Gene name	Forward primer	Reverse primer
Pla2g7	GCACCAGAACTTTGACGACTT	CGAAGCTTTGTTGGTGAGGT
Ctgf	CTGTGCCTGCCATTACAACTG	GTGTCCCTTACTTCCTGGCTT
Col1a1	GAGTACTGGATCGACCCTAACCA	GACGGCTGAGTAGGGAACACA
Col3a1	TCCCCTGGAATCTGTGAATC	TGAGTCGAATTGGGGAGAAT
Anf	CACAGATCTGATGGATTTCAAGA	CCTCATCTTCTACCGGCATC
Bnp	GAAGGTGCTGTCCCAGATGA	CCAGCAGCTGCATCTTGAAT
Mcp1	CCTGGATCGGAACCAAATGA	ACCTTAGGGCAGATGCAGTTTTA
Tnfα	AAGGGGATTATGGCTCAGGGT	TTGATGGTGGTGCATGAGAGG
Il12p40	TCCACTTGGCCTTATGCTGTT	AGGCCACGAGCACATGAAATA
Nlrp3	TGCCCATACCTTCAGTCTTGT	GCCACAAACCTTCCATCTAGC
Il1β	TCACAAGCAGAGCACAAGCC	GCATTAGAAACAGTCCAGCCC
Il18	TTAGGTGGGGAGGGTTTGTG	GCAGCCTCGGGTATTCTGTT
Gapdh	TGGAGAAACCTGCCAAGTATGA	GGTCCTCAGTGTAGCCCAAG

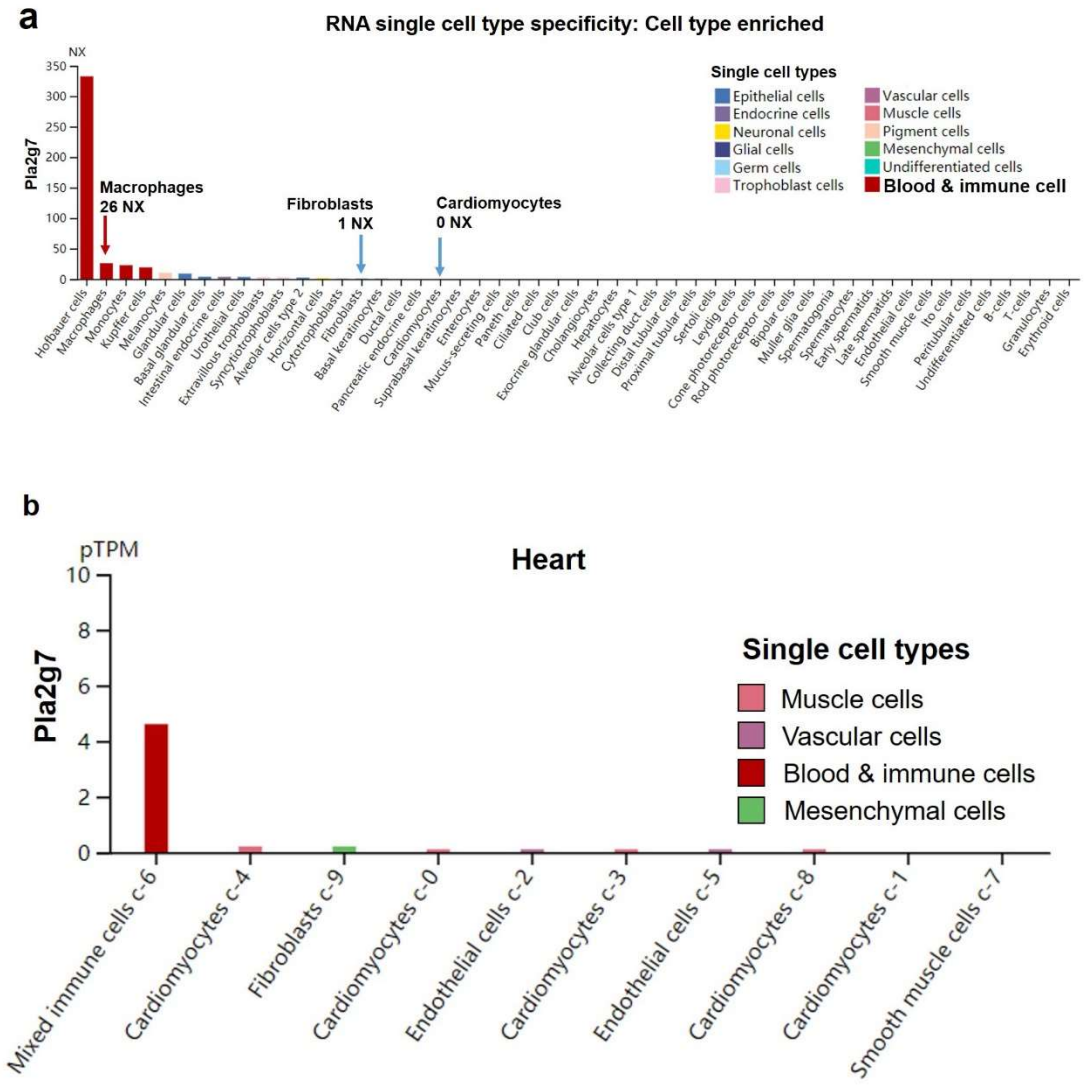
Supplementary Table S1 Primer sequences for RT-PCR.

