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Reporting Summary

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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	Ligand-receptor connectome information for the analysis of PBMCs was extracted from the FANTOM5 network database. For age scoring by pseudobulk RNA-seq we collected data from GSE156707. We then used each list of genes to construct an expression module score, which we referred to as "Adult" or "Young" gene expression module, using the Seurat function AddModuleScore with adult-specific or young-specific gene lists as features (version 3.1.4)
Data analysis	snRNA-seq Analysis: Raw sequencing data were handled by using the l0X Genomics Cell Ranger software (version 3.0.1, www.l0xgenomics.com). Fastq files were mapped to the hg19 genome, and gene counts were quantified by using Cellranger count function. Cell Bender (version 0.1.0) to remove unwanted background. Bent h5 expression matrices from each experiment were then imported into Seurat (version 3.1.4) and merged into a single object. Harmony (version 1.0) was used for batch correction. Dimensionality reduction (UMAP) and clustering were carried out in Seurat (dimensions =20, cluster resolution= 1.5). GO analysis was performed by using the clusterProfiler package (version 3.16.1) DEseq2 was used for pseduobulk RNA-seq analysis All complex Venn diagrams generated with an online tool (http://bioinformatics.psb.ugent.be/webtools/Venn/) MiloR (version 0.99.19) was used for differential abundance testing CellChat package (version 1.1.2) was used for ligand-receptor analysis on tissue snRNA-seq data We next performed differential expression analysis (FindAllMarkers function, Seurat) to aid in the identification of doublets. bedtools (version v2.26.0) was used to count reads CQN (version 1.34.0) was used for data normalization DESeq2 was used to quantify differential accessibility Homer(v4.10.3) was used for motif enrichment analysis (findMotifsGenome.pl) and generation of genome tracks (makeUCSCfile) All snRNA-seq analyses were performed using standard protocols. The pseduo-bulk RNA-seq analysis is available online: https://hbctraining.github.io/scRNA-seq/ lessons/pseudobulk_DESeq2_scrnaseq.html. Custom code used in this study is available from the

corresponding author upon request.
Our data will be available to the scientific community through the CZI supported cellxgene tool that is hosted on the CZI website
ATAC-seq Analysis:
Bowtie2 (version 7.3.0) was used to map reads to the human genome (hg19)
MACS2 (version 2.1.1.20160309) was used to call peaks
Imaging Mass Cytometry Analysis:
MCD Viewer (1.0.560.6) and Visiopharm software (2019.06) were used to convert data into TIFF format and for segmentation of single cells. Individual cells and vessel landmarks were segmented with the use of the Visiopharm software. For normalization, clustering, visualization, and dimensionality reduction we used the R package CATALYST (version 1.12.2).
Histology:
Contrast of both H&E and Masson's Trichrome images were enhanced using the auto-contrast function in Adobe Photoshop, with the same contrast settings applied to each image for consistency.
Immunofluorescence imaging and quantification:
Visualization and image processing (Scale bar, pseudocolor) was performed by using FIJI/ImageJ software (Version 2.3.0/1.53q).
'Eigen' and S4 (lme4) package in R (version 1.1-27.9000) were used to to perform generalized linear mixed effects model and statistical analysis
Quantification tables were generated with Graphpad Prism (Version 9.3.1).
Final figures were constructed with Adobe Illustrator

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

Raw and processed next-generation sequencing data have been deposited at the NCBI GEO under accession number GSE203275. The snRNA-seq data is available online at https://singlecell.broadinstitute.org/single_cell/study/SCP1852/integrated-multiomic-characterization-of-congenital-heart-disease. The Broad single cell portal study number is SCP1852.

