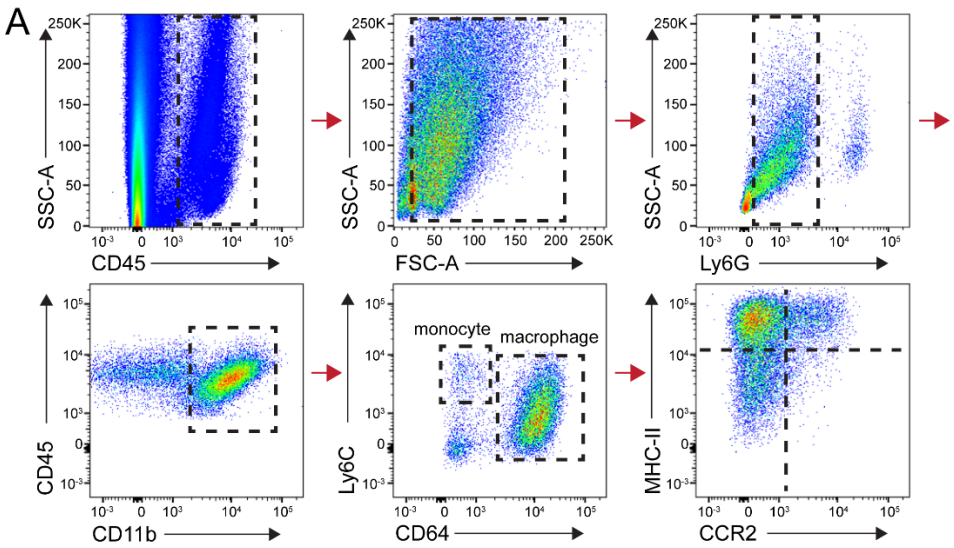
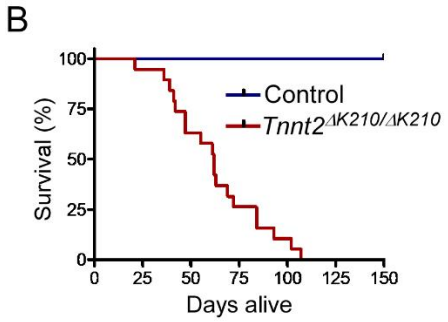
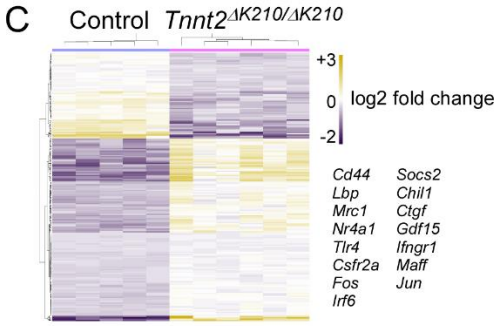
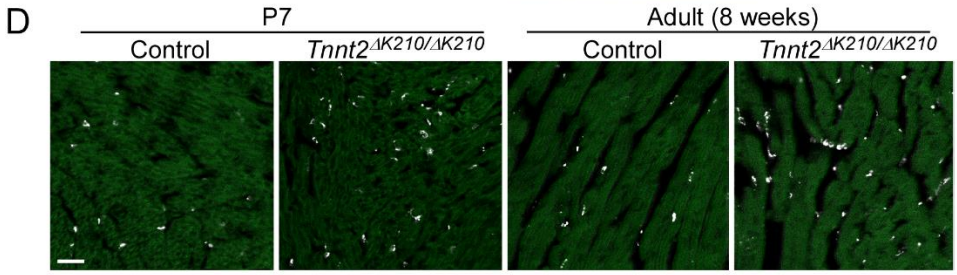
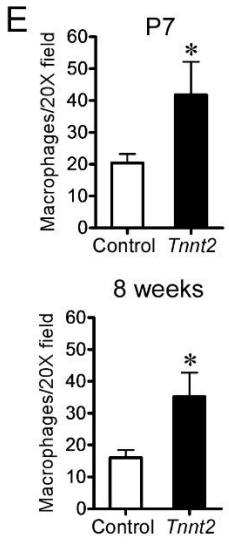

A
SSC-A
CD45
FSC-A
Ly6G
CD11b
Ly6C
monocyte
macrophage
CD64
MHC-II
CCR2


B
Survival (%)
Control
Tnnt2ΔK210/ΔK210
Days alive


C
Control
Tnnt2ΔK210/ΔK210
+3
0
-2
log2 fold change
Cd44
Lbp
Mrc1
Nr4a1
Tlr4
Csfr2a
Fos
Irf6
Socs2
Chil1
Ctgf
Gdf15
Ifngr1
Maff
Jun


D
P7
Adult (8 weeks)
Control
Tnnt2ΔK210/ΔK210
Control
Tnnt2ΔK210/ΔK210


E
P7
Macrophages/20X field
Control
Tnnt2
8 weeks
Macrophages/20X field
Control
Tnnt2

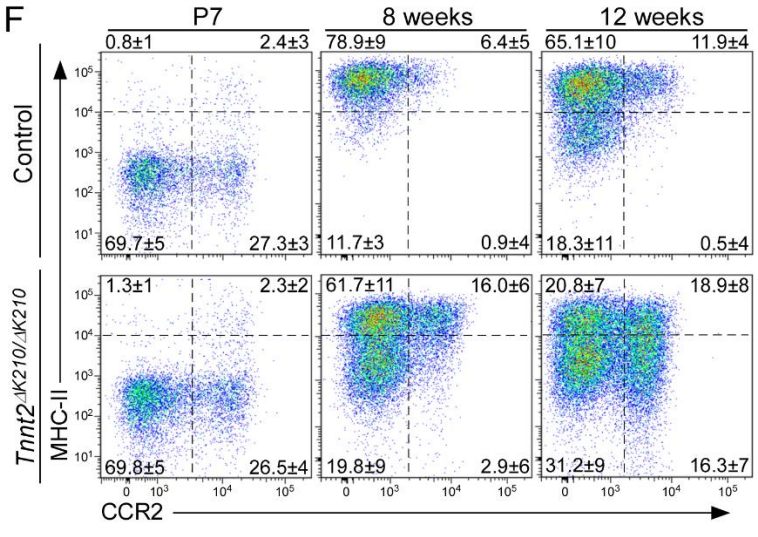

F
P7
8 weeks
12 weeks
Control
Tnnt2ΔK210/ΔK210
MHC-II
CCR2
0.8±1
2.4±3
78.9±9
6.4±5
65.1±10
11.9±4
69.7±5
27.3±3
11.7±3
0.9±4
18.3±11
0.5±4
1.3±1
2.3±2
61.7±11
16.0±6
20.8±7
18.9±8
69.8±5
26.5±4
19.8±9
2.9±6
31.2±9
16.3±7

Figure S1 (related to Figure 1). **Flow cytometry gating scheme and cardiac phenotype of *Tnnt2*$^{\Delta K210/\Delta K210}$ mice across the spectrum of age.** **A**, Flow cytometry gating strategies for cardiac macrophages. **B**, Kaplan-Meier curve showing reduced survival of *Tnnt2*$^{\Delta K210/\Delta K210}$ mice compared to controls (n>20 per group). **C**, Heat map showing genes differentially expressed in control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts at 8 weeks of age (n=5-6 per experimental group). Representative genes related to macrophages and innate immunity that were differentially expressed in *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts compared to controls are displayed. CPM: counts per million. FDR $p<0.05$ (control vs *Tnnt2*) for comparisons. **D-E**, Immunostaining of control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts showing increased numbers of $CD68^+$ (white) macrophages in *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts compared to controls at P7 and 8 weeks of age. Green: cardiac actin. * denotes $p<0.05$ compared to controls. Mann-Whitney test. n=6 per experimental group. **E**, Flow cytometry of $CD45^+CD64^+Ly6G^-$ macrophages showing shifts in macrophage composition in control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts across the spectrum of age. n=6 per experimental group.