	Gene name	Fold change (Ang II/Saline)	Probability
	Pla2g7 (Lp-PLA2)	4.172	0.873
	Pla2g5	0.422	0.838
	Pla2g15	2.625	0.785
	Pnpla2	0.691	0.688
	Pla2g4a	3.826	0.674
	Pla2g12a	0.798	0.531
	Pla2g16	0.836	0.447
	Pla2r1	2.617	0.437
	Pla2g4b	0.083	0.425
	Pla2g2e	3.661	0.423
	Pla2g4e	0.780	0.319
	Pla2g2c	0.472	0.304
	Pla2g10os	13.000	0.274
	Pla2g6	0.899	0.230
	Pla2g2d	0.842	0.196
	Pla2g12b	7.333	0.194
	Pla2g3	1.714	0.166
	Lypla2	1.030	0.149
	Pla2g4c	3.400	0.146
	Pla2g2f	0.437	0.127
	Pla2g4f	2.000	0.115
	Pla2g4d	1.667	0.099
	Pla2g10	0.875	0.097
Housekeeping genes	*Gapdh*	0.846	0.468
	Eif5	1.319	0.557
	Actb	1.569	0.738
	Nono	1.458	0.484

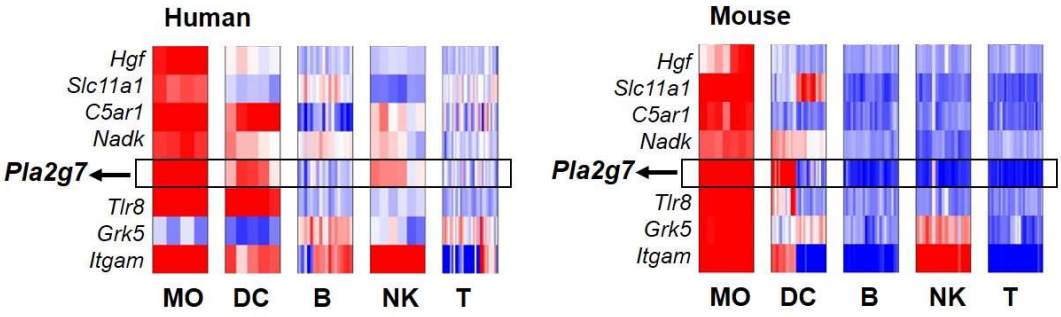
Supplementary Table S2 Ang II-infusion increased *Pla2g7* gene expression in mouse heart tissue. C57BL/6J mice were infused with Ang II (1500 $ng \cdot kg^{-1} \cdot min^{-1}$) or saline for 7 days. Hearts of these mice were collected for RNA-seq analysis. Fold change (FC) and probability of expression change of PLA2 superfamily members and four housekeeping genes (*Gapdh*, *Eif5*, *Actb* and *Nono*) between Ang II-infused and control mouse hearts are shown (n = 3). Fold change ≥ 2 and probability ≥ 0.8 were considered to be statistically significant.

Gene name	Fold change (AngII/Saline)	Probability
Lgals3	2.396	0.901

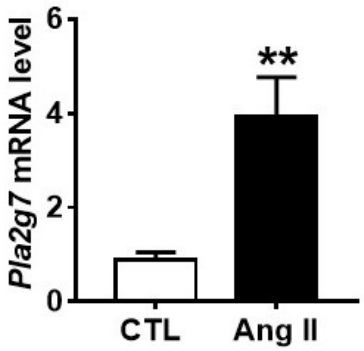
Supplementary Table S3 Ang II increases macrophage specific gene *Lgals3* expression. C57BL/6J mice were infused with Ang II (1500 $ng \cdot kg^{-1} \cdot min^{-1}$) or saline for 7 days. Hearts of these mice were collected for RNA-seq analysis. FC and probability of expression change of *Lgals3* between Ang II-infused and control mouse hearts are shown (n = 3). Fold change ≥ 2 and probability ≥ 0.8 were considered to be statistically significant.