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	Pilot studies were performed to estimate the number of patients required to reproducibly see differences in the single cell genomic assays
Data exclusions	Datasets that didn't match region (ventricle) or chemistry (10X version 3) were excluded from snRNA-seq analysis. All other samples were included based on their diagnosis as described in the manuscript. We only included data from tissues of the left and right ventricles as this is standard in the field.
Replication	Experiments were not performed in replication. We followed standard protocols.
Randomization	Patients were placed into groups based on their diagnosis.
Blinding	Investigators were blinded during data collection for quantification of imaging data (RNA-scope, Immunofluorescence). The pipelines used are by definition blinded to human biases. Moreover, the computational personnel were blinded to the identity and diagnosis of the individual patient

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

(Also see supplemental table S18)
SMA 141Pr , 1A4, Fluidigm, 3141017D
Vimentin 143Nd, RV202, Fluidigm, 3143029D
CD14 144Nd, EPR3653, Fluidigm, 3144025D
CD33 145Nd , Polyclonal, Fluidigm, 3145017D
CD163 147Sm , 3147021D, Fluidigm, 3147021D
CD11b 149Sm, EPR1344, Fluidigm, 3149028D
PD-L1 150Nd, E1L3N, Fluidigm, 3150031D
CD31 151Eu , EPR3094, Fluidigm, 3151025D
CD45 152Sm , CD45-2B11, Fluidigm, 3152016D
CD4 156Gd , EPR6855, Fluidigm, 3156033D
CD73 158Gd , EPR6115, Fluidigm, 3158031D
CD68 159Tb , KP1, Fluidigm, 3159035D
CD20 161Dy , Polyclonal, Fluidigm, 3161029D
CD8a 162Dy , D8A8Y, Fluidigm, 3162035D
c-Myc 164Dy , 9.00E+10, Fluidigm, 3164025D
p-H2AX 165Ho , N1-431, Fluidigm, 3165036D
Ki67 168Er , B56, Fluidigm, 3168022D
Collagen type 1 169Tm, Polyclonal, Fluidigm, 3169023D
CD3 170Er , Polyclonal, Fluidigm, 3170019D
p-ERK 171Yb , D13.14.4E, Fluidigm, 3171021D
PD-L2 172Yb , D7U89C, Fluidigm, 3172031D
CD25 175Lu , EPR6452, Fluidigm, 3175036D
p-Histone H3 176Yb , HTA28, Fluidigm, 3176024D
CD196 163Dy (IMC), Polyclonal, Fluidigm, 3163029D
Ir DNA-Intercalator, Fluidigm, 201192A
Ir DNA-Intercalator, Fluidigm, 201192A
YAP, NB110-58358(polyclonal), Novus Bio, NB110-58358
cTNT, EPR3696, abcam, ab239917
CD31, EPR3094, abcam, ab207090
Ki67, 8D5, Novus, NBP2-22112
Collagen type 1, Fluidigm, 3169023D
Vimentin, RV202, Novus, NBP1-97672
pHistone H3 [Ser28], HTA28, BioLegend, 641002
SMA, D4K9N, CST, 19245BF
Lyz, EPR2994(2), abcam, ab185129
UEA1, na, vector, L-1060-5
Anti-Human CD68 -159Tb, (KP1), Fluidigm, 3159035D
Anti-Human/Mouse CD11b-149Sm, (EPR1344), Fluidigm, 3149028D
Anti-Human CD163 -147Sm, (EDHu-1), Fluidigm, 3147021D
Anti-Human CD45 -152Sm, (D9M8I), Fluidigm, 3152018D
WGA, other, Vector Lab, L-1020-10
Yap, Novus, NB110-58358
c-Myc, EMD Millipore, 06-340
PTX3, Abcam, 90806
Vimentin, Alexa Fluor 488 conjugated, Abcam, 185030
anti-Rabbit IgG Biotinylated, Vector Labs, BA-1100
anti-Rat IgG Alexa Fluor 546, Thermo Fisher, A11081
Streptavidine, Alexa Fluor 488, Thermo Fisher, S32354
Streptavidine, Alexa Fluor 647, Thermo Fisher, S32357
Wheat Germ Agglutinin (WGA)-Rhodamine, Vector Labs, RL-1022