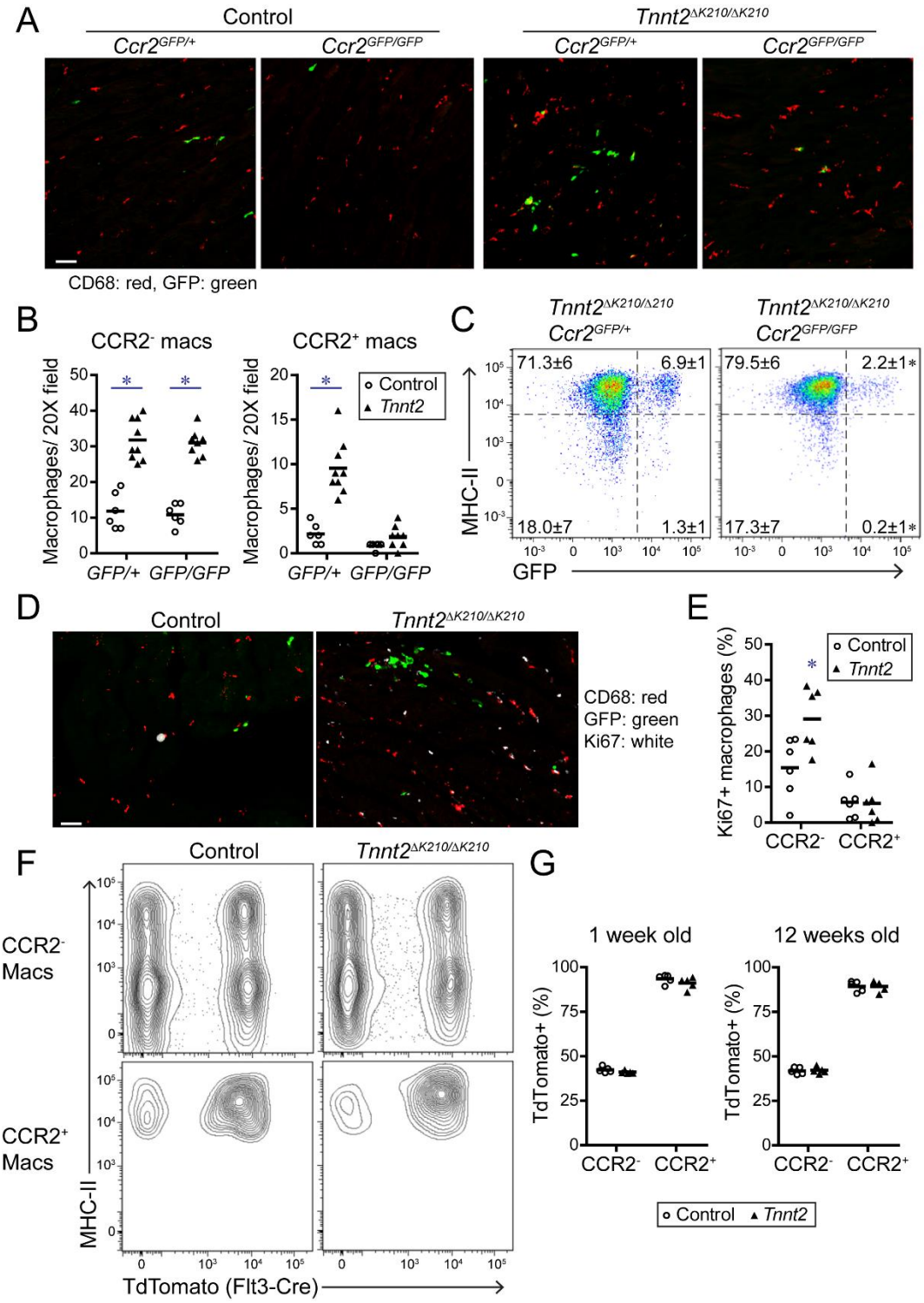
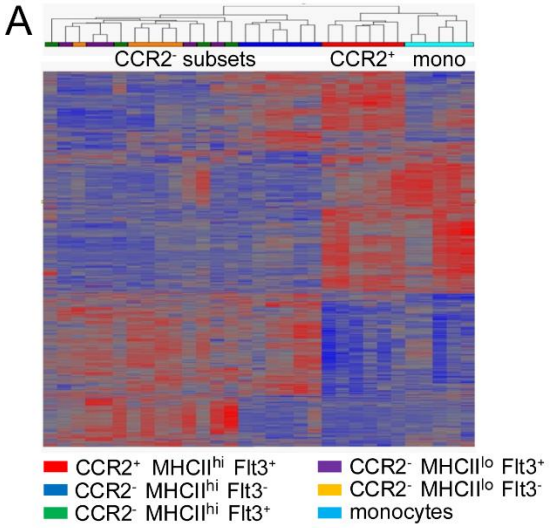
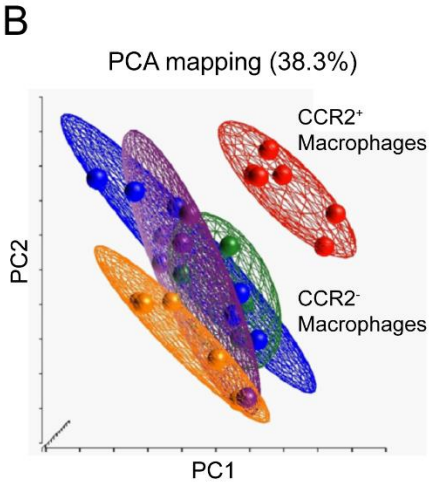
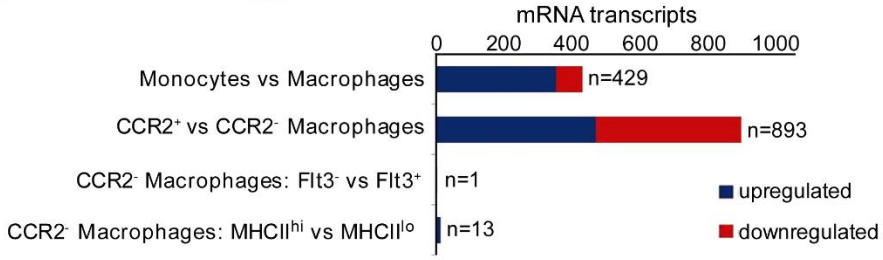

