1 **Supplemental Materials**

2 **PPARγ Agonist Pioglitazone Prevents Hypoxia-induced Cardiac Dysfunction By**

3 **Reprogramming Glucose Metabolism**

4

5 **Supplementary**

6 **Tables 1-2 and Figures 1-4**

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9 Yijin Wang[1†], Ru Zhang[2†], Qian Chen[1], Zhangwen Lei[3], Caiyu Shi[1], Yifei Pang[3], Shan'an

10 Zhang[4], Linjie He[5], Longtao Xu[4], Jinliang Xing[5*], Haitao Guo[5*]

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12 [1]College of Life Sciences, Northwest University, Xi'an, 710069, China

13 [2]The Key Laboratory of Aerospace Medicine, Ministry of Education, Fourth Military Medical

14 University, Xi'an, 710069, China

15 [3]School of Medicine, Northwest University, Xi'an, 710069, China

16 [4]College of Basic Medicine, Fourth Military Medical University, Xi'an, 710032, China

17 [5]State Key Laboratory of Cancer Biology and Department of Physiology and Pathophysiology,

18 Fourth Military Medical University, Xi'an, 710032, China

19 [†]This represents these authors contributed equally to this work.

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21 *Correspondence to: Haitao Guo and Jinliang Xing, State Key Laboratory of Cancer Biology

22 and Department of Physiology and Pathophysiology, Fourth Military Medical University, 169

23 Changle West Road, Xi'an 710032, China. Email: haitaoguo@fmmu.edu.cn and

24 xingjl@fmmu.edu.cn.

27 **Supplementary Tables**

28 **Supplementary Table 1**

29 **Primary antibodies used for western blotting**

Antibody	Target species	Working dilutions	Catalog No.	Supplier
GLUT1	Rabbit	WB: 1/1000	A6982	ABclonal, Wuhan, China
HK2	Rabbit	WB: 1/1000	A20829	ABclonal, Wuhan, China
PKM2	Rabbit	WB: 1/1000	A0268	ABclonal, Wuhan, China
LDHA	Rabbit	WB: 1/1000	A1146	ABclonal, Wuhan, China
PDH	Rabbit	WB: 1/1000	ab168379	Abcam, Cambridge, UK
P-PDH	Rabbit	WB: 1/1000	ab177461	Abcam, Cambridge, UK
PDK4	Rabbit	WB: 1/1000	A13337	ABclonal, Wuhan, China
HIF-1α	Rabbit	WB: 1/1000	ab179483	Abcam, Cambridge, UK
PPARγ	Rabbit	WB: 1/1000	16643-1-AP	Proteintech, Wuhan, China
α-actin	Rabbit	WB: 1/3000	A2319	ABclonal, Wuhan, China
AKT	Rabbit	WB: 1/1000	AP0140	ABclonal, Wuhan, China
p-AKT	Rabbit	WB:1/1000	4060	CST, Boston, USA
p-70S6	Rabbit	WB:1/1000	2708	CST, Boston, USA
p-p70S6	Mouse	WB:1/1000	9206	CST, Boston, USA

30

31 **Supplementary Table 2**

32 **Primer sequences used in RT-PCR**

Gene		Sequences
HIF-1α (mouse)	Forward	GCGAGAACGAGAAGAAAGATG
	Reverse	GTGGCAACTGATGAGCAAGC
actin (mouse)	Forward	AACAGTCCGCCTAGAAGCAC
	Reverse	CGTTGACATCCGTAAAGACC

