nature portfolio

Corresponding author(s): Gordana Vunjak-Novakovic

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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	NIS-Elements (Nikon)
Data analysis	All software used to analyse the data is commercial or open-source: Excel (Microsoft), Prism (GraphPad), MATLAB (MathWorks), CoBI (CFD Research), FlowJo (BD Biosciences), SOLIDWORKS Flow Simulation (SolidWorks), IVIS Living Image (PerkinElmer), GSEA (UC San Diego and Broad Institute), Transcriptome Analysis Console (Thermo Fisher Scientific). The custom code for the analyses of pixel movement can be obtained at https://www.nature.com/articles/s41596-019-0189-8.

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

Source data for all graphs in the Main Figures and in the Extended Data Figures are available as Supplementary Information. All raw and analysed datasets generated during the study are 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	All sample sizes were determined on the basis of our previous studies with the same tissues (heart, bone, liver, and skin).
Data exclusions	No data were excluded from the analyses.
Replication	All quantitative data were obtained in replicated experiments, and the findings were reproduced from one experiment to another.
Randomization	Engineered tissues were randomly allocated into the experimental groups and analytical assays.
Blinding	The investigators as well as facilities providing specific analytical assessments were blinded to experimental-group allocation.

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-VE-Cadherin: Sino Biological; Catalog# 10433-MM01; Clone 01; Dilution 1:250
Anti-VE Cadherin: Abcam; Catalog # ab33168; Clone N/A; Dilution 1:250
Anti-Actin alpha 2: Thermo Fisher Scientific; Catalog # 701914; Clone 7H1L69; Dilution 1:100
Anti-Cytochrome P450 CYP3A4: Millipore; Catalog # AB1254; Clone N/A; Dilution 1:50
Anti-Albumin:Thermo Fisher Scientific; Catalog # A80-229F; Clone N/A; Dilution 1:100
Anti-Keratin 14: Biolegend; Catalog # PRB-155P; Clone N/A; Dilution 1:100
Anti-Vimentin: Santa Cruz Biotechnology; Catalog # sc-6260; Clone V9; Dilution 1:100
Anti-Bone sialoprotein II: Millipore Sigma; Catalog # AB1854; Clone N/A; Dilution 1:500
Anti-Osteocalcin: Millipore Sigma; Catalog # AB10911; Clone N/A; Dilution 1:500
Anti-CD45: Biolegend; Catalog # 304006; Clone HI30; Dilution 1:100
Anti-CD14: Biolegend; Catalog # 301834; Clone M5E2; Dilution 1:100
Anti-ITGAM (CD11b): Biolegend; Catalog # 301324; Clone ICRF44; Dilution 1:100
Anti-CD68: Biolegend; Catalog # 333807; Clone Y1/82A; Dilution 1:100
Anti-Troponin T: Thermo Fisher Scientific; Catalog # BS-10648R; Clone N/A; Dilution 1:50
Goat anti-Mouse: Thermo Fisher Scientific, Catalog # A-11029; Clone N/A; Dilution 1:400
Goat anti-Rabbit: Thermo Fisher Scientific, Catalog # A-11012; Clone N/A; Dilution 1:200
Rabbit anti-Human: Thermo Fisher Scientific, Catalog # PA1-28834; Clone N/A; Dilution 1:500

Validation

All antibodies used in this study were validated, and detailed information can be found on the manufacturers' websites:

Anti-VE-Cadherin: https://www.sinobiological.com/antibodies/human-ve-cadherin-10433-mm01
Anti-VE Cadherin: https://www.abcam.com/ve-cadherin-antibody-intercellular-junction-marker-ab33168.html
Anti-Actin alpha 2: https://www.thermofisher.com/antibody/product/alpha-Actinin-2-Antibody-clone-7H1L69-Recombinant-Monoclonal/701914
Anti-Cytochrome P450 CYP3A4: https://www.emdmillipore.com/US/en/product/Anti-Cytochrome-P450-Enzyme-CYP3A4-