A
Control
Tnnt2ΔK210/ΔK210
Ccr2GFP/+
Ccr2GFP/GFP
Ccr2GFP/+
Ccr2GFP/GFP
CD68: red, GFP: green
B
CCR2- macs
CCR2+ macs
Macrophages/ 20X field
Control
Tnnt2
GFP/+
GFP/GFP
C
Tnnt2ΔK210/Δ210
Ccr2GFP/+
Tnnt2ΔK210/ΔK210
Ccr2GFP/GFP
71.3±6
6.9±1
18.0±7
1.3±1
79.5±6
2.2±1*
17.3±7
0.2±1*
MHC-II
GFP
D
Control
Tnnt2ΔK210/ΔK210
CD68: red
GFP: green
Ki67: white
E
Ki67+ macrophages (%)
Control
Tnnt2
CCR2-
CCR2+
F
Control
Tnnt2ΔK210/ΔK210
CCR2- Macs
CCR2+ Macs
MHC-II
TdTomato (Flt3-Cre)
G
1 week old
12 weeks old
TdTomato+ (%)
CCR2-
CCR2+
Control
Tnnt2

Figure S2 (related to Figure 1). **Recruitment dynamics and origins of cardiac macrophages in control and *Tnnt2*$^{\Delta K210/\Delta K210}$ mice. A**, Immunostaining for CD68 (red) and GFP (green) in control (*Ccr2*$^{GFP/+}$), *Ccr2*$^{GFP/GFP}$, *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/+}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/GFP}$ hearts at 8 weeks of age. Representative images of n=6-8 per experimental group. Scale bar 20μm **B**, Quantification of CCR2^{-} and CCR2^{+} macrophages in the LV myocardium of *Ccr2*$^{GFP/+}$, *Ccr2*$^{GFP/GFP}$, *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/+}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/GFP}$ hearts. * denotes $p<0.05$ compared to control (Mann-Whitney test). n=6-8 per experimental group. **C**, Flow cytometry of CD45+CD64+Ly6G- macrophages in *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/+}$ and *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/GFP}$ hearts at 8 weeks of age showing specific reductions in only CCR2^{+} macrophages. * denotes $p<0.05$ compared to *Tnnt2*$^{\Delta K210/\Delta K210}$ *Ccr2*$^{GFP/GFP}$ hearts (Mann-Whitney test). n=6 per experimental group. **D**, Immunostaining for CD68 (red), GFP (green), and Ki67 (white) in control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts at 8 weeks of age showing increased proliferation of CCR2^{-} macrophages in *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts. n=6 per experimental group. Scale bar 20μm. **E**, Quantification of the percent of CCR2^{-} and CCR2^{+} macrophages that expressed Ki67. * denotes $p<0.05$ compared to controls (Mann-Whitney test). n=6-8 per experimental group. **F-G**, Flow cytometry of CD45^{+}CD64^{+}Ly6G^{-} macrophages in control (*Flt3-cre Roas26-tdTomato*) and *Tnnt2*$^{\Delta K210/\Delta K210}$ *Flt3-cre Rosa26-tdTomato* hearts at 1 week and 12 weeks of age showing that the percent of CCR2^{-} and CCR2^{+} macrophages derived from definitive hematopoietic progenitors (tdTomato^{+}) remains unchanged between control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts. B, E, G: each data point represents a biologically independent replicate (n=5-6 per experimental group).





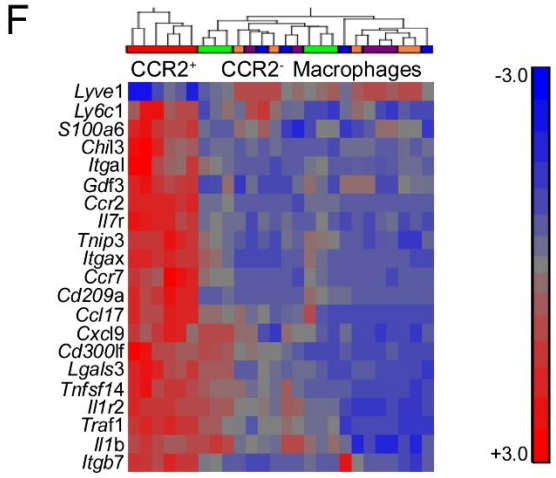


D

CCR2+ Macrophages	p-value
Antigen processing/presentation	9.0 e-10
Immune response	4.6 e-9
Angiogensis	1.6 e-8
Inflammatory response	4.3 e-6
T-cell costimulation	6.8 e-4
Integrin signaling	8.4 e-4

E

CCR2- Macrophages	p-value
Endocytosis	6.8 e-5
Transport	1.5 e-4
Nervous system development	2.2 e-3
Cell migration	2.6 e-3
Cell adhesion	2.8 e-3



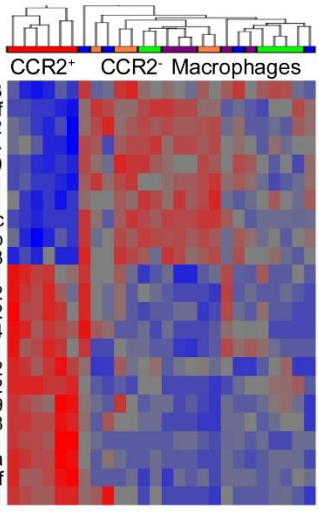


Figure S3 (related to Figure 1)**. CCR2^{-} and CCR2^{+} macrophages have distinct gene expression profiles in dilated cardiomyopathy. A**, Hierarchical Clustering of CCR2^{+}MHCII^{hi}Flt3^{+}, CCR2^{-}MHCII^{lo}Flt3^{-}, CCR2^{-}MHCII^{hi}Flt3^{-}, CCR2^{-}MHCII^{lo}Flt3^{+}, CCR2^{-} MHCII^{hi}Flt3^{+}, and CCR2^{+}Ly6C^{hi} monocytes FACS sorted from 8-week-old *Tnnt2*$^{\Delta K210/\Delta K210}$ mice. n=5-7 per experimental group. **B**, Principal component analysis (PCA) highlighting that CCR2^{+}MHCII^{hi}Flt3^{+} macrophages cluster independently from each of the CCR2^{-} macrophage populations. Each data point represents biologically independent samples. **C**, Bar graph showing the number of differentially expressed genes (FDR $p<0.05$, fold change>1.5) for each of the listed comparisons. Blue: upregulated in *Tnnt2*$^{\Delta K210/\Delta K210}$ mice. Red: down regulated in *Tnnt2*$^{\Delta K210/\Delta K210}$ mice. **D**, Pathways enriched in CCR2^{+} and CCR2^{-} (all subgroups combined) macrophages. **F**, Heat maps listing individual genes differentially expressed in CCR2^{+} and CCR2^{-} macrophages. Scale bar denotes fold change.

