

## 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 All imaging was performed using ImageXpress (Molecular Devices). RNA, ChIP and ATAC-seq data was collected from IGM Gneomics Center @ UCSD.

Data analysis All imaging analysis was performed using MetaXpress (Molecular Devices) analysis suite, all codes used to analyze RNA, ChIP and ATAC-seq data are available at <https://github.com/smurph50>

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 have been made publicly available

## 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	Sample size varied depending on experiments. For cell based immunofluorescence quantification n>8 per condition, for mouse experiments for each experimental arm has a least n=10, for RNA and ChIP-seq n=2, for single cell ATAC-seq >8500 cells per condition were analyzed for each experimental arm. For RT-QPCR all data is derived from biological triplicates.
Data exclusions	No data exclusion was performed
Replication	All in vitro and in vivo experiments were replicated in at least three independent experiments. For RNA, Chip and scATAC-Seq data was derived from biological duplicates.
Randomization	For in vivo work (infarcted hearts), injection, sample processing and quantification was randomized
Blinding	For in vivo work, operator was blinded to the experimental conditions for injection, sample processing and quantification. Similarly, for data analysis operator was blinded to the experimental conditions.

## 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

### Methods

n/a	Involved in the study	n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies	<input type="checkbox"/>	<input checked="" type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines	<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology	<input type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms		
<input type="checkbox"/>	<input type="checkbox"/> Human research participants		
<input type="checkbox"/>	<input type="checkbox"/> Clinical data		
<input type="checkbox"/>	<input type="checkbox"/> Dual use research of concern		

## Antibodies

Antibodies used	rabbit anti-ATF7IP (Sigma, HPA023505, 1:200); rabbit anti-ATF7IP (Invitrogen, PA5-54811, 1:200); rabbit anti-JUNB (Abcam, Ab128878, 1:200); rabbit anti-SP7/OSTERIX (Abcam, Ab22552, 1:500); mouse anti-ZNF207 (Sigma, SAB1412396, 1:500); rabbit anti-TAGLN (Abcam, Ab14106, 1:800); guinea pig polyclonal anti-Vimentin (Progen, GP53, 1:100); mouse anti-VIMENTIN (Santa Cruz Biotechnology, sc-373717, 1:800); goat polyclonal anti-TAGLN (GeneTex, GTX89789, 1:800); rabbit polyclonal anti-TNNT2 (Sigma, HPA017888, 1:100); mouse anti-ACTN2 (Sigma, A7811, 1:800); goat anti-PECAM1 (H3) (Santa Cruz Biotechnology, Sc1506, 1:200); rabbit anti-MAP2 (Abcam, Ab32454, 1:200); and mouse anti-TUJ1 (R&D Systems, MAB1195, 1:200); rabbit anti-NANOG (Abcam, ab109250, 1:200). Secondary antibodies were: Alexa Fluor 488 goat-anti-rabbit IgG (H+L) (Invitrogen, A11008, 1:1000); Alexa Fluor 488 donkey-anti-mouse IgG (H+L) (Invitrogen, A21202 1:1000); Alexa Fluor 488 goat anti-Guinea Pig IgG (H+L) (Invitrogen, A 11073 1:100); Alexa Fluor 568 goat-anti-mouse IgG (H+L) (Invitrogen, A10037, 1:1000); Alexa Fluor 568 donkey anti-goat IgG (H+L) (Invitrogen, A11057, 1:1000); Alexa Fluor 680 donkey-anti-mouse IgG (H+L) (Invitrogen, A10038, 1:1000); and Alexa Fluor 680 donkey-anti-rabbit IgG (H+L) (Invitrogen, A10043, 1:1000); rabbit anti-Collagen I (Abcam, Ab21286, 1:50).
Validation	Rabbit anti-ATF7IP (Sigma, HPA023505, 1:200); rabbit anti-ATF7IP (Invitrogen, PA5-54811, 1:200); rabbit anti-JUNB (Abcam, Ab128878, 1:200); rabbit anti-SP7/OSTERIX (Abcam, Ab22552, 1:500); mouse anti-ZNF207 (Sigma, SAB1412396, 1:500); rabbit anti-TAGLN (Abcam, Ab14106, 1:800) were validated by siRNA-mediated KD. -Rabbit anti-TAGLN (Abcam, Ab14106, 1:800); guinea pig polyclonal anti-Vimentin (Progen, GP53, 1:100); mouse anti-VIMENTIN (Santa Cruz Biotechnology, sc-373717, 1:800); goat polyclonal anti-TAGLN (GeneTex, GTX89789, 1:800); rabbit polyclonal anti-TNNT2 (Sigma, HPA017888, 1:100); mouse anti-ACTN1 (Sigma, A7811, 1:800); goat anti-PECAM1 (H3) (Santa Cruz Biotechnology, Sc1506, 1:200) were validated previously in the Colas lab using a iPSC cardiac differentiation protocol described in Cunningham et al 2017, ensuring no staining overlap between cardiac (ACTN1, TNNT2), fibroblasts (TAGLN, VIMENTIN) and endothelial (PECAM-1) markers.