33
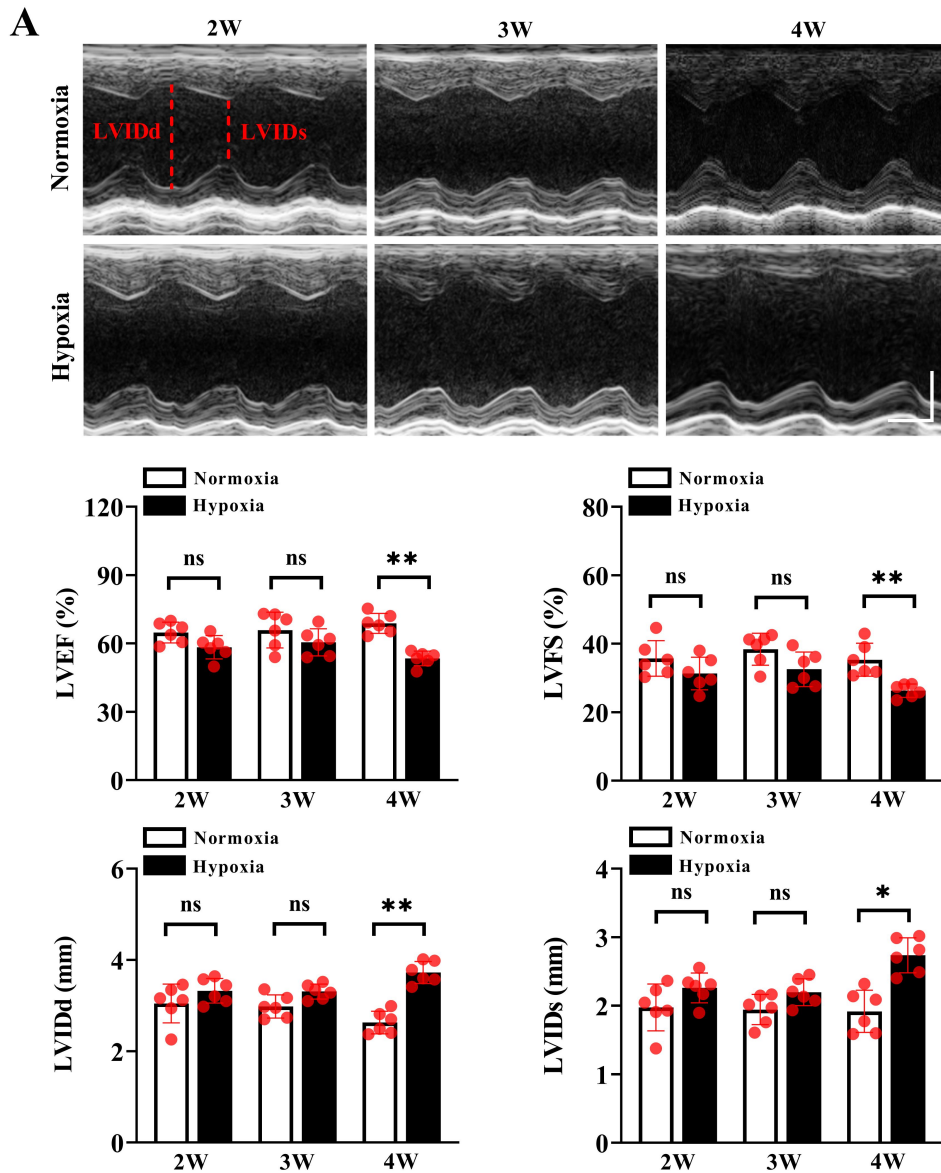
Supplementary Figures

Supplementary Figure 1. Pioglitazone prevents hypoxia-induced cardiac left ventricular dysfunction. (A) Representative echocardiographic images and data analysis of left ventricular (LV) ejection fraction (LVEF), LV fractional shortening (LVFS), and LV systolic and diastolic internal dimension (LVIDs/d) under normoxic and hypoxic conditions ($n = 6$). LVIDd and LVIDs were annotated with red dotted lines. Scale bars, vertical 2mm and horizontal 50ms. $^*P < 0.05$, $^{**}P < 0.01$ in control group under normoxia *vs*. hypoxia.