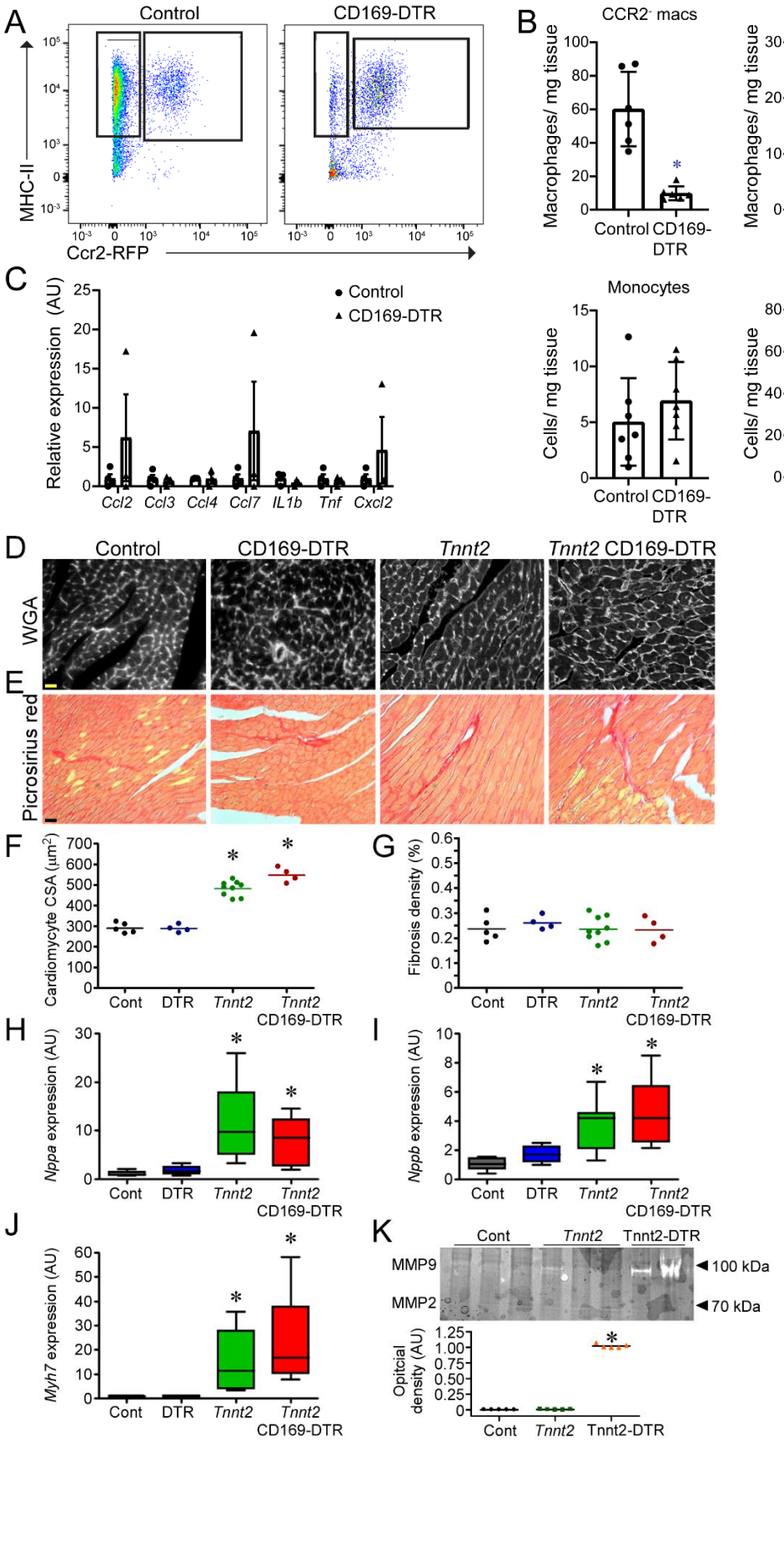

A
Control
CD169-DTR
MHC-II
Ccr2-RFP
B
CCR2⁻ macs
CCR2⁺ macs
Macrophages/ mg tissue
Control
CD169-DTR
C
Control
CD169-DTR
Relative expression (AU)
Ccl2
Ccl3
Ccl4
Ccl7
IL1b
Tnf
Cxcl2
Monocytes
Neutrophils
Cells/ mg tissue
D
Control
CD169-DTR
Tnnt2
Tnnt2 CD169-DTR
WGA
E
Picrosirius red
F
Cardiomycyte CSA (μm²)
Cont
DTR
Tnnt2
Tnnt2 CD169-DTR
G
Fibrosis density (%)
H
Nppa expression (AU)
I
Nppb expression (AU)
J
Myh7 expression (AU)
K
Cont
Tnnt2
Tnnt2-DTR
MMP9
MMP2
100 kDa
70 kDa
Opitcial density (AU)

Figure S4. CCR2$^-$ macrophage ablation and adverse LV remodeling (related to Figures 2-4). **A**, Flow cytometry of macrophages (CD45$^+$Ly6G$^-$CD11b$^+$CD64$^+$) isolated from the hearts of control (*Cx3cr1-GFP/+ Ccr2-RFP/+*) and CD169-DTR (CD169-DTR *Cx3cr1-GFP/+ Ccr2-RFP/+*) mice. n=6 per experimental group. **B**, Quantification of flow cytometry data showing depletion of CCR2$^-$ macrophages and no changes in the abundance of CCR2$^+$ macrophages, monocytes, or neutrophils. Each data point denotes a biologically independent sample (n=6 per experimental group). * denotes $p<0.05$ compared to controls (Mann-Whitney test). **C**, Quantitative RT-PCR for chemokine and cytokine mRNA expression in CCR2$^+$ macrophages isolated from control (*Cx3cr1-GFP/+ Ccr2-RFP/+*) and CD169-DTR (CD169-DTR *Cx3cr1-GFP/+ Ccr2-RFP/+*) hearts. Each data point denotes a biologically independent sample (n=4-6 per experimental group). No statistically significant differences were observed (Mann-Whitney test). **D-E**, Wheat germ agglutinin (WGA, D) and Picrosirius red (E) staining of control, CD169-DTR, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR hearts after 3 weeks of DT treatment. Scale bar 20μm **F-G**, Quantification of cardiomyocyte cross-sectional area and fibrotic density in the hearts of control, CD169-DTR, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR mice after 3 weeks of DT treatment. * denotes $p<0.05$ compared to controls. Each data point represents a biologically independent replicate. **H-J**, Box and whisker plots of *Nppa*, *Npp*b, and *Myh7* mRNA expression in control, CD169-DTR, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR hearts after 3 weeks of DT treatment. * denotes $p<0.05$ compared to controls. n=5-6 per experimental group. **K**, Gelatinase activity assay showing minimal metallomatrix proteinase (MMP) activity in control and *Tnnt2*$^{\Delta K210/\Delta K210}$ hearts. Tnnt2-DTR mice (DT-cardiomyocyte ablation model) treated with DT were included as a positive control as they display marked increase in MMP activity following cardiomyocyte cell death and resultant inflammatory cell infiltration. * denotes $p<0.05$ compared to controls. Each data point represents a biologically independent replicate. n=4-9 per experimental group.

