

Figure S1. Lactate levels over time and immunofluorescence after drug treatment. (A) Lactate levels measured at different time points during reperfusion (n=5). (B and C) The level of intracellular lacylation observed by immunofluorescence and quantitative analyzes (n=3). These data were representative results of three repetitions at least. Data are expressed as the mean \pm SD. *P<0.05 and **P<0.01. H/R, hypoxia/reoxygenation; DCA, dichloroacetate; NaLac, sodium lactate; ns, not significant.

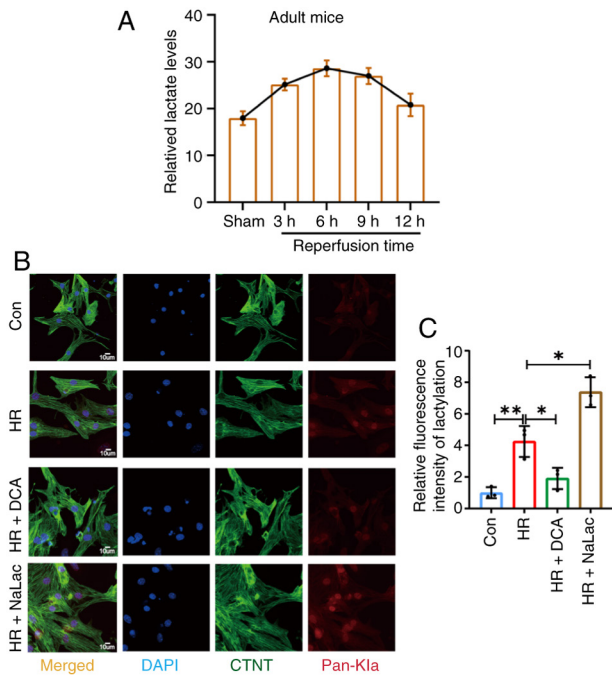


Figure S2. Level of IDH2 K275 lactylation is elevated in I/R myocardium. (A) Heat map of metabolomics analysis. (B) The level of IDH2 lactylation *in vivo* (n=5) and *in vitro* model (n=3) detected by immunoprecipitation experiment and semi-quantitative analyses. (C and D) Quantification of IDH2 lactylation levels after drug treatment or plasmid transfection (n=3). These data were representative results of three repetitions at least. Data are expressed as the mean \pm SD. *P<0.05 and **P<0.01. IDH2, isocitrate dehydrogenase 2; I/R, ischemia-reperfusion; H/R, hypoxia/reoxygenation; DCA, dichloroacetate; NaLac, sodium lactate; WT, wild-type; ns, not significant.

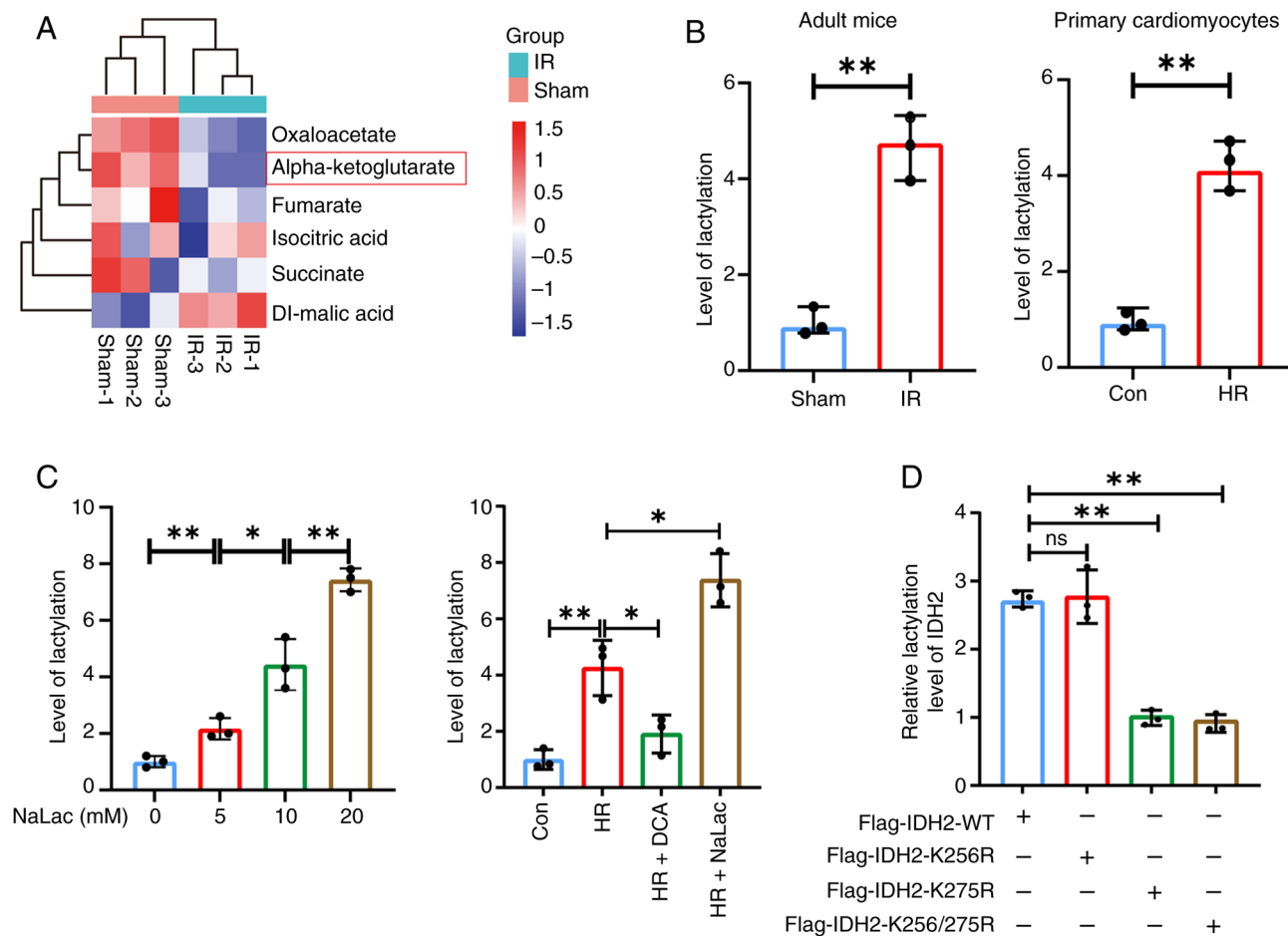


Figure S3. α -KG treatment effectively promotes AMPK pathway activation and alleviates mitochondrial oxidative damage. (A and B) Western blot for detecting IDH2 protein level after lentivirus transfection and semi-quantitative analyzes (n=3). (C and D) Western blot for the detection of the proteins related to mitochondrial disorder after the addition of exogenous α -KG and semi-quantitative analyzes (n=3). These data were representative results of three repetitions at least. Data are expressed as the mean \pm SD. * P <0.05, ** P <0.01 and *** P <0.001. α -KG, α -ketoglutaric acid; AMPK, adenosine 5'-monophosphate-activated protein kinase; IDH2, isocitrate dehydrogenase 2; H/R, hypoxia/reoxygenation; p-, phosphorylated; DRP1, dynamin-related protein 1; MnSOD2, manganese superoxide dismutase 2; sh-, short hairpin; NC, negative control.