Antibody,MM_NF-AB1254
Anti-Albumin: https://www.thermofisher.com/antibody/product/Human-Albumin-Antibody-Polyclonal/A80-229F
Anti-Keratin 14: https://www.biolegend.com/en-us/products/keratin-14-polyclonal-antibody-purified-10953?GroupID=GROUP26
Anti-Vimentin: https://www.scbt.com/p/vimentin-antibody-v9
Anti-Bone sialoprotein II: https://www.emdmillipore.com/US/en/product/Anti-Bone-Sialoprotein-II-Antibody,MM_NF-AB1854
Anti-Osteocalcin: https://www.emdmillipore.com/US/en/product/Anti-Osteocalcin-Antibody,MM_NF-AB10911
Anti-CD45: https://www.biolegend.com/en-us/products/fitc-anti-human-cd45-antibody-707?GroupID=BLG5926
Anti-CD14: https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-human-cd14-antibody-7653?GroupID=BLG10263
Anti-ITGAM (CD11b): https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-human-cd11b-antibody-7325
Anti-CD68: https://www.biolegend.com/en-us/products/pe-anti-human-cd68-antibody-4845
Anti-Troponin T: https://www.thermofisher.com/antibody/product/Troponin-T-Antibody-Polyclonal/BS-10648R
Goat anti-Mouse: https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11029
Goat anti-Rabbit: https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11012
Rabbit anti-Human: https://www.thermofisher.com/antibody/product/Rabbit-anti-Human-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/PA1-28834

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	The human hiPSC line, WTC-11, was obtained from Bruce Conklin, Gladstone Institute, through a Material Transfer Agreement. Peripheral blood mononuclear cells (PBMCs) were obtained from the New York Blood Center. We purchased the following cell lines: Normal human dermal fibroblasts (NHDF) from Lonza, Catalog # PCS-201-012 iCell Hepatocytes from CDI, Catalog # C1023 Mesenchymal stromal cells (MSCs) from Lonza, Catalog # PT-2501 Human umbilical venous endothelial cells (HUVECs) from Angio-Proteomie, Catalog # cAP-0001RFP
Authentication	The WTC-11 line has been characterized in a previously published manuscript (Kreitzer et al., Am J Stem Cells, 2013) and its certificate can be obtained at https://www.coriell.org/0/Sections/Search/Sample_Detail.aspx?Ref=GM25256. For peripheral blood mononuclear cells: https://www.nybc.org/products-and-services/blood-products/research-products All other cells were validated, and detailed information can be found on the manufacturers' websites: Normal human dermal fibroblasts: https://www.atcc.org/products/pcs-201-012#generalinformation iCell Hepatocytes: https://www.fujifilmcdi.com/icell-hepatocytes-20-01279-ghpc01279 Mesenchymal stromal cells: https://bioscience.lonza.com/lonza_bs/US/en/Primary-and-Stem-Cells/p/000000000000186706/hMSC---Human-Mesenchymal-Stem-Cells Human umbilical vein endothelial cells: https://www.angioproteomie.com/ccp3099-rfp-expressing-human-umbilical-veinendothelial-c-cap-0001rfp.htm
Mycoplasma contamination	The cells were regularly tested for mycoplasma.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cells were used.

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	All samples were collected and washed with a FACS buffer (1 mm EDTA and 2% FBS in PBS), filtered through a 40-um mesh cell strainer, and stained prior to acquisition on the Bio-Rad ZE5 Cell Analyzer or Agilent NovoCyte Quanteon. The circulating cells were collected from primary human peripheral blood donors and subjected to magnetic cell sorting for CD14 (Miltenyi Biotec) prior to use.
Instrument	Bio-Rad ZE5 Cell Analyzer and Agilent NovoCyte Quanteon
Software	FlowJo 10.6.1 (BD Biosciences)
Cell population abundance	> 98% CD14+, ITGAM (CD11b)+ cells were used after magnetic cell sorting.

Gating strategy

Multiple gating strategies were used for analysis. First gating for total cells and single cells (removing doublets), then for DRAQ5+ cells to account for live cells and to distinguish from debris.

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