Validation

(Also see supplemental table S18)
Antibody,validation statements,References
SMA 141Pr , Pathologist-verified on: Human FFPE, Human Frozen; Fluidigm tested on: Human FFPE, Human Frozen, Mouse FFPE;
Apllication: IMC paraffin, IMC frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods
Vimentin 143Nd,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature
Methods

CD14 144Nd, Pathologist-verified on: Human FFPE, Human Frozen; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD33 145Nd ,N/A, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD163 147Sm ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD11b 149Sm, Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

PD-L1 150Nd,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD31 151Eu ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD45 152Sm ,N/A, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD4 156Gd ,Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE; Apllication: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD73 158Gd ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD68 159Tb , Reactivity: Human; Application: IMC Paraffin, IMC Frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD20 161Dy ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD8a 162Dy ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

c-Myc 164Dy ,N/A, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

p-H2AX 165Ho , Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

Ki67 168Er , Pathologist-verified on: Human FFPE, Human Frozen; Fluidigm tested on: Human FFPE, Human Frozen, Mouse FFPE; Apllication: IMC paraffin, IMC frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

Collagen type 1 169Tm, Pathologist-verified on: Human FFPE, Human Frozen; Fluidigm tested on: Human FFPE, Human Frozen, Mouse FFPE; Apllication: IMC paraffin, IMC frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD3 170Er , Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

p-ERK 171Yb , Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

PD-L2 172Yb ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD25 175Lu ,Reactivity: Human; Application: IMC paraffin, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

p-Histone H3 176Yb , Reactivity: Human, Mouse, Rat; Application: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

CD196 163Dy (IMC),N/A, Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

YAP, publications tested in 5 confirmed species: Human, Mouse, Rat, Canine, Zebrafish and 9 applications: ChIP, ChIP-seq, ICC/IF, IHC, IHC-F, IHC-P, IP, KD, WB. , [PMID: 28581498] (IHC, WB, IP, Mouse), [PMID: 28406163] (KD, ICC/IF, WB, Human)

cTNT, Suitable for: WB, ICC, IHC-P; Reacts with: Human; WB: THP-1 and Jurkat cell lysates IHC-P: Human kidney tissue and human muscle tissue ICC: Jurkat cells , PMID: 6339421, PMID: 9490273, PMID: 22156833, PMID: 24096620

CD31,tested applications: suitable for IHC-in human muscle tissue, Xue (2019) Oncol Rep, Ren (2014) Biomed Res Int, He (2014) Biomed Res Int , Shu (2014) Int J Mol Sci, Hofmann (2012) PLoS One, Balcells (2010) Circulation

Ki67,Use in Rabbit reported in scientific literature (PMID:33691202). Human reactivity reported in the scientific literature (PMID: 23777661). Rat reactivity reported in scientific literature (PMID: 23447644). Porcine reactivity reported in scientific literature (PMID: 27046485).,

Vimentin,N/A,[PMID: 27474370]

pHistone H3 [Ser28], WB - Quality tested CyTOF®, ICC - Verified IP, ICFC - Reported in the literature, not verified in house; Each lot of this antibody is quality control tested by Western blotting , Lun XK et al. 2019. Mol Cel. 74(5):1086-1102 . Damond N, et al. 2019. Cel Metab. 29:755. Godde N, et al. 2014. PLoS Genet. 10:1004323. Tognetti M, et al. 2021. Cel Systems. 12(5):401-418.e12.

