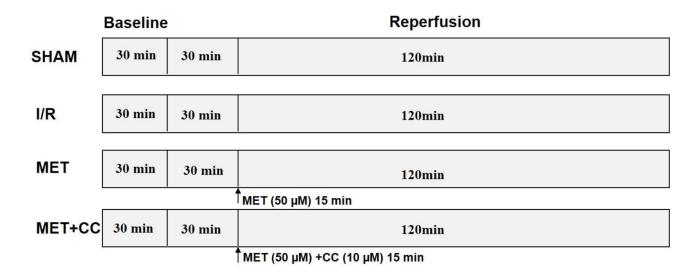
Supplementary Figures



Supplementary Figure 1. Schematic illustration of the experimental protocol in Langendoff IR model. All the groups underwent the same surgical operation. (1) SHAM: rats were subjected to 3h continuous perfusion; (2) IR: rats received 30min equilibrium period, 30min ischemia period, followed by 2h reperfusion period; (3) MET: rat hearts were perfused with K-H solution saturated with 50 μ M metformin for 15 min besides ischemia/reperfusion; (4) MET+CC: rat hearts were perfused with K-H solution saturated with 50 μ M metformin combined with 10 μ M Compound C for 15 min besides ischemia/reperfusion.

	Hypoxia	Reoxygenation
SHAM	3 h	3 h
H/R	3 h	3 h
MET+veh	3 h	3 h
	[†] MET (5 mM) 30min	
MET+nigericin	3 h	3 h
·	↑MET (5 mM) +nigericin (20 µM) 30min	

Supplementary Figure 2. Schematic illustration of the experimental protocol in vitro H/R model. Nigericin initially dissolved in ethanol and diluted with DMEM to a final concentration of 20 μmol/l. (1) SHAM: neonatal rat ventricular myocytes (NRVMs) were subjected to 3h continuous oxygenation; (2) H/R: NRVMs received 3h hypoxia period, followed by 3h reoxygenation period; (3) MET+veh: NRVMs were subjected to 5 mM metformin for 30 min besides hypoxia/reoxygenation; (4) MET+nigericin: NRVMs were subjected to 5 mM metformin combined with 20 μM nigericin for 30 min besides hypoxia/reoxygenation.