A

EFP

B

42
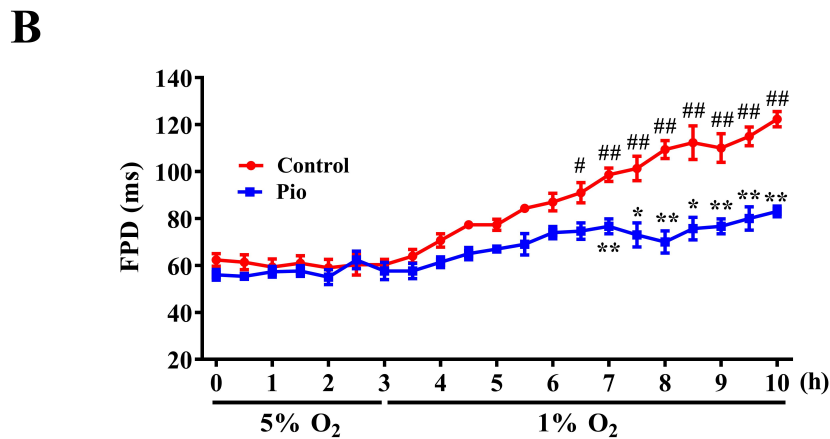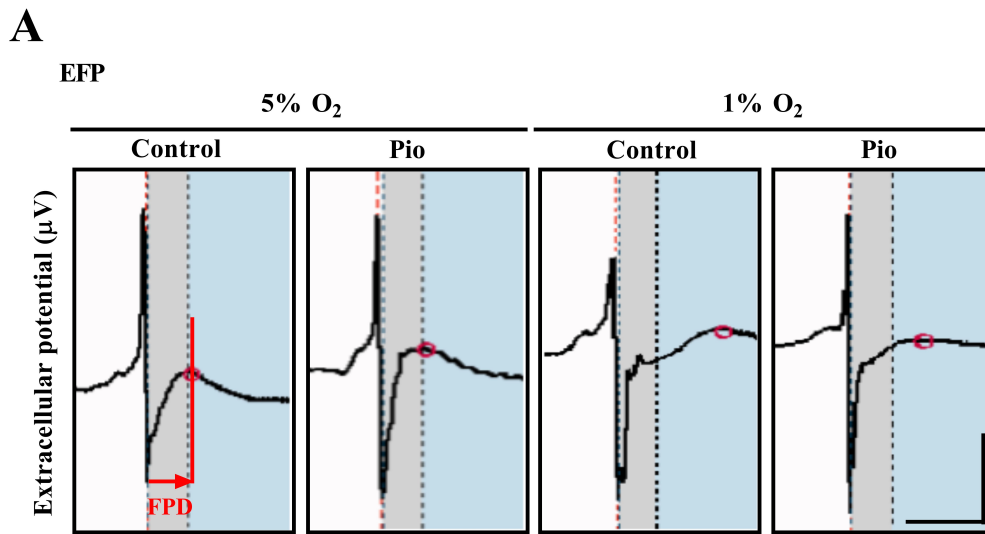
Supplementary Figure 2. Effect of pioglitazone on the extracellular field potential signal in cardiomyocytes under hypoxia. (A) Representative field potential wave tracings in control and pioglitazone (pio)-treated cardiomyocytes under 5% O_2 and 1% O_2. The field potential duration (FPD) was labeled with red arrows. Scale bars, vertical 20μV and horizontal 150ms. (B) The recordings of FPD in cardiomyocytes. Data were from three independent experiments. *$P < 0.05$, **$P < 0.01$ in control group *vs*. pio group under 1% O_2. #$P < 0.05$, ##$P < 0.01$ in control group under 5% O_2 *vs*. 1% O_2.

