

Legends to supplemental figures

Suppl. Figure 1. Effects of DOX±peroxynitrite scavengers on time course of myocardial iNOS expression, 3-nitrotyrosine formation and caspase 3/7 activity *in vivo*.

Upper panels: Effects of scavengers on the time course of DOX-induced myocardial iNOS protein expressions. **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX; n=4/group

Middle panel: Effects of scavengers on the time course of DOX-induced nitrotyrosine formation from heart lysate measured by ELISA. For quantitative data, **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX; n=6/group.

Bottom panel: Effects of scavengers on the time course of DOX-induced cleaved caspase 3/7 activity from heart lysate. For quantitative data, **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX; n=6/group.

Suppl. Figure 2. Time course of the myocardial dysfunction *in vivo* following DOX (20 mg/kg. i.p.) administration

The DOX-induced depression of cardiac function is evident after day 3, which corresponds to markedly increased myocardial nitrotyrosine formation and cell death (see also suppl. Fig. 1)

Results are mean±SEM of 6 to 10 experiments in each group. **P*<0.05 vs vehicle.

Suppl. Figure 3. Effects of DOX±peroxynitrite scavengers on myocardial eNOS, nNOS expressions *in vivo*.

Effects of DOX±peroxynitrite scavengers on myocardial eNOS and nNOS protein and mRNA expressions 5 days following the drug treatments. **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX; n=6/group for protein samples and n=9 for mRNA samples.

Suppl. Figure 4. Effects of DOX±peroxynitrite scavengers on mitochondrial membrane potential measured by TMRE *in vitro*. The yellow color in the bottom line shows colocalization of mitotracker green (green color, upper line) with TMRE (red color, middle line).

Suppl. Figure 5. Effects of DPI, apocynin, allopurinol and SOD-PEG on DOX induced cell death.

Cell death was measured in H9c2 cardiomyocytes treated with 5µM DPI, 200 µM apocynin, 10 µM allopurinol and 3000U/ml cell permeable SOD-PEG in the presence or without DOX. **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX; n=4/group.

Suppl. Figure 6. Effects of catalase-PEG on DOX and hydrogen peroxide (H₂O₂)-induced cell death.

A) Effects of catalase-PEG on DOX-induced apoptosis and necrosis measured by flow cytometry in H9c2 cardiomyocytes. Representative data from 4 experiments analyzed. **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX;

B) Effects of Catalase-PEG on H₂O₂-induced apoptosis and necrosis measured by flow cytometry in H9c2 cardiomyocytes. Representative data from 4 experiments analyzed. **P* <0.05 vs. vehicle, #*P*<0.05 vs DOX.

Suppl. Figure 7. Effects of nitric oxide donors on DOX-induced apoptosis/necrosis *in vitro*.

Effects of nitric oxide donors SNP and SIN-1 (50 and 20 μM) on DOX-induced apoptosis/necrosis measured by flow cytometry in H9c2 cardiomyocytes. Representative data from 4 experiments analyzed. **P* <0.05 vs. vehicle, # *P*<0.05 vs DOX; n=4/group.

Suppl. Figure 8: Effects of NO donor on DOX-induced nitrotyrosine formation measured by flow cytometry in H9c2.

Effect of NO donor on DOX-induced nitrotyrosine formation in H9c2 measured by flow cytometry. Peroxynitrite (ONOO⁻) at 100μM for 2h was used as positive control in flow cytometry. **P* <0.05 vs. vehicle, # *P*<0.05 vs DOX; n=4/group.