SMA, Species reactivity is determined by testing in at least one approved application (e.g., western blot); Approved Applications: IHC-Leica® Bond™, Immunofluorescence (Frozen), Immunohistochemistry (Paraffin), Western Blotting ,N/A

Lyz, Knock-out validated; Suitable for: ICC/IF, WB, IHC-P; WB: THP-1, HepG2, RAW 264.7 and HL-60 whole cell lysate; Human spleen tissue lysate; Natural human Lysozyme protein. IHC-P: Human tonsil, spleen, lung, kidney, brain, breast and heart tissues; Mouse spleen and small intestine tissues. ICC/IF: THP-1 cells. ,PubMed: 32896624; PubMed: 33688393; PubMed: 33949881; PubMed: 33154092; PubMed: 33186749

UEA1, Applications: Immunohistochemistry / Immunocytochemistry, Immunofluorescence, Blotting Applications, Glycobiology ,

Anti-Human CD68 -159Tb, Reactivity: Human; Application: IMC Paraffin, IMC Frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

Anti-Human/Mouse CD11b-149Sm, Pathologist-verified on: Human FFPE; Fluidigm tested on: Human FFPE, Mouse FFPE; Apllication: IMC paraffin , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

Anti-Human CD163 -147Sm, Reactivity: Human; Application: IMC Paraffin, IMC Frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

Anti-Human CD45 -152Sm, Reactivity: Human; Application: IMC Paraffin, IMC Frozen , Chang (2017) Current Protocols in Cytometry, Geisen (2014) Nature Methods

WGA, Applications: Immunohistochemistry / Immunocytochemistry, Immunofluorescence, Blotting Applications, Glycobiology, Mitogenic Stimulation ,

c-Myc, validated in ChIP, ICC, IP, WB to detect Myc also known as Transcription factor p64, avian myelocytomatosis viral oncogene homolog, myc proto-oncogene protein; Routinely evaluated by western blot on A431 lysates from EGF-stimulated human A431 cells, human A431 cells and HeLa nuclear extract. , PMID: 25895029, 25522242, 24786788, 24870930,24510096

PTX3, Suitable for: WB, IHC-Fr; WB: HUVEC, 3T3-L1 and MDA-MB-231 whole cell lysate. LPS, Brefeldin treated HUVEC whole cell lysate. Mouse and rat placenta tissue lysate. IHC-Fr: Mouse and rat placenta tissue. , PMID: PubMed: 33633222, PubMed: 33907853, PubMed: 33952272, PubMed: 32883960

Vimentin, Alexa Fluor 488 conjugated , Suitable for: ICC/IF, Flow Cyt (Intra), ICC/IF: HeLa and wildtype HAP1 cells. Flow Cyt (intra): wildtype HAP1 cells; Knockout validated , PMID: PubMed: 31109359, PubMed: 31164563, PubMed: 28849024, PubMed: 26807167
Wheat Germ Agglutinin (WGA)-Rhodamine, Applications: Immunofluorescence, Glycobiology ,

