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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	10x genomics; BD FACSDIVA (v8.0.1)
Data analysis	Cell Ranger (v2.1); ImageJ (c1.48); Flowjo (v10); Vevolab (Seura1.7.2); Prism (v7) Seurat (v.2.3.0); Scran (V.1.6.2); Scater (v.1.6.0); Monocle 2; MPath; gProfiler (http://www.biit.cs.ut.ee/gprofiler/)

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

we have uploaded all the single cell RNA sequencing data (mouse) to the NCBI as requested (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE119355). We have also uploaded our gene array data (human) to NCBI as well (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE119515).

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample size was determined during experimental design based on the type of measurements made (flow vs echocardiogram) and our extensive experience with data variation with each technique. A power calculation was not done.
Data exclusions	No data exclusions were performed following analysis. Mice were excluded from the study if a failed myocardial infarction surgery was determined. This exclusion criteria was predetermined.
Replication	All experiments were repeated with >2 independent experiments and all replications were reproducible.
Randomization	All mice for this study were randomized to make sure litter-mates were used in all experiments where possible.
Blinding	Blinding for experiments was accomplished by segregating treatment groups by ear tag number only. Data analysis was performed by a second investigator with no knowledge of the tags associated to treatment groups for all functional experiments.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☐	☒ Human research participants

Methods

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

Antibodies

Antibodies used

Mouse antibodies used:
CD45 (30-F11); Cat# 103126; Dilution 1:250
CD64 (X54-5/7.1); Cat # 139306; Dilution 1:250
CD11c (N418); Cat # 117334; Dilution 1:250
MHC-II (AF6-120.1); Cat # 116415; Dilution 1:250
CD11b (M1/70); Cat # 101222; Dilution 1:250
Timd4 (RMT4-54); Cat # 130009; Dilution 1:250
Ly6C (HK1.4); Cat # 128024; Dilution 1:250
CD115 (AFS98); Cat # 135505; Dilution 1:250
Ly6g (1A8) Cat # 127623; Dilution 1:250
F4/80 (CI:A3-1); Cat # 123124; Dilution 1:250
CD4 (RM4-5); Cat # 100536; Dilution 1:250
CD8a (53-6.7); Cat # 100708; Dilution 1:250
CD3e (145-2c11); Cat #100309; Dilution 1:250
BrdU (Bu20a); Cat # 339812 ; Dilution 1:25
TruStain CD16/CD32 FC Block (93). Cat # 101320; Dilution 1:100
CD68 (FA-11); Cat #137001; Dilution 1:100

Human Antibody used:
CD45 (HI30); Cat # 304028; Dilution 1:250
MerTK (2B10C42); Cat #367603; Dilution 1:250
CD14 (M5E2); Cat # 301806; Dilution 1:250
CD64 (10.1); Cat #305005; Dilution 1:250

CCR2 (K036C2); Cat # 357207; Dilution 1:250
HLA-DR (L243). Cat # 307626; Dilution 1:250

All antibodies listed above were purchased from Biolegend with the exception of
CCR2 (475301) (R&D Systems); Cat #FAB5538A; Dilution 1:10
Lyve1 (ALY7) (eBiosciences); Cat # 13-0443-82; Dilution 1:250 (flow); Dilution 1:100 (IF)
B220 (RA3-6B2); Cat # 553088; Dilution 1:250
BV421-SA (BD Biosciences); Cat # 563259; Dilution 1:200

Validation

All antibodies were validated by us using appropriate FMO/isotype controls for flow cytometry. All antibodies had validation statement provided on the website of the manufacturer.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

Mice: both male and female mice were used. Ages are specified for each experiment. All mice ordered from Jackson Laboratory. Strains: C57BL/6 (#000664); CCR2KO (#004999); RosaTd (#007914); RosaDTR (#007900); Cx3cr1-CreER-YFP (#021160); Cx3cr1-CreER (#020940);

Wild animals

Wild animals were not used.

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.

Human research participants

Policy information about studies involving human research participants

Population characteristics

Human cardiac tissue samples were obtained from the Washington School of Medicine from patients with end-stage cardiomyopathy during the time of implantation of the left ventricular assist device. Informed consent was received from all patients and approved by the Washington University IRB panel. After LV apical core segment was removed, prior to placement of the inlet cannula, the cardiac tissue was immediately placed into cold RPMI media. Patients had end-stage cardiomyopathy, from an ischemic etiology. There was no additional co-variate information provided for these samples

Recruitment

Pilot study, n=6 patient. These patients were recruited while in hospital awaiting LVAD implantation by a nurse coordinator. The only exclusion criteria was active infection or immunosuppressive medications. There were no obvious study selection biases that would have influenced the results except for the sample size (n=6), thereby increasing variability.

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

Mice were sacrificed by CO2 inhalation. Hearts were perfused with 20mL of cold PBS. Hearts, lungs, livers, and brains were chopped finely and digested, while shaking, for 1hr at 37°C in DMEM containing collagenase I (450 U/mL), DNase I (60 U/mL), and hyaluronidase (60 U/mL) enzymes (all Sigma)12. The digested material from heart, liver and brain was filtered through 40uM filters and pelleted by centrifugation (400xg for 5min at 4°C) in HBSS supplemented with 2% bovine serum + 0.2% BSA. Red blood cells (RBCs) were lysed in ACK lysis buffer (Invitrogen) for 5min at room temperature and resuspended in FACs buffer (PBS containing 2% FCS and 2mM EDTA). Liver was filtered and resuspended into 40% Percoll. Brain was filtered and resuspended into 40% Percoll mixed over top of 80% Percoll. Pellets were resuspended, RBCs were lysed, and samples were resuspended as above. Finally, blood was collected in syringes containing 50□L heparin, RBCs were lysed, and pellets were resuspended as above. Single-cell suspensions were then stained for cell-surface markers using antibodies listed in the 'antibodies used' section. Cells were stained in 50uL FACS buffer with 0.2uL antibody per sample, with the exception of 5□L of CCR2 antibody, for 30min at 4°C. Cells were washed and resuspended in 400uL FACs buffer to be run by flow cytometry

Instrument

BD LSRII-OICR BGRV

Software

FlowJo

Cell population abundance

Sorted MFs represented ~1% of the total cell population from heart tissue samples. Purity was determined by flow cytometry

Cell population abundance	and confirmed in our data analysis.
Gating strategy	For all experiments an initial gaiting strategy was used to gait on live (based on SSC-A/FSC-A) cells followed by two double exclusion gates (FSC-W/FSC-H and SSC-W/SSC-H) and a total CD45+ gate. Subsequent gates are defined in the figures/figure legends.

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