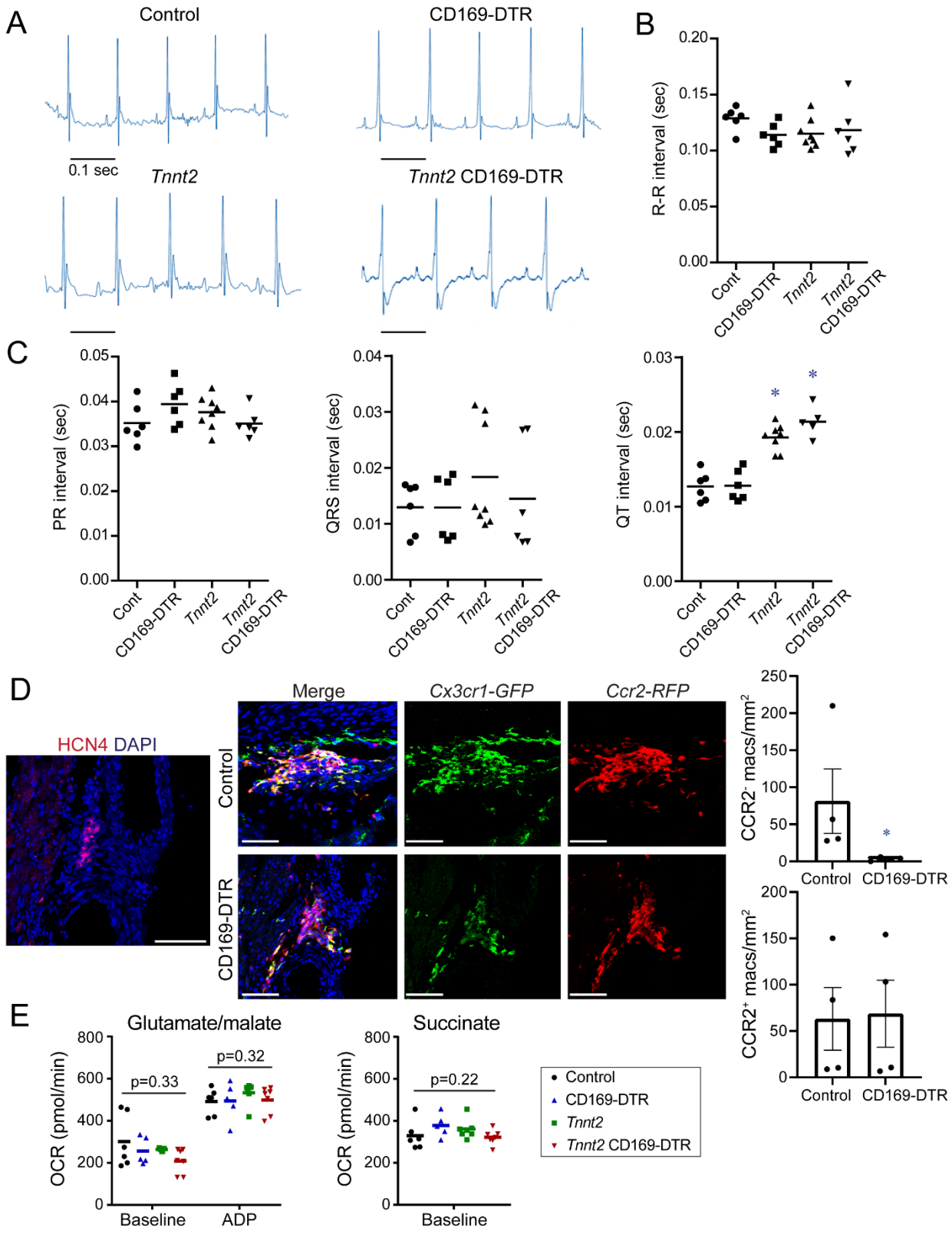

A
Control
CD169-DTR
0.1 sec
Tnnt2
Tnnt2 CD169-DTR
B
R-R interval (sec)
0.20
0.15
0.10
0.05
0.00
Cont
CD169-DTR
Tnnt2
Tnnt2 CD169-DTR
C
PR interval (sec)
0.05
0.04
0.03
0.02
0.01
0.00
QRS interval (sec)
0.04
0.03
0.02
0.01
0.00
QT interval (sec)
0.03
0.02
0.01
0.00
*
D
HCN4 DAPI
Merge
Cx3cr1-GFP
Ccr2-RFP
Control
CD169-DTR
CCR2- macs/mm2
250
200
150
100
50
0
Control
CD169-DTR
CCR2+ macs/mm2
200
150
100
50
0
E
Glutamate/malate
OCR (pmol/min)
800
600
400
200
0
p=0.33
p=0.32
Baseline
ADP
Succinate
p=0.22
Control
CD169-DTR
Tnnt2
Tnnt2 CD169-DTR

Figure S5 (related to Figures 2-4). **Telemetry, atrioventricular node macrophages, and myocardial metabolism following CCR2^{-} macrophage depletion. A**, Representative ECG tracings of control, CD169-DTR, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR hearts after 3 weeks of DT treatment. **B-C**, Quantification of R-R, PR. QRS, and QT intervals in each experimental group. Prolongation of the QT interval was observed in *Tnnt2*$^{\Delta K210/\Delta K210}$ and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR hearts compared to controls. * denotes $p<0.05$ compared to controls. Each data point represents a biologically independent replicate. 6-8 mice per experimental group. **D**, *Left*, representative image of HCN4 immunostaining (red) showing staining in the atrioventricular node. DAPI: blue. Scale bar 100μm. *Center*, immunostaining for GFP (green) and RFP (red) in the atrioventricular node of control (*Cx3cr1-GFP/+ Ccr2-RFP/+*) and CD169-DTR (CD169-DTR *Cx3cr1-GFP/+ Ccr2-RFP/+*) mice. The atrioventicular node region was identified in serial sections using HCN4 staining. DAPI: blue. Scale bar 50μm. Right, quantification of CCR2^{-} and CCR2^{+} macrophages in the atrioventricular node of control (*Cx3cr1-GFP/+ Ccr2-RFP/+*) and CD169-DTR (CD169-DTR *Cx3cr1-GFP/+ Ccr2-RFP/+*) mice. * denotes $p<0.05$ compared to controls. Each data point represents a biologically independent replicate (n=4). All immunostaining studies were performed in 4 independent specimens. **E,** Oxygen consumption rate (OCR) in mitochondria isolated from the hearts of control, CD169-DTR, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ CD169-DTR mice after 3 weeks of DT treatment. Mitochondria were provided either glutamate/malate or succinate substrates. ADP was added to measure maximal OCR. Each data point represents mitochondria preparations from an individual hearts. n=5-6 mice per experimental group.