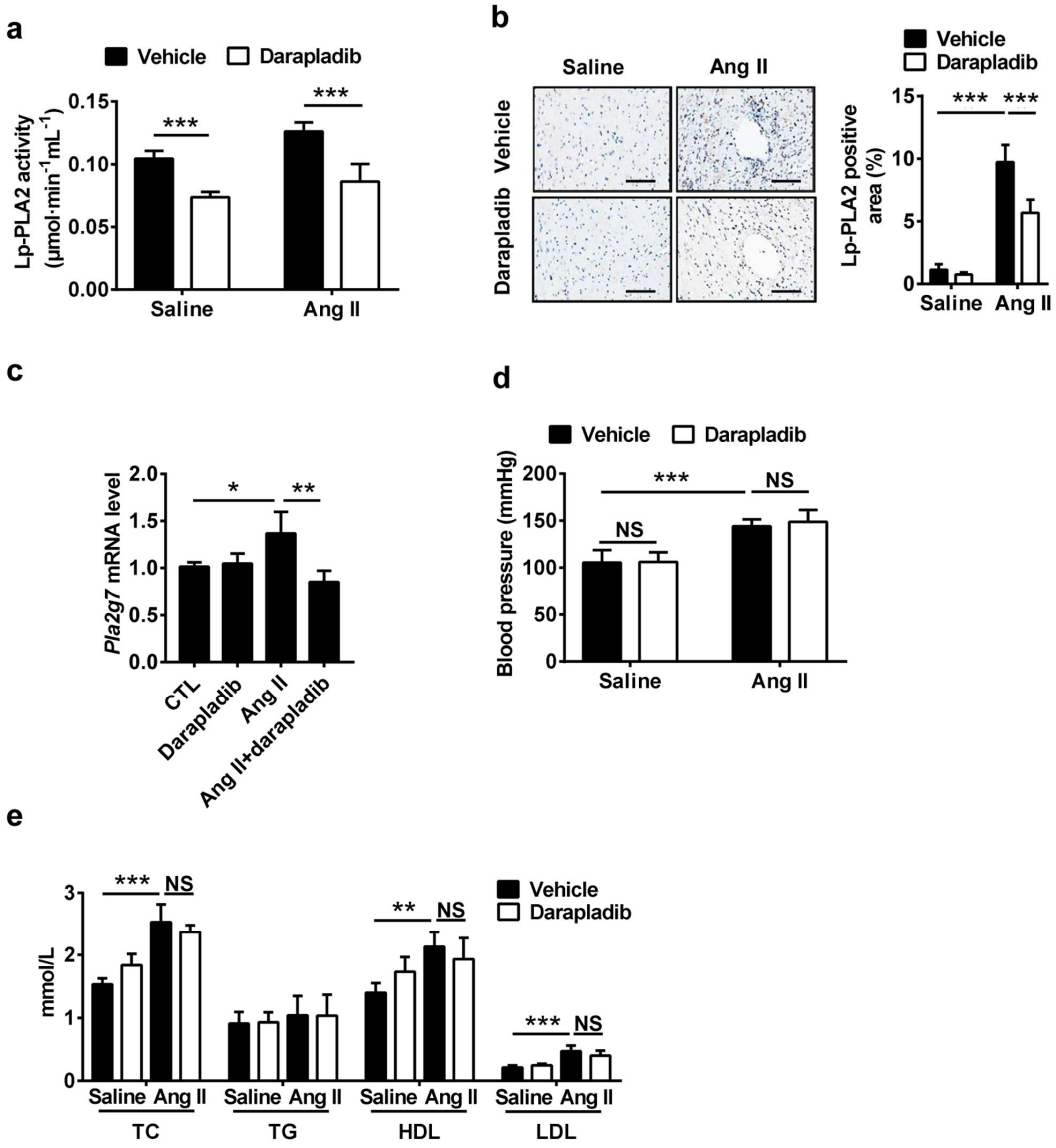
Supplementary Figure S1 Single cell type *Pla2g7* expression in Human Protein Atlas. (a) A summary of single cell *Pla2g7* expression (Normalized eXpression, NX) from all single cell types. **(b)** Single cell *Pla2g7* expression in cell types from heart tissue. Barchart shows pTPM levels in each cluster of single cells. Color-coding is based on cell type groups, each consisting of cell types with functional features in common. Please note that the same cell type may be found in several clusters (Human Protein Atlas, http://www.proteinatlas.org).



