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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	Flow cytometry was collected with a BD FACS Canto (BD Bioscience). qRT-PCR was run using a Mini Cycler PCR instrument (Bio-rad Laboratories). Cell ultrastructure was visualized with transmission electron microscope (JEOL). Sequencing was performed on the Illumina NovaSeq 6000 platform. Transthoracic echocardiography was performed using a Vevo 2100. An inverted microscope (Olympus IX71) and laser confocal scanning microscope (Olympus, FV3000) were used for observing the morphology of CSps and the stained images, respectively.
Data analysis	Flow cytometry data was analyzed by Flow Jo software (BD Bioscience). Image J software was used for section quantification and cell morphology measurements. Olympus FV31S-SW software and Bruker MI SE were both used for analysis. Statistical analysis was performed using GraphPad Prism version 9.0 software. Gene expression pathway was performed using R package clusterProfiler.

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](#)

RNA-seq data generated for CDCs cultured on the PS, ULA, and OPC substrates have been deposited in GEO under accession number: GSE223508

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, 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.

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

For in vivo animal sample size was performed with 8 rats from each group. For in vitro experiments sample size was performed with a minimum of 3 independent experiments. The number of independent experiments is required to perform statistical analysis.

Data exclusions

No data was excluded.

Replication

Each experimental protocol was successfully replicated a minimum of three times.

Randomization

All samples were randomly selected and assigned to each group for analysis.

Blinding

For in vivo animal experiments, investigators were blinded to surgical procedures, injections, and analysis. Blinding was not feasible for in vitro experiments since implementation needed treatment groups to be revealed to the researcher as part of the study design for accurate execution. Recording the outcomes assessments was done with the utmost objectivity at all times. Results were trustworthy, there were numerous assessments of the results, high levels of agreement among the various assessors, and instrumentation was used that allowed for objective quantification. Together, these steps reduce the possibility of bias affecting data processing and interpretation.

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

Methods

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

Antibodies

Antibodies used

CD31 Servicebio Cat#: GB11063-3
 CD34 Abcam Cat#: ab81289
 CD90 Abcam Cat#: ab225
 CD105 Abcam Cat#: ab156756
 Sca-1 Abcam Cat#: ab51317
 KDR Santacruz Cat#: sc6251
 Alexa Fluor 488 goat anti-mouse IgG Abcam Cat#: ab150113
 Alexa Fluor 488 goat anti-rabbit IgG Abcam Cat#: ab150077
 Alexa Fluor 594 goat anti-rabbit IgG Abcam Cat#: ab150080
 HRP-labeled Anti-Rabbit IgG antibodies Cell Signal Technology Cat#: 7074
 HRP-labeled Anti-Rat IgG antibodies anti-mouse Cell Signal Technology Cat#: 7076
 caspase-1 Abcam Cat#: ab1872
 β -actin Abcam Cat#: ab8226
 CD68 ZhengNeng Cat#: 360018
 Cardiac troponin T (cTnT) Abcam Cat#: ab209813
 Smooth muscle alpha-actin (α -SMA) Abcam Cat#: ab1878

Validation

Following manufactures' instructions

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

Cells were derived from primary tissue explants from hearts of 4-week-old male Sprague Dawley rats provided by Guangdong Medical Laboratory Animal Center.

Authentication

To validate cardiosphere derived cells, cell morphological examination, growth characteristics, and surface marker characteristics were performed.

Mycoplasma contamination

Not tested for mycoplasma.

Commonly misidentified lines
(See [ICLAC](#) register)

No commonly misidentified lines were used.

Animals and other research organisms

Policy information about [studies involving animals; ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals

3-month-old female Sprague Dawley (Vital River)

Wild animals

No wild animals were used.

Reporting on sex

Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.

Field-collected samples

No field-collected samples were used.

Ethics oversight

All animal studies were performed in accordance with the ethical guidelines of the National Guide for the Care and Use of Laboratory Animals and approved by Jinan University Animal Care and Use Committee (Approval numbers: I ACUC-20210113-06).

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

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

For cell analysis, cells were fixed in a 75% ethanol solution for 10 minutes at room temperature after being collected and then labeled with antibodies.

Instrument

BD FACSCanto

Software

Flow-Jo

Cell population abundance

10,000 events per sample were recorded

Gating strategy

Gating was set based on the commercially available secondary antibody or isotype controls. The background was gated to 2% or less based on secondary control.

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