A

IMP

Pio + 1% O$_2$

Pio + GW9662 + 1% O$_2$

Pio + KC7F2 + 1% O$_2$

B

C

D

EFP

E

50
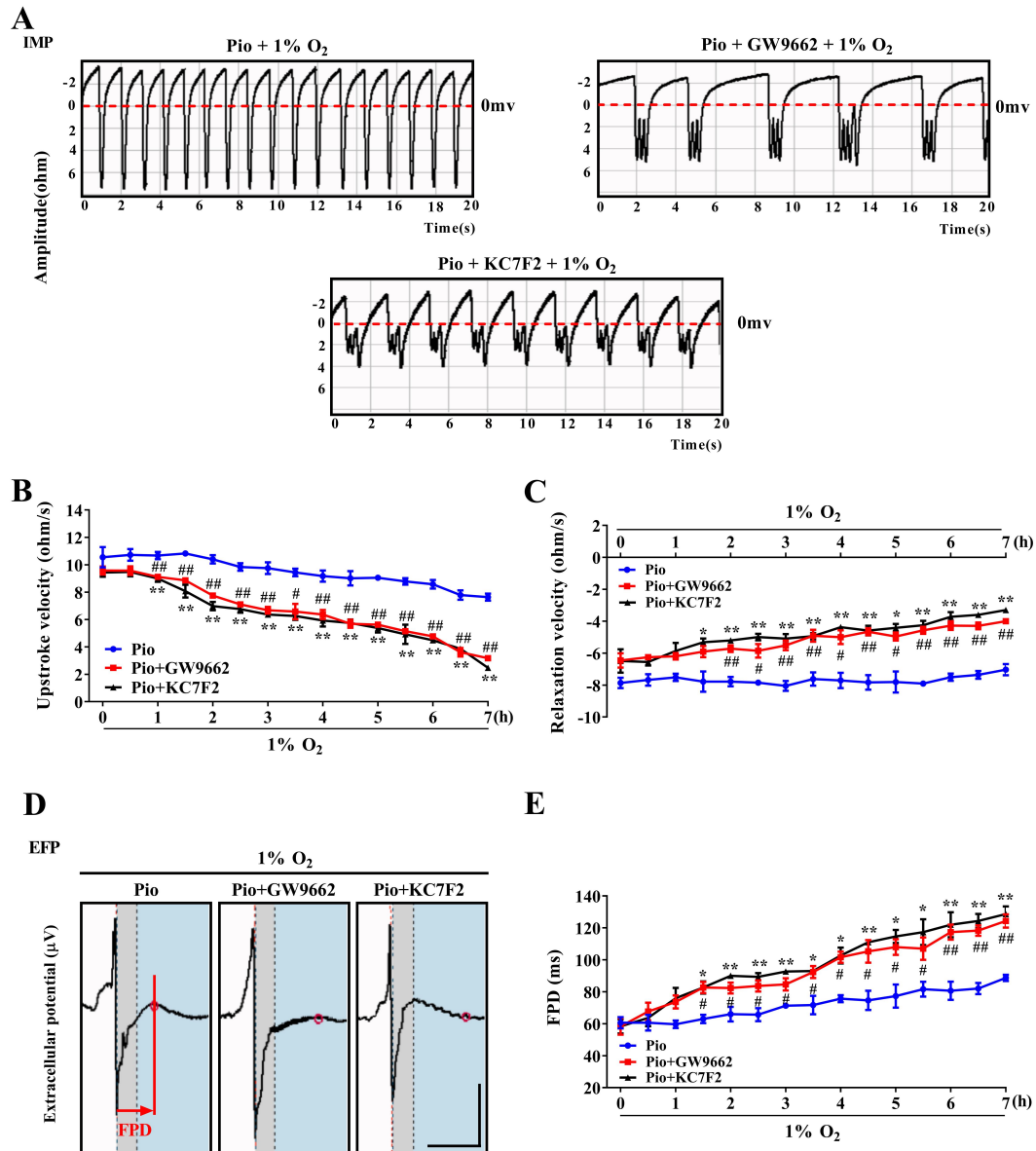
Supplementary Figure 3. The PPARγ agonist pioglitazone promotes cardiomyocyte

contractility and induces changes in cardiomyocyte electrophysiological activity under

hypoxia by modulating the HIF-1α pathway. (A) Representative tracings of intracellular

membrane potential (IMP) in cardiomyocytes treated with pio alone, pio combined with

GW9662, and pio combined with KC7F2 under 1% O$_2$. (B-C) Recordings of IMP upstroke

velocity (B) and IMP relaxation velocity (C) in cardiomyocytes with treatment as indicated.