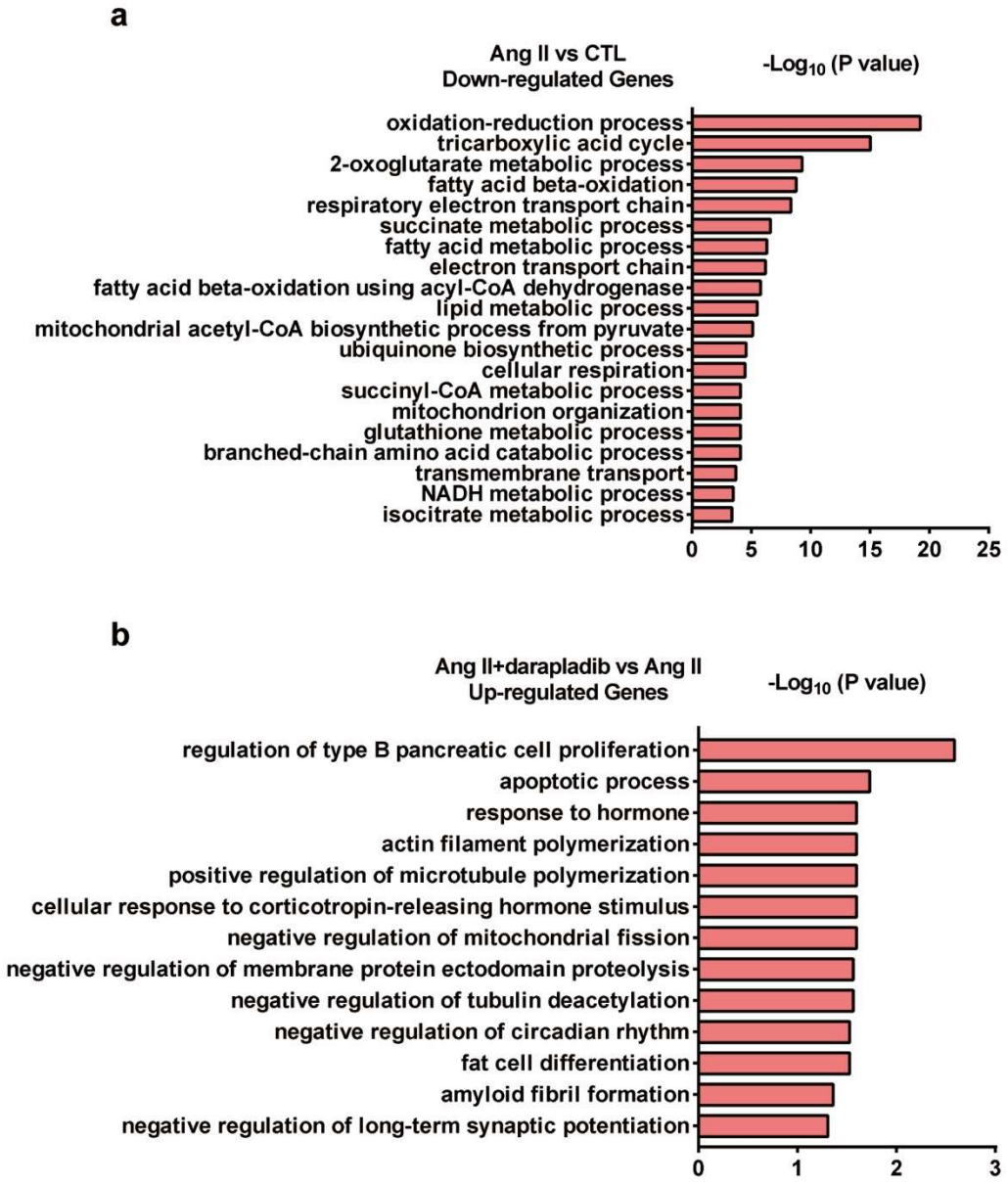
Supplementary Figure S2 Compares the expression of *Pla2g7* expression in human and mouse immune cell lineages, and their co-regulated gene modules (Immunological Genome Project, www.immgen.org). MO, monocyte; DC, dendritic cell; B, B cell; NK, natural killer cell; T, T cell.



Supplementary Figure S3 Ang II increased *Pla2g7* expression in macrophage *in vitro*. Macrophages were stimulated with Ang II (100 nmol/L) for 24 h, and *Pla2g7* expression was detected by RT-PCR (n = 3). Data are presented as mean ± SD, and n represents the number of animals. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.



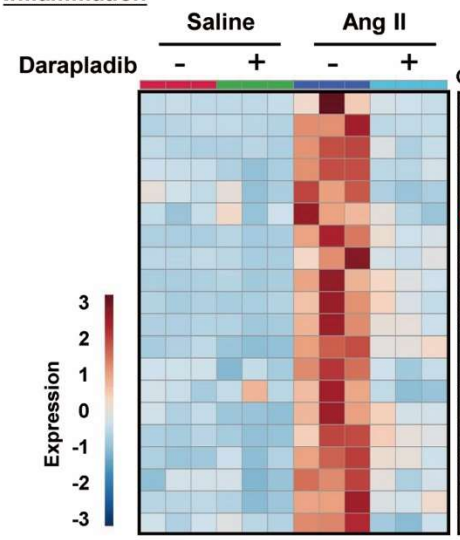
Supplementary Figure S4 Effects of darapladib on Lp-PLA2 activation, hypertension, and plasma lipid upon Ang II stimulation. (a) Analysis of plasma Lp-PLA2 activity (n = 6). **(b)** Immunohistochemical staining of Lp-PLA2 in heart tissues and quantification (n = 5; scale bar = 200 μm). **(c)** *Pla2g7* expression in macrophages, which were pretreated with darapladib (100 nmol/L) for 1 h, and Ang II (100 nmol/L) stimulated for 24 h *in vitro* (n = 4). **(d)** Blood pressure in mice receiving darapladib or vehicle intragastric administration after 7 days of Ang II infusion (n = 6). **(e)** Plasma total cholesterol (TC), total glyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels are shown (n = 6). Data are presented as mean ± SD, and n represents the number of animals. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.