Human research participants

Policy information about studies involving human research participants

Population characteristics	See Supplemental S1 and Table 1

P1,Partial Atrioventricular Canal (PAVC), Repair of PAVC, 2y/10m/12d,M;
P2,Hypoplastic Left Heart Syndrome (HLHS) - MS/AA,Norwood/Sano,0y/0m/4d,F;
P3,Dilated Cardiomyopathy (DCM),Berlin LVAD Placement, 0y/5m/21d, M, age at demise 2 yr 9 mo;
P4,Supracardiac Total Anomalous Pulmonary Venous Return (TAPVR),TAPVR Repair,0y/0m/1d,M;
P5,Tetralogy of Fallot (TOF) with Pulmonary Stenosis, Complete TOF Repair (Valve Sparing), 0y/3m/26d, M;
P8,Hypoplastic Left Heart Syndrome (HLHS) - MS/AS, Norwood/Sano (Bilateral PAB at birth), 0y/2m/3d,M, age at demise 1 yr 5 mo;
P10, TOF/PS,TOF repair,0y/5m/26d, F;
P20, Tetralogy of Fallot (TOF) with Pulmonary Stenosis (PS),TOF Repair (Transannular Patch), 0y/1m/10d, M;
P22, Bicuspid aortic valve, aortic stenosis s/p subaortic membrane resection w/ recurrent aortic and subaortic stenosis and AI, Ross Konno,3y/10m/13d,M;
P25, Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,Norwood/BTS 0y/0m/7d,F;
P26, Tetralogy of Fallot (TOF) with Pulmonary Stenosis (PS),TOF Repair (Transannular Patch) 0y/3m/3d,M;
P27, Perimembranous Ventricular Septal Defect (VSD),VSD closure 1y/4m/28d, M;
P28, Tetralogy of Fallot with Pulmonary Atresia (TOF/PA) TOF Repair, RV-PA Conduit Placement 0y/8m/9d,F;
P32, DCM/LVNC,Heartware LVAD,10y/10m/19d F;
P33, Tetralogy of Fallot with Pulmonary Atresia (TOF/PA) TOF Repair (Transannular Patch) 0y/7m/3d,F;
P34, subaortic membrane, coarctation s/p subaortic membrane resection, arch advancement in infancy w/ worsening subaortic stenosis, subaortic membrane resection, partial septal myomectomy 17y/10m/9d,M;
P35, Sinus venosus ASD and PAPVR Warden Procedure,1y/11m/12d,M;
P36, Dilated Cardiomyopathy (DCM),Heartware LVAD Placement,17y/3m/13d,M;
P37, T21, LV-dominant CAVC, small arch s/p coarct repair, PA band, s/p Glenn, s/p Glenn takedown AV canal repair, RV bundle resection,3y/9m/13d, F;
P39, Tetralogy of Fallot (TOF) / Absent Pulmonary Vein Syndrome,RV-PA conduit replacement, LPA/RPA repair, 2y/0m/7d,M;
P40, Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,Heart Transplant,4y/4m/20d, M, age at demise 6 yr, 2 mo;
P41, DCM with VAD,Heart Transplant,12y/7m/2d, M;
P42, Partial Anomalous Pulmonary Venous Return (PAPVR), PAPVR repair, right sided MAZE procedure,42y/9m/24d,M;
P43, Shone's Variant Mitral Valve Replacement (Previously Arch Repair, MV repair),18y/4m/22d,M;
P45, Hypoplastic Left Heart Syndrome (HLHS) - MS/AS,Norwood/BTS 0y/0m/7d,M;
P49, Dilated Cardiomyopathy (DCM),Heart Transplant,13y/5m/21d,M;
P61, TOF/PS,TOF repair,0y/7m/4d,M;
P63, Tetralogy of Fallot (TOF) with Pulmonary Stenosis (PS),TOF Repair (Transannular Patch) 0y/5m/20d, F;
P64, Hypoplastic Left Heart Syndrome (HLHS) -- HLH variant (DORV/non-commited VSD/hypoplastic arch/good size ventricles) VAD placement / Fontan Completion, 3y/3m/17d, M;
P66, Dilated Cardiomyopathy (DCM),Heartware LVAD insertion and ECMO wean,17y/0m/20d,M, age at demise 18 yo;
P69, Dilated Cardiomyopathy (DCM)/Left Ventricular Non-Compaction Cardiomyopathy (LVNC),Heart Transplant (on VAD prior to transplant), 0y/7m/15d, F;
P70, Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,VAD placement / Fontan Completion, 6y/3m/28d, F;
P75, Dilated Cardiomyopathy (DCM),Heartware LVAD placement,16y/2m/25d,M;
P77, Heterotaxy, complete AVSD, DORV, infradiaphragmatic TAPVR, s/p SV palliation with Fontan with acute on chronic HF, VAD placement, AV valve repair,22y/4m/27d,M;
P84, HLHS (MA/AA) s/p Glenn, TV replacement, s/p VAD Heart Transplant,1y/3m/25d, M;
P85, Dilated Cardiomyopathy (DCM),Berlin Placement,0y/5m/16d, M;
P86, Hypertrophic Cardiomyopathy, Heart Transplant,11y/3m/12d,F;
P89, Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,Berlin VAD Placement,0y/9m/3d,F;
P91, Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,Heart Transplant,0y/9m/8d,F;
P92, Dilated Cardiomyopathy (DCM),Heart Transplant,0y/6m/10d, M;
P93, HLHS s/p Fontan with HF LVAD placement,16y/11m/2d,M;
P95, Tetralogy of Fallot (TOF) with Pulmonary Stenosis (PS),TOF Repair (Transannular Patch) 0y/4m/3d, M;
P96, DCM/LVNC s/p VAD,Heart Transplant,18y/5m/12d,M;
P100,DCM/LVNC s/p VAD,Heart Transplant,13y/8m/23d,F;
P106,DORV/remote-VSD s/p PA banding, s/p DKS/Glenn, RCA injury with HF, Heart Transplant,5y/6m/10d, M;
P108,DCM s/p VAD Heart Transplant,17y/5m/19d,M;
P114,Hypoplastic Left Heart Syndrome (HLHS) - MS/AA, absent LAD,Norwood/Sano,0y/0m/9d,M, Age at demise 7 months;
P121,TOF TOF repair,12 mo, Male,Alive;
P138,Hypoplastic Left Heart Syndrome (HLHS) - MS/AS,Norwood/Sano,8 do,Male,Alive;
P147,TOF TOF repair,9 mo,Female,Alive;
P148,Hypoplastic Left Heart Syndrome (HLHS) - MA/AA,Norwood/Sano,6 do,Female, Alive;
P162,Hypoplastic Left Heart Syndrome (HLHS) - MS/AA,Norwood/Sano,3 do,Female,Alive;
3B62D, Donor, 3y/9m/15d, F, Age at demise 3y/9m/15d;
FC3CB, Donor, 9y/8m/3d,F, Age at demise 9y/8m/3d;
13-198,Donor, 11y M, Age at demise 11 y;
13-235,Donor, 11y F, Age at demise 11 y;
LVAdult2,Donor, Adult, UNK;
LVAdult3,Donor, Adult, UNK;
Donor 1 Donor, Adult, UNK;

