images) Bruker DMX 360 (acquisition of NMR spectra) Orbitrap Fusion Lumos (Mass spectrometry)
Data analysis	ImageJ v1.52q (Confocal image analysis: nascent matrix area and volume) BoneJ v1.4.2 (open source ImageJ plugin available at http://bonej.org/) Matlab vR2016a (AFM output processing) GraphPad Prism 8 (plotting, statistical analysis) Microsoft Excel v16.37 (data handling) Adobe Illustrator v2020 (figure preparation) Topspin 1.3 (NMR analysis) Maxquant V.1.6.3.4. (Mass spectrometry 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 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

All the data generated or analyzed during this study are included within this article or references cited and its Supplementary Information. Additional information is available from the corresponding author on 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

Life sciences study design

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

Sample size	No statistical methods were used to determine sample size. Sample size was determined based on previous literature available in the same subject area and previous observations from our lab (ref: Loebel Nat Mater. doi: 10.1038/s41563-019-0307-6; McLeod Scientific Reports doi: 10.1038/srep38852 (2016); Chaudhuri Nat Mater. doi: 10.1038/nmat4489). The analysis involved averaging over several experimental repeats and the results were successfully reproduced.
Data exclusions	No data were excluded from analyses.
Replication	All experiments were successfully repeated at least two times with similar results. At least three laboratory members have performed the nascent matrix staining.
Randomization	Randomization methods did not apply to this study as there were no clinical populations or patients involved. Immunostaining were acquired by taking randomly distributed fields of view across the entire area of the hydrogel.
Blinding	The investigators were not blinded to allocation during experiments and outcome measurements. Our data analyses are based on objectively measurable data (nascent protein thickness, area and volume). Blinding does not affect these data values.

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	anti-collagen type IV (1:200, Thermo Fisher Scientific Cat# MA1-22148, RRID:AB_558482, clone COL-94, lot#TI2627961), anti-collagen I (1:200, Abcam Cat# ab138492, RRID:AB_2861258, lot# GR247379-42), Alexa Fluor-594/647 IgG H&L (1:200, Abcam Cat# ab150080, RRID:AB_2650602/ab150143, RRID:AB_2893233)
Validation	anti-collagen I, species reactivity for human collagen I indicated on manufacturer's website (ref. Herberg Nanotheranostics 2018 doi: 10.7150/ntno.23354); anti-collagen IV, species reactivity for human collagen IV indicated on manufacturer's website (ref. Sun Nat Methods 2015 doi: 10.1038/nmeth.3210).