Supplementary Figure S5 RNA-seq analysis of mouse cardiac tissues. GO analysis of biological process for the set of genes downregulated in the Ang II group compared with the saline group **(a)**, and the genes upregulated in the darapladib+Ang II group compared with the Ang II group **(b)** (n = 3). *P* adj < 0.05 is considered to be different.

a

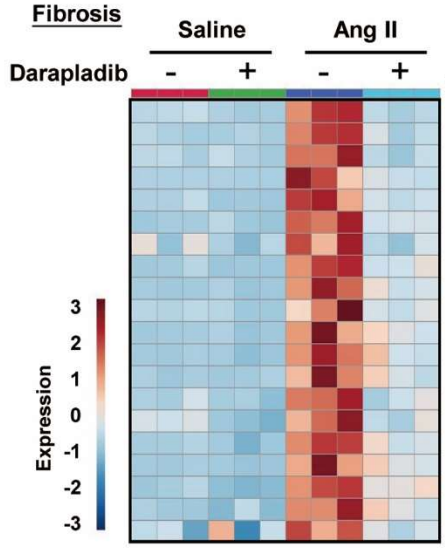
Inflammation



Gene	Ang II+darapladib vs Ang II		Ang II vs CTL	
	Log_2FC	*P* adj	Log_2FC	*P* adj
Cemip	-3.21E+00	3.82E-03	4.99E+00	7.72E-05
Cdk1	-2.87E+00	4.56E-11	3.32E+00	1.06E-13
Ccnb1	-2.81E+00	2.73E-05	3.82E+00	2.20E-11
Rad51	-2.02E+00	9.34E-03	1.95E+00	2.77E-03
Plau	-1.68E+00	3.93E-07	1.14E+00	2.33E-04
Ccl2	-1.68E+00	5.39E-03	1.90E+00	2.60E-05
Fn1	-1.49E+00	2.20E-08	2.94E+00	3.01E-65
Col18a1	-1.48E+00	1.01E-03	2.09E+00	1.22E-10
Col1a1	-1.28E+00	7.45E-04	3.09E+00	1.02E-41
Sfrp2	-1.21E+00	1.29E-02	2.39E+00	2.27E-14
Sfrp1	-1.13E+00	2.30E-04	2.06E+00	2.86E-21
Thbs1	-1.04E+00	1.95E-05	2.43E+00	1.92E-27
Hmgb2	-1.02E+00	2.34E-05	9.52E-01	4.25E-07
Edn1	-8.65E-01	2.06E-02	7.15E-01	1.84E-02
Igf1	-8.62E-01	2.81E-02	1.38E+00	8.19E-08
Col16a1	-7.93E-01	4.93E-02	1.95E+00	4.20E-13
S100a11	-7.88E-01	1.49E-04	1.51E+00	5.77E-24
Adcyap1r1	-7.23E-01	1.79E-02	9.00E-01	3.87E-04
Mcam	-7.18E-01	3.54E-02	1.13E+00	6.32E-09
Dnmt1	-6.14E-01	3.62E-02	5.63E-01	2.68E-03

b

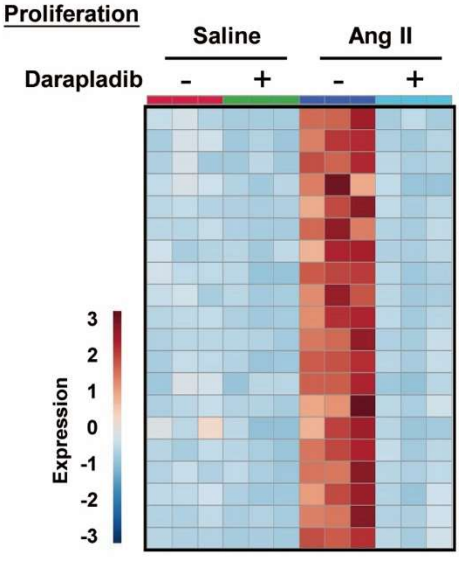
Fibrosis



Gene	Ang II+darapladib vs Ang II		Ang II vs CTL	
	Log_2FC	*P* adj	Log_2FC	*P* adj
Ccna2	-3.29E+00	4.53E-15	2.82E+00	1.08E-21
Ccnb1	-2.81E+00	2.73E-05	3.82E+00	2.20E-11
Troap	-2.81E+00	1.96E-04	2.74E+00	2.03E-06
Tnc	-2.62E+00	1.23E-10	5.36E+00	7.15E-54
Adam12	-2.18E+00	2.80E-09	3.03E+00	1.52E-15
Acan	-2.03E+00	9.98E-04	4.54E+00	1.96E-07
Cdc6	-1.91E+00	2.22E-02	1.45E+00	4.87E-02
Col12a1	-1.74E+00	4.61E-07	3.48E+00	8.15E-26
Fn1	-1.49E+00	2.20E-08	2.94E+00	3.01E-65
Col18a1	-1.48E+00	1.01E-03	2.09E+00	1.22E-10
Col1a1	-1.28E+00	7.45E-04	3.09E+00	1.02E-41
Col3a1	-1.27E+00	2.04E-03	2.81E+00	4.35E-59
Sfrp2	-1.21E+00	1.29E-02	2.39E+00	2.27E-14
E2f1	-1.19E+00	1.46E-02	1.44E+00	8.52E-05
Thy1	-1.12E+00	2.88E-03	1.06E+00	7.05E-06
Col5a1	-1.12E+00	2.37E-07	1.90E+00	2.76E-39
Col1a2	-1.09E+00	4.71E-03	2.64E+00	1.21E-30
Thbs1	-1.04E+00	1.95E-05	2.43E+00	1.92E-27
Wisp2	-1.02E+00	6.77E-03	2.07E+00	4.01E-17
Spon2	-1.01E+00	3.27E-03	1.50E+00	6.15E-05

