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	HPLC: Alliance HPLC System; Western blot: Amersham Imager 680 and ImageJ; PCR: BIO-RAD C1000 Touch Thermal Cycler; Rt-PCR: CFX96 Touch Deep Well Real-Time PCR System; Microscope for immunostaining: Olympus X-Cite 120; Echocardiography analysis: Vevo 3100 High-Resolution Micro-Ultrasound System.
Data analysis	Image J 1.48v, SPSS, GraphPad Prism 8.3.0.

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 are provided with this paper

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	No human participants were involved in this study.
Population characteristics	No human participants were involved in this study.
Recruitment	No human participants were involved in this study.
Ethics oversight	No human participants were involved in this study.

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	Software G Power (Faul, Erdfelder, Lang and Buchner, 2007) was used for sample size calculation. In detail, the sample sizes were chosen based on our experience with mouse model and cell experiment in our previous published studies (Zhang et al. Nat Commun. PMID: 29215012 and Zhao et al. Nat Commun. PMID: 35115536).
Data exclusions	No data were excluded.
Replication	Each western blot, qRT-PCR and immunostaining were repeated at least three independent times. The exact number of animal experiment was performed is stated in the corresponding figure legend.
Randomization	Simple Random Sampling. Basically, assign numbers to participants, or treatments, and use a random number table to choose participants and treatment groups.
Blinding	The investigators were blinded to group allocation during data collection and analysis.

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	Name (Manufacturer, Cat #, Dilutions) Western blot: mouse anti-KYNU (Santa Cruz Biotechnology, sc-390360, 1:500) mouse anti-KAT1 (Santa Cruz Biotechnology, sc-271709, 1:500)

mouse anti-GAPDH (Santa Cruz Biotechnology, sc-137179, 1:2000)
rabbit anti-KMO (Proteintech, 10698-1-AP, 1:500)
mouse anti-YAP1 (Cell Signaling Technology, 4912S, 1:500)
mouse anti-phospho-YAP (ser 127, Cell Signaling Technology, 4911S, 1:500)
rabbit anti-phospho-Erk1/2 (Thr202/Tyr204, Cell Signaling Technology, 9911S, 1:500)
rabbit anti-Erk1/2 (Cell Signaling Technology, 9911S, 1:500)
mouse anti-Cyclin B1 (Santa Cruz Biotechnology, 245, 1:500)
rabbit anti-c-Myc (Cell Signaling Technology, 13987, 1:500)
rabbit anti-phospho-Src (Cell Signaling Technology, Tyr527, 2105S, 1:500)
rabbit anti-Src (Cell Signaling Technology, 2108S, 1:500)
rabbit anti-p-Src (Tyr416, Cell Signaling Technology, 2101S, 1:500)
rabbit anti-p-Histone H3 (Ser10) (Cell Signaling Technology, 9701L, 1:500)
rabbit anti-Histone H3 (Cell Signaling Technology, 9715S, 1:500)
Immunostaining:
rabbit anti-p-Histone H3 (Ser10) (Cell Signaling Technology, 9701L, 1:100)
rabbit anti-KI67 (Abcam, ab16667, 1:100)
rabbit anti-VEGFA (Abcam, ab46154, 1:100)
mouse anti-smooth muscle α-actin (Sigma-Aldrich, F3777, 1:100)
rabbit anti-CD31 (Cell Signaling Technology, 77699, 1:100)
mouse anti-cardiac troponin T (cTnT,Thermo Scientific, MS-295-P1, 1:100)
rat anti-IDO1 (Novus, NB100-77696, 1:100)
mouse anti-IDO1 (Millipore, 05-840, 1:100)
mouse anti-AHR (Santa Cruz Biotechnology, sc-133088, 1:100).
ChIP:
mouse anti-AHR (Santa Cruz Biotechnology, sc-133088, 2ug/IP)
anti-IgG (Santa Cruz Biotechnology, sc-515946, 2ug/IP)

Secondary antibodies:
goat anti-mouse IgG-HRP (Cell Signaling, #96714,1:2000).
goat anti-rat IgG-HRP (Cell Signaling, #98164,1:2000).
donkey anti-rabbit IgG-HRP (Invitrogen, 31458, 1:2000)
Alexa Fluor 488, donkey anti rabbit (Invitrogen, A-11055,1:500)
Alexa Fluor 488, donkey anti rat (Invitrogen, A-48262,1:500)
Alexa Fluor 488, donkey anti goat (Invitrogen, A-11055,1:500)
Alexa Fluor 488, donkey anti-mouse (Invitrogen, A-32766,1:500)
Alexa Fluor 555, goat anti-rabbit (Invitrogen, A-32732,1:500)
Alexa Fluor 555, goat anti-mouse (Invitrogen, A-32727,1:500)