Donor 2 Donor, Adult, F;
Donor 3 Donor, 1y/11m, M;
Donor 4 Donor, 4y/5m, M;
Donor 5 Donor, 2y/7m, M

Recruitment

Cardiac tissues and blood samples used in this study were collected during cardiothoracic surgeries performed at Texas Children's Hospital (Houston, TX). With the help of the Heart Center Biorepository at Texas Children's Hospital, consent was obtained from patients with various forms of pediatric heart disease, including HLHS, TOF, DCM, HCM, and AVC defects. The anatomic location of tissue collected was based on the specific surgical repair being performed. All patients participating in this study were randomly selected, or were being treated by physicians at Texas Childrens Hospital in Houston Texas. This information, along with more specific patient information, can be found in Table S1. There was no bias for patients or conditions.
Cardiac tissue samples from donors were collected from the University of Kentucky (Samples UK1/FC3CB and UK2/3B62D) and Washington University in St. Louis (LV198/RV198/13-198 and RV325/13-235). Samples from the University of Kentucky were processed by the Gill Cardiovascular Biorepository after being obtained from terminal organ donors whose hearts could not be used for transplantation because of technical reasons (blood type mismatch, etc.). The local Organ Procurement Organization (OPO), in this case the Kentucky Organ Donor Affiliates (KODA), obtained informed consent from the LARs. This consent allowed the hearts to be used for research if they could not be used as part of clinical care.

Ethics oversight

The protocols for the procurement and use of these patient samples were approved by the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (Protocol Number H-26502). For donor hearts, the local Organ Procurement Organization (OPO), iKentucky Organ Donor Affiliates (KODA), obtained informed consent from the LARs. This consent allowed the hearts to be used for research if they could not be used as part of clinical care.
Samples from Washington University in St. Louis donor families were consented, hearts procured at Med-American Transplant, and entered into the Translational Cardiovascular Biobank & Repository (TCBR) at Washington University School of Medicine (#201104172). For pediatric tissues, consent was obtained from the legal authorized representative and tissues entered into the TCBR (#201104172).

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