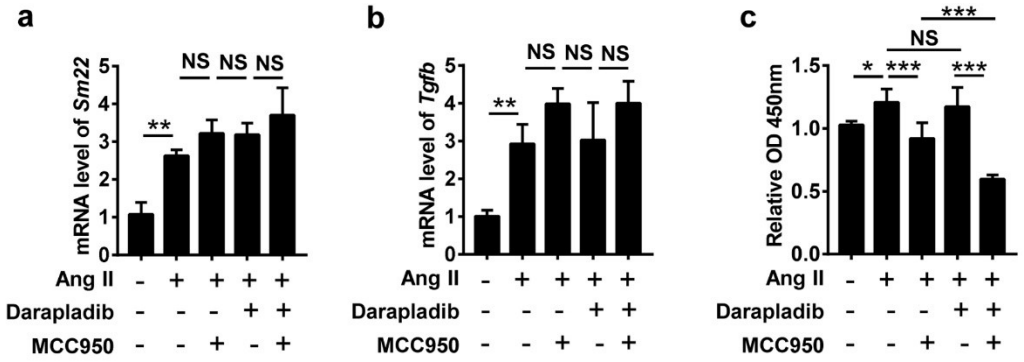
c

Proliferation

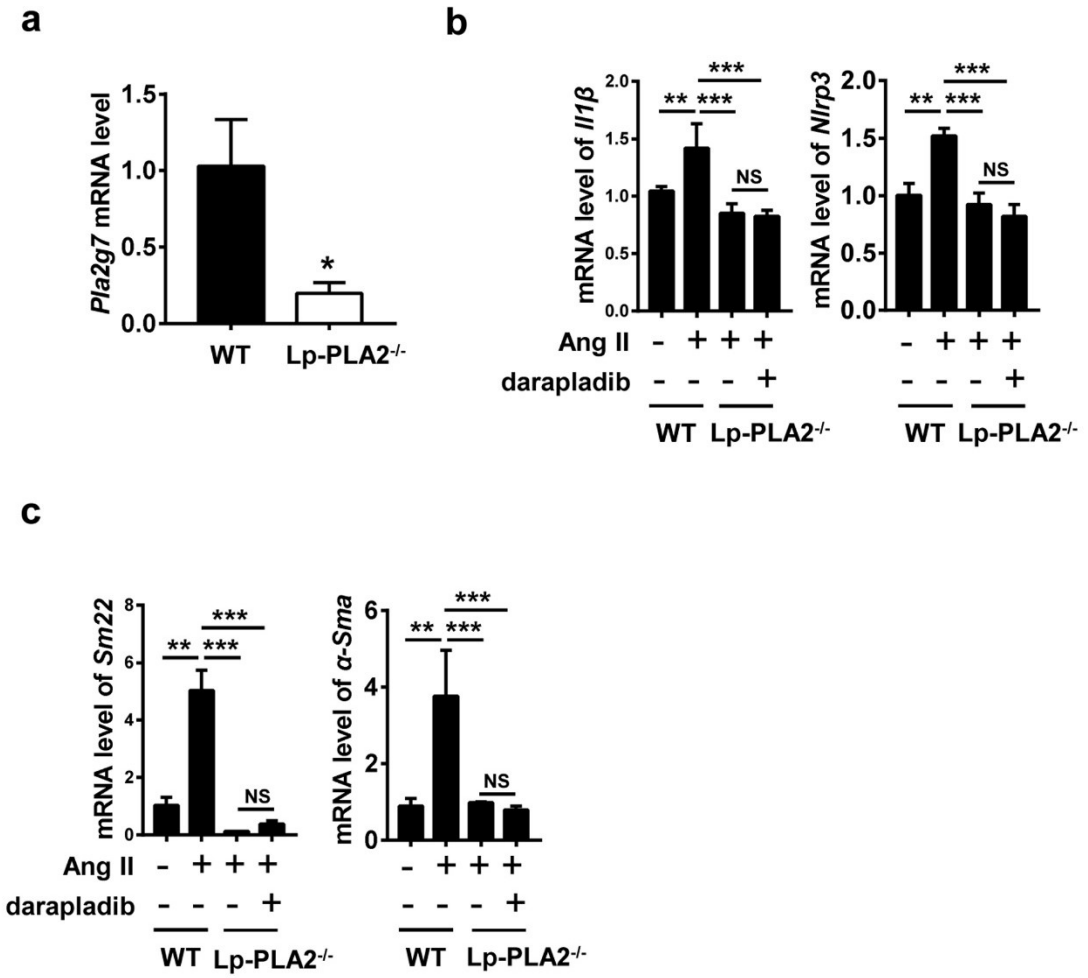


Gene	Ang II+darapladib vs Ang II		Ang II vs CTL	
	Log_2FC	*P* adj	Log_2FC	P adj
Ska1	-4.51E+00	1.92E-02	2.97E+00	1.20E-02
Pbk	-4.09E+00	5.90E-08	2.53E+00	3.74E-05
Cdc25c	-4.00E+00	1.46E-02	3.35E+00	8.68E-03
Mis18bp1	-3.95E+00	3.52E-03	2.13E+00	8.42E-03
Kif18b	-3.59E+00	4.84E-09	3.37E+00	1.42E-10
Cep55	-3.51E+00	2.51E-08	3.06E+00	1.16E-08
Sapcd2	-3.48E+00	2.40E-03	3.27E+00	9.62E-04
Bub1	-3.47E+00	4.32E-05	2.34E+00	3.33E-04
Ckap2	-3.45E+00	2.20E-08	2.56E+00	2.37E-06
Ccna2	-3.29E+00	4.53E-15	2.82E+00	1.08E-21
Fam83d	-3.24E+00	1.05E-05	3.25E+00	5.23E-07
Melk	-3.14E+00	1.17E-05	3.03E+00	4.71E-06
Cdkn3	-3.11E+00	4.67E-05	2.08E+00	1.38E-03
Pimreg	-3.10E+00	1.05E-05	3.33E+00	6.51E-09
