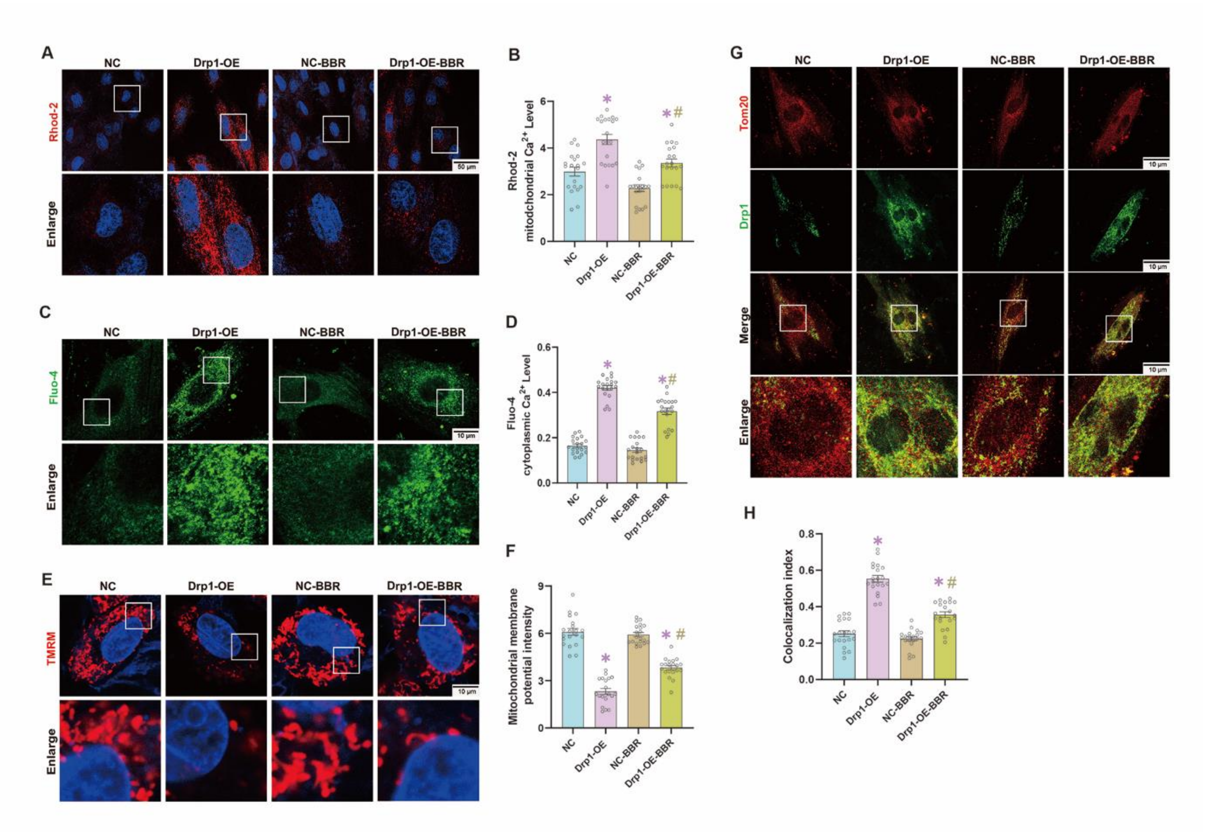
# Supplement materials



**Supplement Figure 1:** Assessment of mitochondrial and cytosolic $Ca^{2+}$ and mitochondrial membrane potential using TMRM as well as co-localization of Drp1 on mitochondria. H9C2 cells were stained with the $Ca^{2+}$ indicators Rhod-2 and Fluo-4, prior to fluorescence detection using confocal microscopy. (A-B) Detection of mitochondrial $Ca^{2+}$ with Rhod-2 strain in H9C2 cells transfected by adenovirus vector (Adv) of Drp1 with or without BBR treatment; (C-D) Detection of cytoplasmic $Ca^{2+}$ with Fluo-4 strain in H9C2 cells transfected by Adv-Drp1 with or without BBR treatment; (E-F) Detection of mitochondrial membrane potential using TMRM straining (red); (G) Representative images of immunofluorescence of H9C2 cells (red: Tom20; green: Drp1); and (H) Menders co-localization index quantitative analysis of Tom20 and Drp1. Mean ± SEM, n=20 cells per group, *$p < 0.05$ vs. NC group, # $p < 0.05$ vs. Drp1-OE group.

Supplement Table 1. Berberine associated genes within given pathways.

| **Pathway** | **Gene** |
|---|---|
| Cell proliferation | GSK3B, TNF, RELA, CASP9, CASP3, AKT1, CCL2, MAPK1, CD36, LDLR, MAP3K5, JUN, TRAF2, PRKCA, SOD2, NFKBIA, IL6, BCL2, CYP1A1, CYCS, FAS, BAX, PPARG, TLR4, NFE2L2 |
| Oxidative stress | CASP9, CCND1, MYC, ERBB2, SPP1, EIF4EBP1, AKT1, MAPK1, EGF, HGF, ITGA1, RPS6, FN1, VEGFC, PRKCA, NGF, IL2, VEGFA, IL4, IL6, COL2A1, CCNE1, BCL2, TLR4 |
| Rhythmic process | TNF, FOXO1, RELA, NFKBIA, CCND1, ACOX1, CASP3, CTNNB1, AKT1, FAS, ACADM, CYP2E1, PPARA, PPARGC1A, TLR4, MAP3K5 |
| Response to lipopolysaccharide | TGFB1, PRKCA, TNF, RELA, CCNE1, MYC, CASP3, BCL2, AKT1, CYCS, MAPK1, FAS, BIRC5, EP300, BAX |
| Heart development | CREBBP, PRKAA1, CDKN1A, CDKN1B, TGFB1, SETD7, PTEN, SLC2A4, SOD2, FOXO1, EGFR, IGF1R, IL6, CCND1, EP300 |
| Glucose homeostasis | SREBF1, GSK3B, PRKAA1, CPT1A, PRKCE, PTEN, SLC2A4, TNF, FOXO1, RELA, NFKBIA, PPARGC1A, SLC27A5 |
| Steroid metabolism | H2AX, H2AW, H2AC8, H2AC6, PARP1, H2AC4, TRAF2, TNF, H2AC11, IFNG, BCL2, FAS, BAX, TLR4 |
| Positive regulation of MAPK | SREBF1, LC2A4, FOXO1, IGF1R, CCND1, HNF4A, EIF4EBP1, PTEN, SLC2A4, AKT1, PPARGC1A |
| Fatty acid metabolism | CPT1A, FABP4, CYP4A10, ADIPOQ, PPARG, CYP4A14, ACADM, CD36, PPARA, SLC27A5 |
| Angiogenesis | EGFR, RELA, IGF1R, VEGFA, IL6, IFNG, ERBB2, AKT1 |
| Cell cycle | AKT1, VEGFC, MAPK1, PRKCA, NGF, EGFR, RELA, |

A set of input genes is highly associated with certain terms, which is statistically measured by Fisher Exact in DAVID system.