

## 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 [Authors & Referees](#) and the [Editorial Policy Checklist](#).

### 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

- The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- An indication of 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 statistics 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
- 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 about [availability of computer code](#)

Data collection

Nikon Elements software 5.11 (confocal microscopy images)  
SoftWoRx 6.1 (images for TFM analysis)  
AMT V542 Advantage image capture software (TEM images)  
Bruker DMX 360 (acquisition of NMR spectra)

Data analysis

ImageJ v1.51m9 (Confocal image analysis: cell aspect ratio, area)  
BoneJ v1.4.2 (open source ImageJ plugin available at <http://bonej.org/>)  
TFM Software (open source ImageJ routines available at <https://sites.google.com/site/qingzongtseng/tfm>)  
Matlab vR2016a (TFM output processing)  
GraphPad Prism 7 (plotting, statistical analysis)  
Microsoft Excel v16.20 (data handling)  
Adobe Illustrator v2017.1.0 (figure preparation)  
Topspin 1.3 (NMR 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

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

## 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       Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/authors/policies/ReportingSummary-flat.pdf](https://www.nature.com/authors/policies/ReportingSummary-flat.pdf)

## Life sciences study design

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

Sample size	Sample size was determined based on previous literature available in the same subject area and previous observations from our lab (ref: Chaudhuri Nat Mater. doi: 10.1038/nmat4489; Khetan Nat Mater. 2013 doi: 10.1038/nmat3586). 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.
Randomization	Randomization methods did not apply to this study as there were no clinical populations or patients involved. Immunostaining and TFM images 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 (cell aspect ratio, fluorescence intensity and nascent protein thickness). Blinding does not affect these data values.

## Reporting for specific materials, systems and methods

### Materials & experimental systems

n/a	Involvement
<input type="checkbox"/>	<input checked="" type="checkbox"/> Unique biological materials
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants

### Methods

n/a	Involvement
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Unique biological materials

Policy information about [availability of materials](#)

Obtaining unique materials      Human bone marrow is commercially available from Lonza.

## Antibodies

Antibodies used      anti-YAP/TAZ (1:200, Santa Cruz sc-101199, clone 63.7, lot# A2017), anti-YAP (1:200, Cell Signaling 14074, clone D8H1X, lot# 2), anti-fibronectin (1:200, Sigma Aldrich F6140, clone FN-3E2, lot# 057M4780V), anti-collagen IV (1:200, ThermoFisher MA1-22148,

clone COL-94, lot# T12627961), anti-collagen I (1:200, Abcam ab138492, lot# GR247379-42), anti-laminin alpha5 (1:200, Abcam b220399, lot# GR3174768-7), anti-paxillin (1:200, BD 610052, clone 349/Paxillin, lot# 7108600), anti-osteocalcin (1:10, R&D MAB1419, clone 190125, lot# IFS0517011), anti-osteocalcin (1:50, Bioss bs-4917R, lot# AG09294227), anti-fatty acid binding protein (FABP6) (1:20, R&D AF3880 polyclonal, lot# YOR011712A), anti-IgG1-k (1:100, 1:400, Millipore MABF1081Z, lot# VP1712138), anti-Integrin alpha2 (1:100, 1:50, 1:25, Millipore MAB1950Z, lot# 2952605), anti-human fibronectin (1:43, 1:86, DHSB HFN7.1, lot# 9/28/17), Alexa Flour-488/594/647 IgG H&L (1:200, Abcam ab150113/ab150080/ab150143).

## Validation

mouse anti-YAP/TAZ, validated for human YAP on manufacturer's data sheet (ref. Cosgrove Nat Mater. 2016 doi: 10.1038/nmat4725, Caliarì 2016 Biomaterials doi: 10.1016/j.biomaterials.2016.06.061); rabbit anti-YAP, validated for human YAP on manufacturer's data sheet (ref. Mou Oncol Rep. 2018 doi: 10.3892/or.2018.6633); anti-fibronectin, species reactivity for human fibronectin indicated on manufacturer's website (ref. Evanko Matrix Biol. 2015 doi: 10.1016/j.matbio.2014.12.001); 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); anti-laminin alpha5, species reactivity for human laminin alpha5 indicated on manufacturer's website; anti-paxillin, species reactivity for human paxillin indicated on manufacturer's website (ref. Cosgrove Nat Mater. 2016 doi: 10.1038/nmat4725); mouse anti-osteocalcin, specificity for human osteocalcin indicated on manufacturer's website (ref. Khetan Nat Mater. 2013 doi: 10.1038/nmat3586); rabbit anti-osteocalcin, specificity for human osteocalcin indicated on manufacturer's website (ref. Liu Int J Mol Med 2018 doi: 10.3892/ijmm.2018.3526); anti-FABP6, specificity for human FABP6 indicated on manufacturer's website (ref. Khetan Nat Mater. 2013 doi: 10.1038/nmat3586); anti-human fibronectin, specificity for human fibronectin indicated on manufacturer's website (ref. Keselowsky PNAS 2005 doi: 10.1073/pnas.0407356102); anti-Integrin alpha2, specificity for human Integrin alpha2 indicated on manufacturer's website (ref. Kaido J Biol Chem 2004 doi: 10.1074/jbc.M411202200); anti-IgG1-k, specificity for human IgG1 indicated on manufacturer's website (ref. Kim Stem Cells 2018 doi: 10.1002/stem.2920).