Ect2	-3.09E+00	1.13E-05	1.63E+00	5.94E-03
Nek2	-3.07E+00	3.08E-06	3.12E+00	2.67E-07
Ccnb2	-3.03E+00	8.50E-11	2.97E+00	2.32E-11
Kntc1	-2.93E+00	4.57E-03	2.54E+00	1.23E-04
Foxm1	-2.91E+00	1.36E-09	3.11E+00	3.19E-19
Cdca3	-2.89E+00	6.18E-08	3.30E+00	8.70E-17

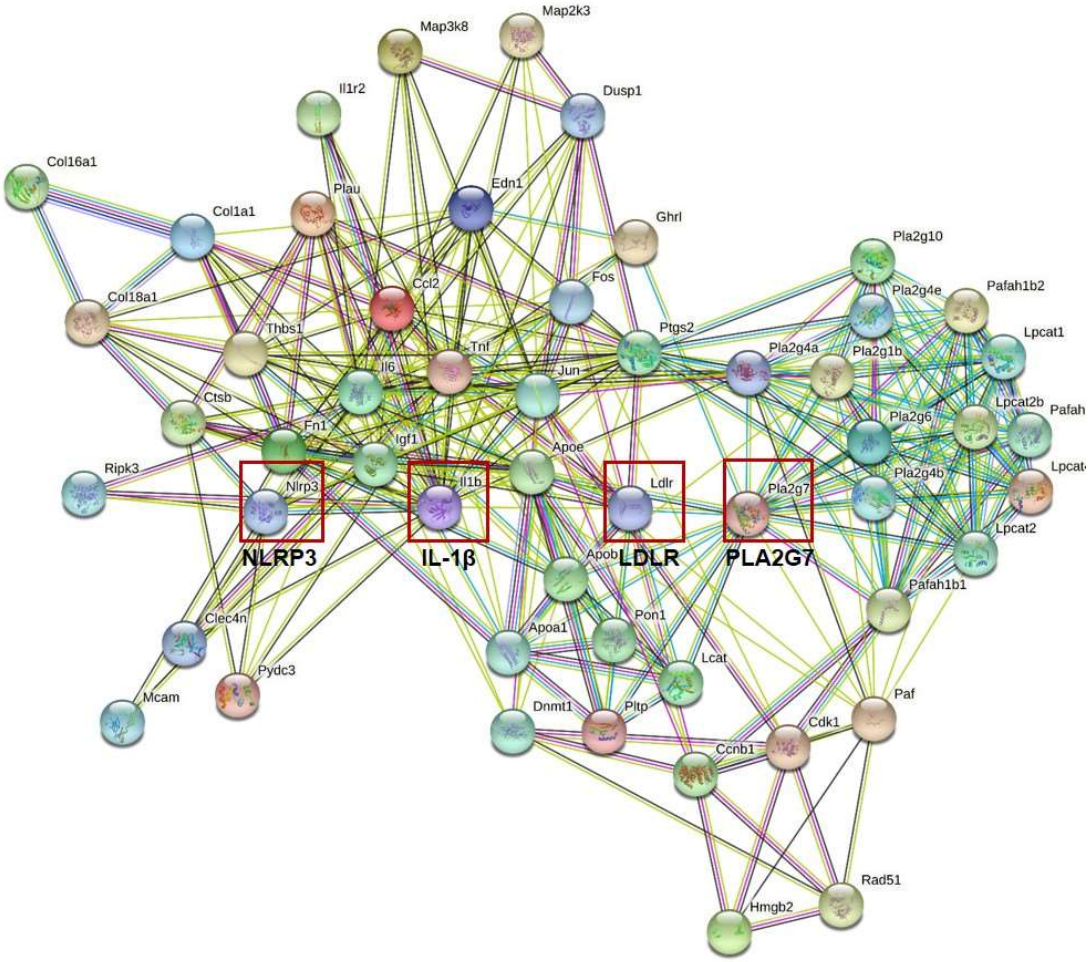
Supplementary Figure S6 Top 20 differentially expressed genes involved in inflammation (a), fibrosis (b), and proliferation (c) are shown. They were all significantly upregulated in the Ang II group compared with the saline group, and downregulated in the Ang II+darapladib group compared with the Ang II group. Genes were listed according to the FC between the Ang II+darapladib group and the Ang II group (n = 3). *P* adj < 0.05 is considered to be different.