-Rabbit anti-MAP2 (Abcam, Ab32454, 1:200); and mouse anti-TUJ1 (R&D Systems, MAB1195, 1:200) were validated in (Mahmoudi et al., 2019). Rabbit anti-Collagen I (Abcam, Ab21286, 1:50). Ab21286 has been referenced in 163 publications.

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	iMEFs were provided by Dr Qian's laboratory, human dermal (CRL-2097, CCD-1079Sk) and aortic endothelial cells (PCS-100-011) were purchased from ATCC
Authentication	Authentication of iMEFs was performed by Dr. Qian and Colas lab, authentication of human dermal fibroblasts and aortic endothelial cells was performed by ATCC
Mycoplasma contamination	All cell lines tested negative for mycoplasma
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

## Palaeontology and Archaeology

Specimen provenance	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.
Specimen deposition	Indicate where the specimens have been deposited to permit free access by other researchers.
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.
<input type="checkbox"/> Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

## Animals and other organisms

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

Laboratory animals	Both male and female C57Bl/6 wild-type mice from the Jackson laboratories (strain 000664) were used for this study.
Wild animals	Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.
Field-collected samples	For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.
Ethics oversight	IACUC-approved and accredited by AAALAC. Animal Welfare Assurance Number A3053-01.

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

## Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics	Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."
Recruitment	Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.
Ethics oversight	Identify the organization(s) that approved the study protocol.

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

## Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	<input type="text" value="Provide the trial registration number from ClinicalTrials.gov or an equivalent agency."/>
Study protocol	<input type="text" value="Note where the full trial protocol can be accessed OR if not available, explain why."/>
Data collection	<input type="text" value="Describe the settings and locales of data collection, noting the time periods of recruitment and data collection."/>
Outcomes	<input type="text" value="Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures."/>

## Dual use research of concern

Policy information about [dual use research of concern](#)

### Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Public health
<input checked="" type="checkbox"/>	<input type="checkbox"/>	National security
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Crops and/or livestock
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Ecosystems
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Any other significant area

### Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Demonstrate how to render a vaccine ineffective
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Confer resistance to therapeutically useful antibiotics or antiviral agents
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Enhance the virulence of a pathogen or render a nonpathogen virulent
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Increase transmissibility of a pathogen
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Alter the host range of a pathogen
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Enable evasion of diagnostic/detection modalities
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Enable the weaponization of a biological agent or toxin
<input checked="" type="checkbox"/>	<input type="checkbox"/>	Any other potentially harmful combination of experiments and agents