Validation

All antibodies were purchased from the commercial vendors, validation information is available from manufactures' websites.
KYNU: https://www.scbt.com/p/kynureninase-antibody-e-5?requestFrom=search
KMO: https://www.ptglab.com/products/KMO-Antibody-10698-1-AP.htm
KAT1:https://www.scbt.com/p/kat-i-antibody-b-8?requestFrom=search
GAPDH: https://www.scbt.com/p/gapdh-antibody-a-3?requestFrom=search
YAP1:https://www.cellsignal.com/products/primary-antibodies/yap-antibody/4912
phospho-YAP: https://www.cellsignal.com/products/primary-antibodies/phospho-yap-ser127-antibody/4911?site-search-type=Products&N=4294956287&Ntt=4911s&fromPage=plp&_requestid=3944763
phospho-Erk1/2:https://www.cellsignal.com/products/primary-antibodies/phospho-erk1-2-pathway-antibody-sampler-kit/9911?site-search-type=Products&N=4294956287&Ntt=9911s&fromPage=plp&_requestid=3944828
Erk1/2:https://www.cellsignal.com/product/productDetail.jsp?productId=9911
Cyclin B1: https://www.scbt.com/p/cyclin-b1-antibody-gns1?requestFrom=search
c-Myc: https://www.cellsignal.com/product/productDetail.jsp?productId=13987
phospho-Src: https://www.cellsignal.com/products/primary-antibodies/phospho-src-tyr527-antibody/2105?site-search-type=Products&N=4294956287&Ntt=2105s&fromPage=plp&_requestid=3944995
Src:https://www.cellsignal.com/product/productDetail.jsp?productId=2108
phospho-Src: https://www.cellsignal.com/products/primary-antibodies/phospho-src-family-tyr416-antibody/2101?site-search-type=Products&N=4294956287&Ntt=2101s&fromPage=plp&_requestid=3945133
phospho-Histone H3 (Ser10): https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h3-ser10-antibody/9701?site-search-type=Products&N=4294956287&Ntt=9701l&fromPage=plp&_requestid=3945513
Histone H3: https://www.cellsignal.com/products/primary-antibodies/histone-h3-antibody/9715?site-search-type=Products&N=4294956287&Ntt=9715s&fromPage=plp&_requestid=3945584
rphospho-Histone H3 (Ser10): https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h3-ser10-antibody/9701?site-search-type=Products&N=4294956287&Ntt=9701l&fromPage=plp&_requestid=3945673
KI67: https://www.abcam.com/ki67-antibody-sp6-ab16667.html
VEGFA: https://www.abcam.com/vegfa-antibody-ab46154.html
smooth muscle α-actin: https://www.sigmaaldrich.com/US/en/product/sigma/f3777?gclid=EAIaIQobChMIqpiEzYa_-QIVvRXUAR297wdyEAAYASAAEgLu_fD_BwE
CD31:https://www.cellsignal.com/products/primary-antibodies/cd31-pecam-1-d8v9e-xp-rabbit-mab/77699?site-search-type=Products&N=4294956287&Ntt=77699%29&fromPage=plp&_requestid=3945762
Troponin T: https://www.fishersci.com/shop/products/lab-vision-troponin-t-cardiac-isoform-ab-1-mouse-monoclonal-antibody-200-g-ml-bsa-azide/MS295P1

IDO1 : https://www.novusbio.com/products/indoleamine-23-dioxygenase-ido-antibody-mido-48_nb100-77696
IDO1 :https://www.emdmillipore.com/US/en/product/Anti-IDO-Indoleamine-23-Dioxygenase-Antibody-clone-10.1,MM_NF-05-840
AHR: https://www.scbt.com/p/ah-receptor-antibody-a-3
IgG: https://www.scbt.com/p/igg-antibody-d-1?requestFrom=search
goat anti-mouse IgG-HRP: https://www.cellsignal.com/products/secondary-antibodies/goat-anti-mouse-igg1-fc-gamma-specific-antibody-hrp-conjugate/96714?site-search-type=Products&N=4294956287&Ntt=96714&fromPage=plp&_requestid=3949520
goat anti-rat IgG-HRP: https://www.cellsignal.com/products/secondary-antibodies/goat-anti-rat-igg-light-chain-specific-antibody-hrp-conjugate/98164
donkey anti-rabbit IgG-HRP): https://www.thermofisher.com/search/results?query=31458&focusarea=Search%20All
Alexa Fluor 488, donkey anti rabbit): https://www.thermofisher.com/antibody/product/Donkey-anti-Goat-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11055
Alexa Fluor 488, donkey anti rat): https://www.thermofisher.com/antibody/product/Goat-anti-Rat-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A48262
Alexa Fluor 488 (donkey anti goat): https://www.thermofisher.com/antibody/product/Donkey-anti-Goat-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11055
Alexa Fluor 488 (donkey anti-mouse): https://www.thermofisher.com/antibody/product/Donkey-anti-Mouse-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A32766
Alexa Fluor 555 (goat anti-rabbit): https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A32732
Alexa Fluor 555 (goat anti-mouse): https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A32727

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The primary neonatal mouse cardiomyocytes (CMs) were isolated and cultured according the protocol of the Primary Cardiomyocyte Isolation Kit (Thermo Fisher Scientific). The isolation of primary neonatal (P1) mouse cardiac microvascular endothelial cells (MCECs) was performed as described (PMID: 27404385).
Authentication	Both the primary cardiomyocytes and cardiac microvascular endothelial cells were authenticated by immunostaining and morphology, through staining of CM or EC specific markers.
Mycoplasma contamination	Cells test negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

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	Ido1 flox/flox, Ahr ko, Cdh5Cre, TntCre and Myh11Cre mice with C57BL/6 background were obtained from The Jackson Laboratory. All experiment animals used are postnatal 0-4 weeks with old both sex, if not specific delineated in this paper. All mice were kept in a controlled temperature (21.8 ± 0.7°C) and humidity (49.16 ± 2.37%) environment with a 12-h light/dark cycle and fed a rodent diet with free access to water.
Wild animals	No wild animals were used in this study.
Reporting on sex	All male mice were used in this study.
Field-collected samples	No field collected samples were used in this study.
Ethics oversight	All animal protocols were approved by the Georgia State University Committee on the Use and Care of Animals.

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