

Figure S1. DOX-treatment on COX5B expression and cardiac function. **A.** Western blot analysis of COX5B expression in H9c2 cells treated with 0.5 μ M DOX for 24 h. **B.** The changes of cardiac functional parameters (LVEF and FS) at different time post DOX treatment. Data are expressed as mean \pm SEM. * $P < 0.05$ vs. the normal control (CON) group.

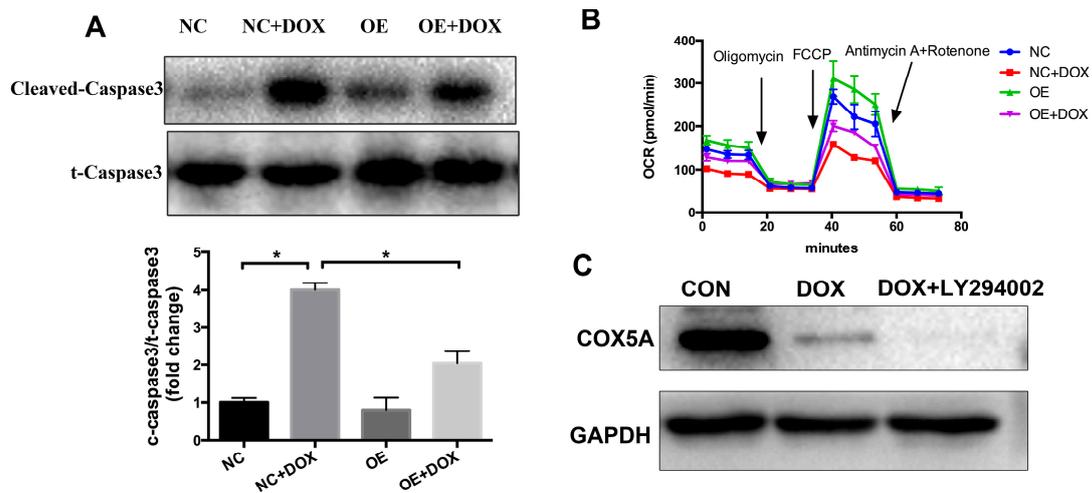


Figure S2. COX5A alleviates DOX-induced cardiomyocyte apoptosis and mitochondrial dysfunction *in vitro*. **A.** Western blot analysis of the protein level of cleaved caspase-3/t-caspase 3. **B.** OCR measurements by means of the Seahorse™ XFe96 extracellular flux analyzer at baseline and after addition of oligomycin, FCCP, and rotenone+antimycin A. **C.** LY294002 (10 μ M) was used to pre-treat H9c2 cells for 2 hours, followed by continued treatment with 0.5 μ M DOX for 24 hours. The expression of COX5A was detected using Western blot analysis. The results showed that treatment of DOX led to a significant decrease in the expression of COX5A, whereas combination treatment with DOX+LY294002 resulted in an even more substantial reduction of COX5A compared to DOX group alone. Data are expressed as mean \pm SEM. * $P < 0.05$.

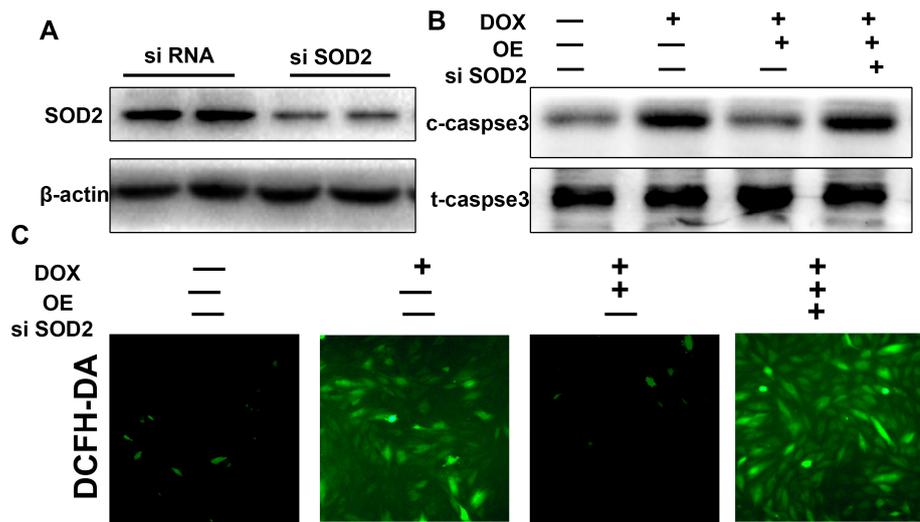


Figure S3. COX5A alleviates DOX-induced cardiomyocyte apoptosis and oxidative stress via upregulation of SOD2. **A.** Western blot analysis of the protein level of SOD2. **B.** Western blot analysis of the protein level of cleaved caspase-3 and t-caspase-3. **C.** DCFH-DA staining to detect ROS level.