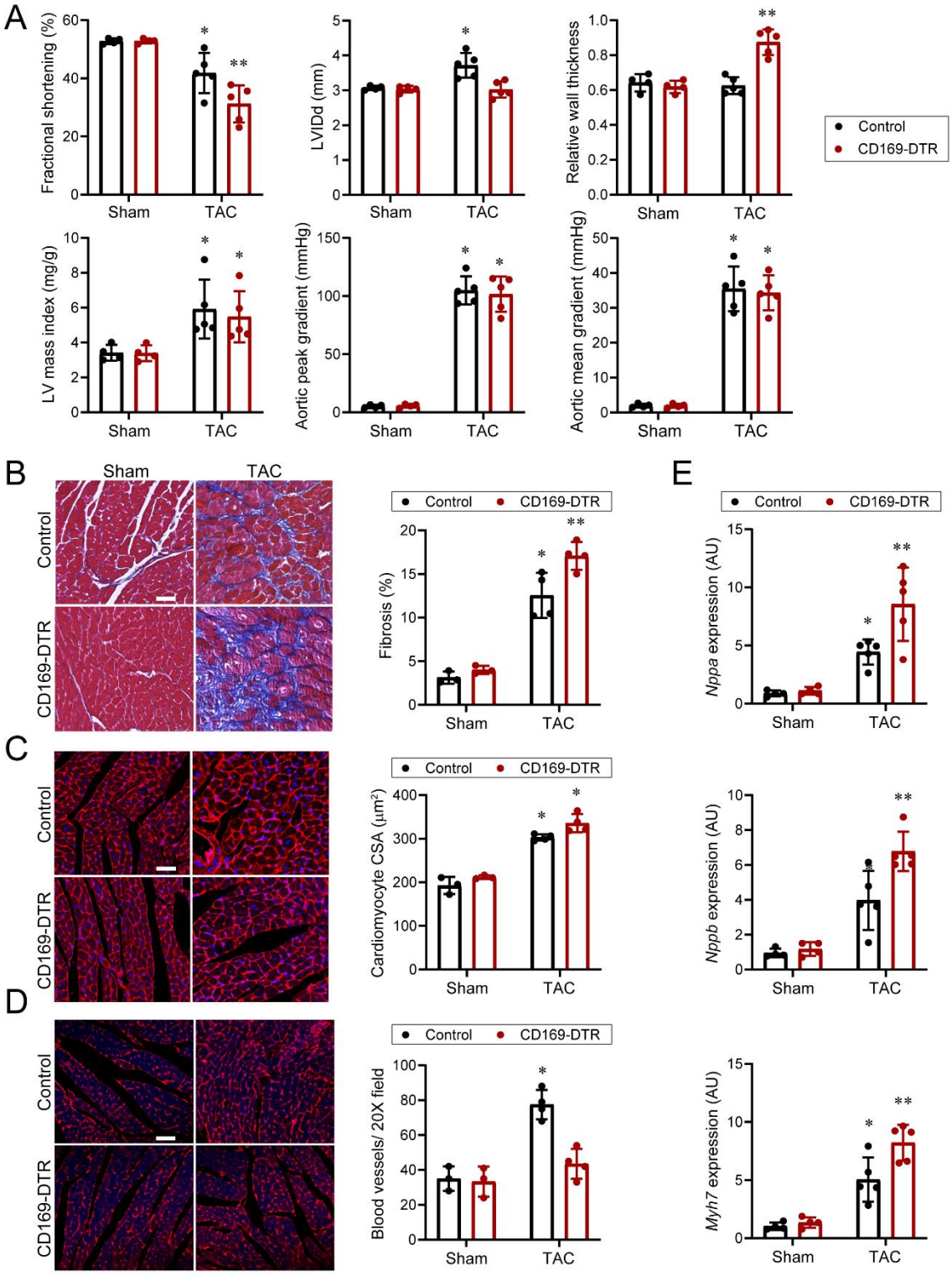

A
Fractional shortening (%)
LVIDd (mm)
Relative wall thickness
LV mass index (mg/g)
Aortic peak gradient (mmHg)
Aortic mean gradient (mmHg)
Sham
TAC
Control
CD169-DTR
B
C
D
E
Fibrosis (%)
Cardiomyocyte CSA (μm²)
Blood vessels/ 20X field
Nppa expression (AU)
Nppb expression (AU)
Myh7 expression (AU)

Figure S6 (related to Figures 2-4). **CCR2^{-} Macrophages Promote Adaptive Remodeling following Pressure Overload. A**, Echocardiographic analysis of control and CD169-DTR mice performed 4 weeks after sham surgery or transverse aortic constriction (TAC). * denotes $p<0.05$ compared to control, ** denotes $p<0.05$ compared to control TAC group (ANOVA, post-hoc Tukey). n=4-5 per experimental group. LVIDd: LV end diastolic dimension. **B-D**, Quantification of myocardial fibrosis (B, Trichrome staining, scale bar 20μm), cardiomyocyte cross-sectional area (C, WGA staining, scale bar 20μm), and myocardial microvascular density (D, CD34 staining, scale bar 40μm) in control and CD169-DTR hearts 4 weeks after sham surgery or TAC. * denotes $p<0.05$ compared to control, ** denotes $p<0.05$ compared to control TAC group. Each data point represents a biologically independent sample. **E**, RT-PCR measuring the expression of *Nppa*, *Nppb*, and *Myh7* mRNA in the hearts of control and CD169-DTR mice 4 weeks after sham surgery or TAC. * denotes $p<0.05$ compared to control, ** denotes $p<0.05$ compared to control TAC group. Each data point represents a biologically independent sample.