Supplementary Figure S7 Darapladib regulated Ang II-induced macrophage inflammation and myofibroblast trans-differentiation by targeting Lp-PLA2. Cardiac fibroblasts were pre-treated with MCC950 (1 μmol/L) or/and darapladib (100 nmol/L) before Ang II (100 nmol/L) stimulation for 24 h. Gene expression of *Sm22* **(a)** and *Tgfb* **(b)** were detected by RT-PCR (n = 3)**. (c)** Cell proliferation was detected by CCK8 assay (n = 6). Data are presented as the mean ± standard deviation, and n represents the number of animals. NS indicates not significant. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.



Supplementary Figure S8 Darapladib regulated Ang II-induced macrophage inflammation and myofibroblast trans-differentiation by targeting Lp-PLA2. (a) Gene expression of *Pla2g7* in the heart of WT mice and Lp-PLA2-knock out mice (n = 3). BMDMs from WT and Lp-PLA2-knock out mice were primed with LPS (100 ng/mL) for 3 h, then treated with darapladib (100 nmol/L) for 1 h before stimulation with 100-nmol/L Ang II for 24 h to detect gene expression of *Nlrp3* and *Il1β* (n = 3) **(b)**. Macrophages were treated as in **b**, and the supernatants were collected. Starved fibroblasts were cultured in different macrophage supernatants respectively for 24 h. The mRNA levels of *Sm22* and *α-Sma* were detected by RT-PCR **(c)**. *Sm22*, smooth muscle protein 22-alpha. Data are presented as the mean ± standard deviation, and n represents the number of animals. NS indicates not significant. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.



Supplementary Figure S9 Protein-protein interaction (PPI) network analysis. Key genes regulated by darapladib detected in our study and associated genes found from related literature were put into STRING for network construction. Apoa1, Apolipoprotein A-I; Apob, Apolipoprotein B-100; Apoe, Apolipoprotein E; Ccl2, C-C motif chemokine 2; Ccnb1, E3 ubiquitin-protein ligase CCNB1IP1; Cdk1, Cyclin-dependent kinase 1; Clec4n, C-type lectin domain family 6 member A; Col16a1, Collagen alpha-1(XVI) chain; Col18a1, Collagen alpha-1(XVIII) chain; Col1a1, Collagen alpha-1(I) chain; Ctsb, Cathepsin B; Dnmt1, DNA (cytosine-5)-methyltransferase 1; Dusp1, Dual specificity protein phosphatase 1; Edn1, Endothelin-1; Fn1, Fibronectin; Fos, Proto-oncogene c-Fos; Ghrl, Appetite-regulating hormone; Hmgb2, High mobility group protein B2; Igf1, Insulin-like growth factor I; Il1b, Interleukin-1 beta; Il1r2, Interleukin-1 receptor type 2; Il6, Interleukin-6; Jun,

Transcription factor AP-1; Lcat, Phosphatidylcholine-sterol acyltransferase; Ldlr, Low-density lipoprotein receptor; Lpcat1, Lysophosphatidylcholine acyltransferase 1; Lpcat2, Lysophosphatidylcholine acyltransferase 2; Lpcat2b, Lysophosphatidylcholine acyltransferase 2B; Lpcat4, Lysophospholipid acyltransferase LPCAT4; Map2k3, Dual specificity mitogen-activated protein kinase kinase 3; Map3k8, Mitogen-activated protein kinase kinase kinase 8; Mcam, Cell surface glycoprotein MUC18; Nlrp3, nucleotide-binding oligomerization domain-like receptor with pyrin domain 3; Paf, PCNA-associated factor; Pafah1b1, Platelet-activating factor acetylhydrolase IB subunit beta; Pafah1b2, Platelet-activating factor acetylhydrolase IB subunit alpha2; Pafah1b3, Platelet-activating factor acetylhydrolase IB subunit alpha1; Pla2g10, Group 10 secretory phospholipase A2; Pla2g1b, Phospholipase A2; Pla2g4a, Cytosolic phospholipase A2; Pla2g4b, Cytosolic phospholipase A2 beta; Pla2g4e, Cytosolic phospholipase A2 epsilon; Pla2g6, 85/88 kDa calcium-independent phospholipase A2; Pla2g7, Platelet-activating factor acetylhydrolase; Plau, Urokinase-type plasminogen activator; Pltp, Phospholipid transfer protein; Pon1, Serum paraoxonase/arylesterase 1; Ptgs2, Prostaglandin G/H synthase 2; Pydc3, Pyrin domain-containing protein 3; Rad51, DNA repair protein RAD51 homolog 1; Ripk3, Receptor-interacting serine/threonine-protein kinase 3; Thbs1, Thrombospondin-1; Tnf, Tumor necrosis factor.