## ChIP-seq

### Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links <i>May remain private before publication.</i>	<input type="text" value="GEO Accession # is GSE183124"/>
Files in database submission	<input type="text" value="SP7_1.fq.gz, SP7_2.fq.gz, JUNB_1.fq.gz, JUNB_2.fq.gz, ATF7IP_1.fq.gz, ATF7IP_2.fq.gz, ZNF207_1.fq.gz, ZNF207_2.fq.gz, SP7_1.bed, SP7_2.bed, JUNB_1.bed, JUNB_2.bed, ATF7IP_1.bed, ATF7IP_2.bed, ZNF207_1.bed, ZNF207_2.bed"/>
Genome browser session (e.g. <a href="#">UCSC</a> )	<input type="text" value="https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg38&amp;lastVirtModeType=default&amp;lastVirtModeExtraState=&amp;virtModeType=default&amp;virtMode=0&amp;nonVirtPosition=&amp;position=chrX%3A15592446%2D15635253&amp;hgsid=1153827823_Cx4aQLxoCE4TxcagY5g5L1NygisD"/>

### Methodology

Replicates	<input type="text" value="2 biological replicates were used."/>
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Sequencing depth	ATF7IP_1.fq.gz 93M reads, ATF7IP_2.fq.gz 84M reads, SP7_1.fq.gz 68M reads, SP7_2.fq.gz 37M reads, JUNB_1.fq.gz 30M reads, JUNB_2.fq.gz 29M reads, ZNF207_1.fq.gz 33M reads, ZNF207_2.fq.gz 30M. All lengths were 76nt.
Antibodies	rabbit polyclonal anti-ATF7IP (Invitrogen, PA5-54811), rabbit monoclonal anti-JUNB (C37F9) (Cell Signaling Technology, 3753S), rabbit anti-SP7/OSTERIX (Abcam, Ab22552), or rabbit polyclonal anti-ZNF207 (Bethyl laboratories, A305-814AM). Normal rabbit IgG (Cell Signaling Technology, 2729) was used as a negative control.
Peak calling parameters	Macs2 callpeak -t "\$file" -c "\$input" -f SAM -g hs -n "\$file" -B -q 0.01
Data quality	Using a cutoff of 0.01 FDR, we identified 91,196 peaks (binding sites) for JUNB, 44,100 for ATF7IP, 19,169 for SP7, and 4135 for ZNF207
Software	Bowtie2 was used for mapping peaks. MACS2 was used to call peaks.

## 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	<i>Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.</i>
Instrument	<i>Identify the instrument used for data collection, specifying make and model number.</i>
Software	<i>Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.</i>
Cell population abundance	<i>Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.</i>
Gating strategy	<i>Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.</i>
<input type="checkbox"/>	Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

## Magnetic resonance imaging

### Experimental design

Design type	<i>Indicate task or resting state; event-related or block design.</i>
Design specifications	<i>Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.</i>
Behavioral performance measures	<i>State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).</i>

### Acquisition

Imaging type(s)	<i>Specify: functional, structural, diffusion, perfusion.</i>
Field strength	<i>Specify in Tesla</i>
Sequence & imaging parameters	<i>Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.</i>
Area of acquisition	<i>State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.</i>
Diffusion MRI	<input type="checkbox"/> Used <input type="checkbox"/> Not used

## Preprocessing

Preprocessing software	<i>Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).</i>
Normalization	<i>If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.</i>
Normalization template	<i>Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.</i>
Noise and artifact removal	<i>Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).</i>
Volume censoring	<i>Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.</i>

## Statistical modeling & inference

Model type and settings	<i>Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).</i>
Effect(s) tested	<i>Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.</i>
Specify type of analysis:	<input type="checkbox"/> Whole brain <input type="checkbox"/> ROI-based <input type="checkbox"/> Both
Statistic type for inference (See <a href="#">Eklund et al. 2016</a> )	<i>Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.</i>
Correction	<i>Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).</i>

## Models & analysis

n/a	Involvement in the study
<input type="checkbox"/>	<input type="checkbox"/> Functional and/or effective connectivity
<input type="checkbox"/>	<input type="checkbox"/> Graph analysis
<input type="checkbox"/>	<input type="checkbox"/> Multivariate modeling or predictive analysis
Functional and/or effective connectivity	<i>Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).</i>
Graph analysis	<i>Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).</i>
Multivariate modeling and predictive analysis	<i>Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.</i>