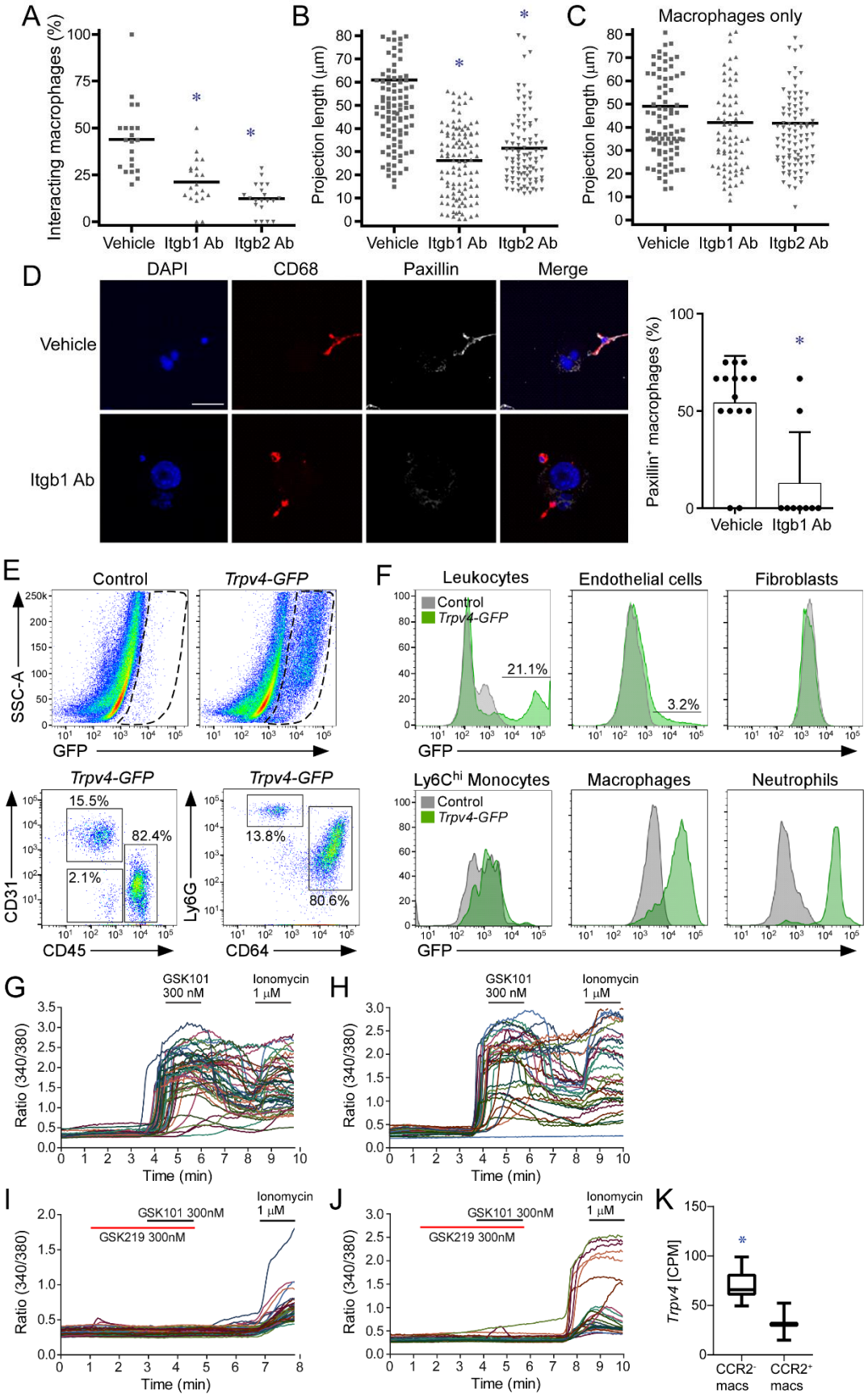

A
Interacting macrophages (%)
Vehicle
Itgb1 Ab
Itgb2 Ab
B
Projection length (μm)
C
Macrophages only
D
DAPI
CD68
Paxillin
Merge
Vehicle
Itgb1 Ab
Paxillin+ macrophages (%)
E
Control
Trpv4-GFP
SSC-A
GFP
CD31
CD45
Ly6G
CD64
15.5%
82.4%
2.1%
13.8%
80.6%
F
Leukocytes
Endothelial cells
Fibroblasts
21.1%
3.2%
Ly6Chi Monocytes
Macrophages
Neutrophils
G
GSK101 300 nM
Ionomycin 1 μM
Ratio (340/380)
Time (min)
H
I
GSK101 300nM
GSK219 300nM
J
K
Trpv4 [CPM]
CCR2- macs
CCR2+ macs

Figure S7 (related to Figures 5-6). **β-integrin mediated macrophage-cardiomyocyte interaction, TRPV4 expression, and TRPV4 activity in cardiac macrophages. A-B**, Quantification of the percent of macrophages interacting with cardiomyocytes (A) and macrophage projection length (B) in co-cultures treated with either isotype antibody (vehicle), Itgb1 neutralizing antibody, or Itgb2 neutralizing antibody. **C**, Quantification of projection length in bone marrow-derived macrophages cultured independently in the presence of isotype antibody (vehicle), Itgb1 neutralizing antibody, or Itgb2 neutralizing antibody. * denotes $p<0.05$ compared to control (AVOVA, post-hoc Tukey). **D**, CD68 (red) and Paxillin (white) immunostaining showing loss of Paxillin expression in cultured macrophages treated with the neutralizing Itgb1 antibody. Blue-DAPI. Scale bar 20μm. Representative images from 4 independent experiments. * denotes $p<0.05$ compared to vehicle control (Mann-Whitney test). Each data point in A-C represents information compiled from 4 experimental replicates. Experiments were repeated 4 times and all data was incorporated into the displayed graphs. **E**, Flow cytometry of *Trpv4-GFP* BAC transgenic hearts showing GFP expression in leukocytes ($CD45^+$), endothelial cells ($CD31^+CD45^-$), neutrophils ($Ly6G^+CD64^-$), and macrophages ($CD64^+Ly6G^-$). Percentages of each cell type as a function of the number of GFP^+ cells is shown. **F**, Histograms showing GFP mean florescent intensity of $CD45^+$ leukocytes, $CD31^+CD45^-$ endothelial cells, $MEFSK4^+CD45^-CD31^-$ fibroblasts, $Ly6C^{hi}$ monocytes, $CD64^+Ly6C^{lo}$ macrophages, and $Ly6G^+$ neutrophils isolated from littermate controls (grey) and *Trpv4-GFP* (green) hearts. Percentages of GFP^+ leukocytes and endothelial cells are shown as a function of total number of leukocytes and endothelial cells, respectively. Data obtained from 3 independent experiments. **G-H**, Ratiometric calcium assays showing that $CCR2^-$ (C) and $CCR2^+$ (D) macrophages isolated from the adult mouse heart by flow cytometry express active TRPV4 channels. GSK101: TRPV4 agonist, Ionomycin: calcium ionophore.**I-J**, Ratiometric calcium assays showing that the TRPV4 antagonist (GSK219) blocks rises in intracellular calcium induced by GSK101 in cardiac $CCR2^-$ (E) and $CCR2^+$ (F) macrophages. Each tracing represents an independently analyzed cell. Tracings were compiled from 3 independent experiments. **K**, *Trpv4* mRNA expression in $CCR2^-$ and $CCR2^+$ cardiac macrophages. RNAseq data derived from Immgen (Immunological Genome, 2020). CPM: counts per million. * denotes $p<0.05$ compared to $CCR2^+$ macrophages (Mann-Whitney test). Data obtained from 5 biologically independent samples per experimental group.

Table S1. (related to Figure 1) **Serial echocardiography of Control and *Tnnt2*$^{\Delta K210/\Delta K210}$ mice**

	Control	*Tnnt2*$^{\Delta K210/\Delta K210}$
Fractional shortening (%)		
7 days	48.7 ± 3.4	28.6 ± 3.4*
14 days	50.6 ± 3.1	26.0 ± 5.5*
28 days	60.7 ± 3.6	30.5 ± 2.9*
8 weeks	52.1 ± 1.3	21.9 ± 3.7*
16 weeks	53.1 ± 2.1	14.2 ± 4.7*
LV diastolic dimension (μm)		
7 days	2.12 ± 0.12	2.18 ± 0.16
14 days	2.28 ± 0.12	2.81 ± 0.23*
28 days	2.77 ± 0.33	3.78 ± 0.27**
8 weeks	3.11 ± 0.44	4.38 ± 0.40**
16 weeks	2.90 ± 0.47	4.39 ± 0.46*
Relative wall thickness		
7 days	0.48 ± 0.08	0.43 ± 0.03
14 days	0.47 ± 0.05	0.49 ± 0.03
28 days	0.60 ± 0.14	0.40 ± 0.04*
8 weeks	0.64 ± 0.10	0.45 ± 0.04*
16 weeks	0.64 ± 0.10	0.47 ± 0.06*
LV mass (mg)		
7 days	21.9 ± 2.9	21.4 ± 5.1
14 days	26.7 ± 3.7	53.0 ± 11.7*
28 days	65.9 ± 4.9	98.3 ± 15.6**
8 weeks	104.5 ± 20.8	179.2 ± 34.1**
16 weeks	98.7 ± 17.6	173.8 ± 29.5*

* denotes p<0.05 compared to control, ** denotes p<0.05 compared to earlier *Tnnt2*$^{\Delta K210/\Delta K210}$ groups (ANOVA, post-hoc Tukey). n=5-6 per experimental group. LV: left ventricle. Mean values and standard deviations are displayed.

