nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio 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	Active foam simulation was performed using framework Mpacts. The software and code is publicly available through https://gitlab.kuleuven.be/mebios-particulate/publications/mpacts-active-foam-dynamics-of-tissue-spheroid-fusion where the 'container registry' contains the exact software version used to rerproduce the results. Images from two-photon microscoy were adjusted for brightness and contrast and registered with descriptor-based registration plugins in ImageJ (https://imagej.net/ij/). The tracking over time of the segmented nuclei was automatically performed using LapTrack (https://github.com/yfukai/laptrack).
Data analysis	All statistical analyses were performed using Python3, including numpy, scipy and pandas. Scripts for statistical analysis are provided in the zenodo repository available at "https://zenodo.org/records/13883906". These include analysis scripts for confocal microscopy, time-lapse two-photon microscopy and fitting procedures of fusion curves for brightfield microscopy as well as scripts for analysis of simulation results.

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 Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

All data is available at the zenodo repository: https://zenodo.org/records/13883906

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The cell pool used comprised of cells of both sexes and it was developed based on biological similarities for basic scientific experimentation. There was no sex-based consideration for the present study as we focused on basic biophysics principles of cell aggregation
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	The studied human periosteum-derived cells (hDPCs) come from a cell pool comprised of multiple donors, with similar biological characteristics (such as population doubling time) and similar bone forming potential. In this study, hPDCs were isolated from periosteal biopsies of two female and four male donors aged between 11 and 17 years old.
Recruitment	hPDCs come from biopsies. We had no control nor involvement in the donor recruitment process.
Ethics oversight	The ethical committee for Human Medical Research (KU Leuven) approved all procedures, and patients' informed consent forms were obtained (S64471). Patient informed written consent was provided by the legal guardian.

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

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	In case of high-throughput brightfield microscopy experiments, sample size could be very large >50, obtaining robust statistics. Two-photon microscopy experiments are extremely time intensive (1 sample takes multiple days of acquisition). In that case, we used n=3.
Data exclusions	Fusion experiments where the two spheroids did not make any contact were discarded from further analyses. A detailed annotated table containing which samples are rejected and any other anomaly is recorded in the zenodo repository. Simulations that failed to complete were excluded from further analyses. This is clearly reported in the manuscript.
Replication	Fusion experiments were repeated multiple times, and these results are presented in the Supplementary information.
Randomization	There was no randomization involved in this study.
Blinding	No blinding was performed, as differences between experimental groups were clearly visible in the microscopy images.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.