The recordings were obtained for 7 hours under 1% O$_2$. (D) Representative field potential

58 wave tracings in cardiomyocytes with treatment as indicated. Field potential duration (FPD)

59 was labeled. Scale bars, vertical 20μV and horizontal 150ms. (E) Recordings of FPD. Data

60 were from three independent experiments. $^{*}P < 0.05$, $^{**}P < 0.01$ in pio group *vs.* pio combined

61 with KC7F2 group under hypoxia. $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ in pio group *vs.* pio combined with

62 GW9662 group under hypoxia.
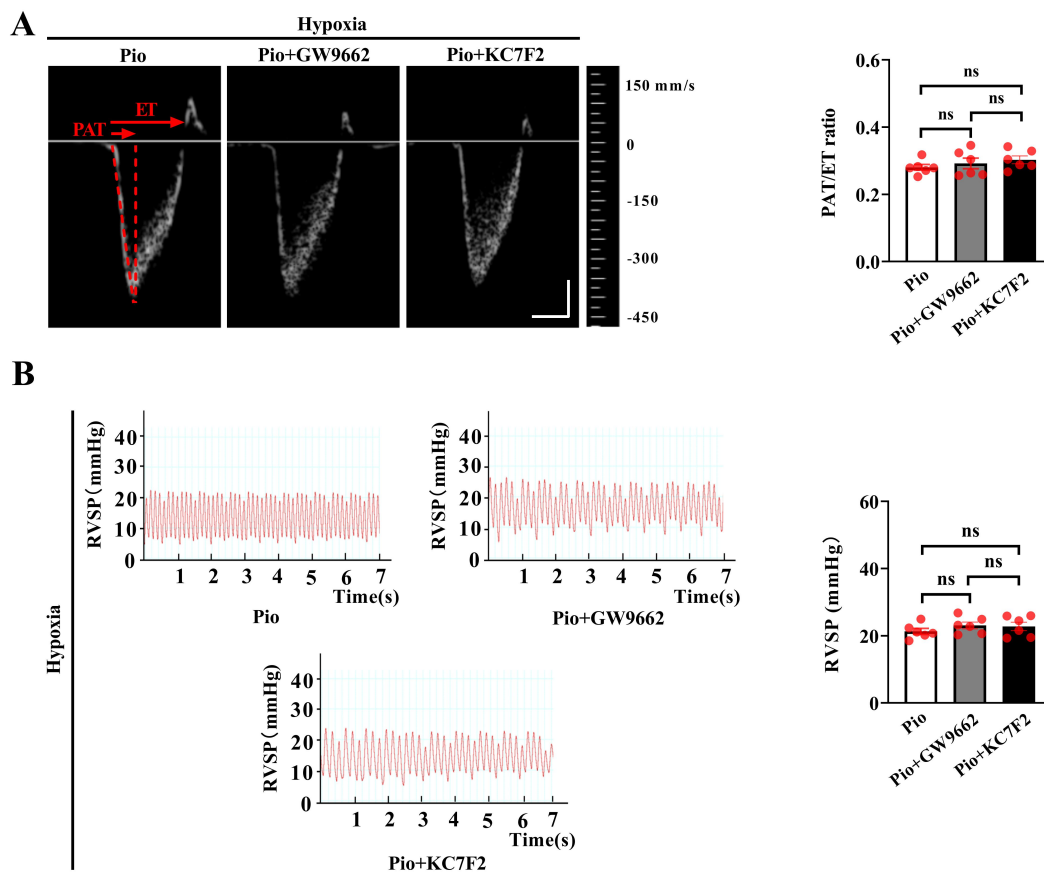
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64 Supplementary Figure 4. Pioglitazone prevents hypoxia-induced pulmonary hypertension (PH)

65 independently of the PPARγ-HIF-1α pathway. (A) Representative echocardiographic images

66 of pulsed-wave doppler of pulmonary artery flow in mice treated with pio and pio combined

67 with GW9662 or KC7F2 under hypoxia, as well as the quantification of the pulmonary artery

68 acceleration time/ejection time ratio (PAT/ET ratio) ($n = 6$). PAT and ET were annotated with

69 red dotted lines. Scale bars, vertical 100 mm/s and horizontal 30 ms. (B) Representative

70 images and the quantification of right ventricular systolic pressure (RVSP) in mice with

71 treatment as indicated ($n = 6$).