Table S2. (related to Figure 2) **Serum chemistries, cytokines, blood counts, and organ weights of control, *CD169-DTR*, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ *CD169-DTR* mice**

	Control		*Tnnt2*$^{\Delta K210/\Delta K210}$	
	-	*CD169-DTR*	-	*CD169-DTR*
BUN (mg)/dL	44.7 ± 7.2	41.6 ± 4.8	40.7 ± 4.8	45.2 ± 5.8
Creatinine (mg/dL)	0.55 ± 0.08	0.51 ± 0.1	0.62 ± 0.07	0.63 ± 0.1
Calcium (mg/dL)	9.3 ± 0.9	10.0 ± 0.7	10.0 ± 0.6	10.4 ± 1.3
Protein (g/dL)	5.5 ± 0.7	5.5 ± 0.7	5.2 ± 0.6	6.0 ± 0.5
Bilirubin (mg/dL)	0.11 ± 0.06	0.13 ± 0.1	0.10 ± 0.06	0.14 ± 0.1
ALT (units/L)	94.7 ± 25	86.0 ± 34	78.4 ± 20	101 ± 31
TNF (ng/μl)	16.0 ± 2.4	15.9 ± 3.2	22.0 ± 3.1*	22.8 ± 4.2*
IL1β (ng/μl)	9.9 ± 1.4	8.7 ± 1.8	14.1 ± 2.6*	11.7 ± 2.9*
WBC (x10^3/μl)	14.3 ± 2.0	12.2 ± 1.5	13.9 ± 2.0	12.0 ± 1.4
Hemoglobin (g/dL)	14.6 ± 1.5	14.0 ± 1.9	14.7 ± 1.4	14.2 ± 1.8
Platelets (x10^3/μl)	893 ± 106	874 ± 190	1011 ± 183	1097 ± 207
Heart/body weight	6.1 ± 0.4	5.5 ± 0.3	9.3 ± 1.3*	10.6 ± 2.8*
Lung/body weight	9.0 ± 1.4	9.4 ± 1.5	8.2 ± 1.3	9.9 ± 1.7

* denotes $p<0.05$ compared to control groups (ANOVA, post-hoc Tukey). n=5-9 per experimental group. ALT: alanine aminotransferase. Mean values and standard deviations are displayed.

Table S3. (related to Figure 2) **Invasive hemodynamics of control, *CD169-DTR*, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ *CD169-DTR* mice.**

	Control		*Tnnt2*$^{\Delta K210/\Delta K210}$	
	-	*CD169-DTR*	-	*CD169-DTR*
Heart rate (beats/minute)				
baseline	266 ± 52	260 ± 72	273 ± 71	308 ± 73
4 ng/min	302 ± 68	288 ± 91	264 ± 54	323 ± 92
8 ng/min	341 ± 103	411 ± 97	330 ± 62	345 ± 84
16 ng/min	505 ± 129	549 ± 30	417 ± 111	484 ± 114
32 ng/min	581 ± 53	621 ± 58	457 ± 122	553 ± 68
64 ng/min	614 ± 38	615 ± 22	554 ± 44	582 ± 58
dP/dt max. (mmHg/sec)				
baseline	5586 ± 1184	5249 ± 1201	1871 ± 490*	2018 ± 778*
4 ng/min	7595 ± 1961	7451 ± 2295	1858 ± 652*	3016 ± 1323*
8 ng/min	11224 ± 2313	11044 ± 2780	4021 ± 1837*	4726 ± 1455*
16 ng/min	16206 ± 1851	15292 ± 1833	4832 ± 1993*	7083 ± 1694*
32 ng/min	17758 ± 1515	17013 ± 2142	5685 ± 2135*	8070 ± 1692*
64 ng/min	17686 ± 1601	18049 ± 1752	7464 ± 2790*	8918 ± 1828*
dP/dt min. (mmHg/sec)				
baseline	-5588 ± 1044	-5236 ± 1134	-2266 ± 637*	-2487 ± 1213*
4 ng/min	-7084 ± 1848	-7374 ± 2487	-2312 ± 954*	-4398 ± 1746*
8 ng/min	-9481 ± 2146	-9599 ± 3043	-5204 ± 2250*	-6529 ± 1572*
16 ng/min	-12926 ± 1713	-11558 ± 2533	-6037 ± 2533*	-8768 ± 1390*
32 ng/min	-12584 ± 1806	-11386 ± 3065	-6841 ± 2255*	-9908 ± 1239
64 ng/min	-12094 ± 2294	-11271 ± 2498	-7855 ± 1911	-10139 ± 1206
LVSP (mmHg)				
baseline	89.1 ± 10	91.4 ± 16	53.7 ± 13	53.7 ± 16
4 ng/min	105 ± 15	107 ± 27	54.4 ± 19	73.7 ± 15
8 ng/min	132 ± 31	114 ± 23	80.1 ± 13	89.5 ± 11
16 ng/min	153 ± 35	130 ± 21	82.9 ± 7.5	95.7 ± 7.5
32 ng/min	155 ± 40	142 ± 31	83.3 ± 6.9	97.2 ± 11
64 ng/min	155 ± 40	147 ± 44	85.8 ± 7.3	101 ± 14
LVEDP (mmHg)				
baseline	7.7 ± 1.4	8.4 ± 2.2	6.8 ± 2.0	5.8 ± 1.4
4 ng/min	9.1 ± 4.1	7.5 ± 2.0	6.2 ± 1.8	7.1 ± 2.1
8 ng/min	7.2 ± 2.6	6.0 ± 1.2	5.6 ± 2.7	8.7 ± 4.5
16 ng/min	5.5 ± 1.9	5.2 ± 1.5	5.2 ± 2.2	7.7 ± 2.7
32 ng/min	4.9 ± 1.2	6.8 ± 5.4	5.5 ± 2.3	8.7 ± 6.0
64 ng/min	6.1 ± 2.4	5.4 ± 2.1	5.2 ± 1.7	8.1 ± 5.5

* denotes $p<0.05$ compared to control groups (ANOVA, post-hoc Tukey). Mice received escalating doses of dobutamine (ng/ml) via intravenous infusion. Measurements were obtained at baseline and indicated dobutamine infusion rates. n=6 per experimental group. dP/dt max: maximum rate of pressure increase, dP/dt min: maximum rate of pressure decease, LVSP: peak LV systolic pressure, LVEDP: LV end diastolic pressure. Mean values and standard deviations are displayed. Data obtained from 9 week old control, *CD169-DTR*, *Tnnt2*$^{\Delta K210/\Delta K210}$, and *Tnnt2*$^{\Delta K210/\Delta K210}$ *CD169-DTR* hearts after 3 weeks of DT treatment.