

Platelet and Erythrocyte Membranes Coassembled Biomimetic Nanoparticles for Heart Failure Treatment

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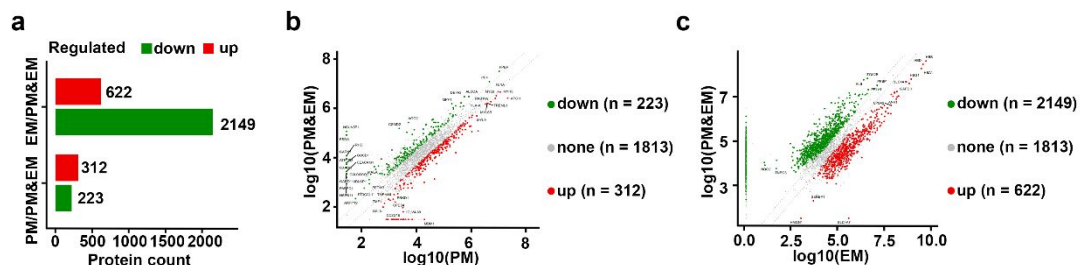


Figure S1 **a** Up and down regulated protein counts in PM vesicles vs. PM&EM vesicles and EM vesicles vs. PM&EM vesicles. **b** Dot plot Up and down regulated protein counts in PM vesicles vs. PM&EM vesicles. **c** Dot plot Up and down regulated protein counts in EM vesicles vs. PM&EM vesicles.

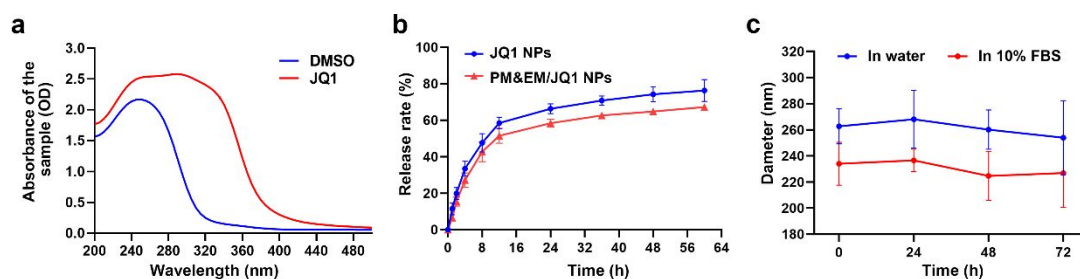


Figure S2 **a** The full spectrums of JQ1 and DMSO. **b** JQ1 release profiles from JQ1 NPs and PM&EM/JQ1 NPs. **c** JQ1 diameter stability in water and 10% FBS.

PM&EM/JQ1 NPs over 64 h in 20% FBS at room temperature measured by a spectrophotometer at the wavelength of 320 nm (mean \pm SD, $n = 3$ independent experiments). **c** The size change tendency of PM&EM/JQ1 NPs in water and medium containing 10% FBS at room temperature (mean \pm SD, $n = 3$ independent experiments).

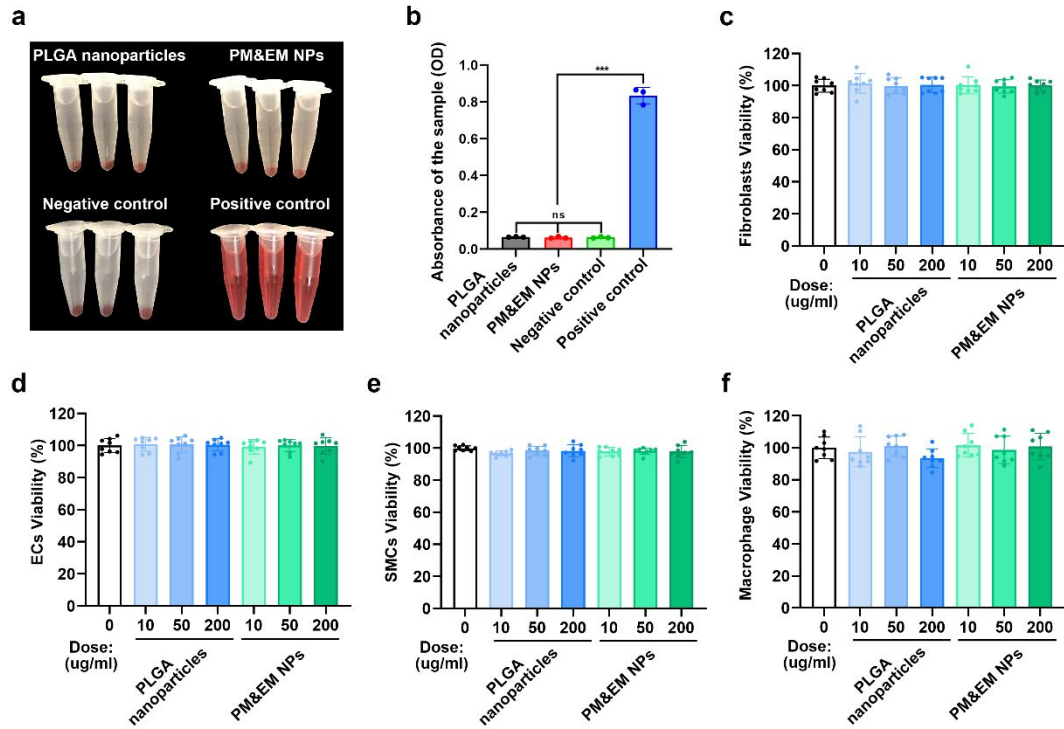


Figure S3 Centrifuged red blood cells after incubation with PLGA NPs and PM&EM NPs. **a, b** The absorbance of the blood sample incubated with PLGA NPs and PM&EM NPs, measured at 540 nm (mean \pm SD, $n = 3$). Cell viability of fibroblasts (**c**), ECs (**d**), SMCs (**e**), and macrophages (**f**) after incubation with various doses of PLGA nanoparticles and PM&EM NPs for 24 h measured by CCK-8 (mean \pm SD, $n = 8$). *** $p < 0.001$, n.s. = not significant, one-way ANOVA, Tukey's multiple comparison test.

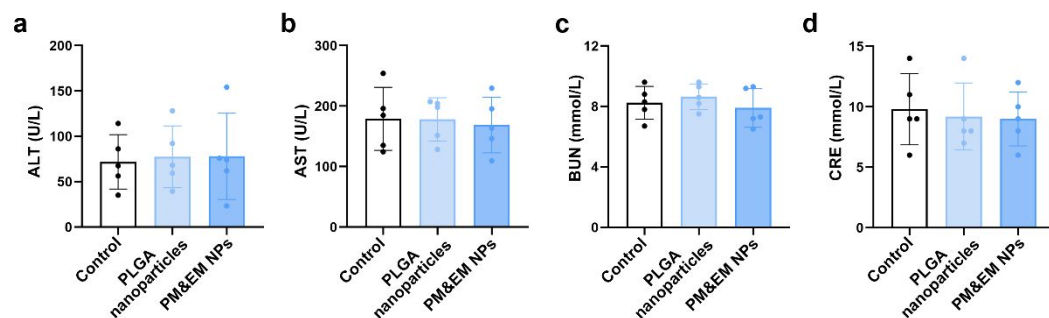


Figure S4 Biochemical markers relevant to hepatic and kidney function (mean \pm SD, $n = 5$ independent experiments). one-way ANOVA, Tukey's multiple comparison test.

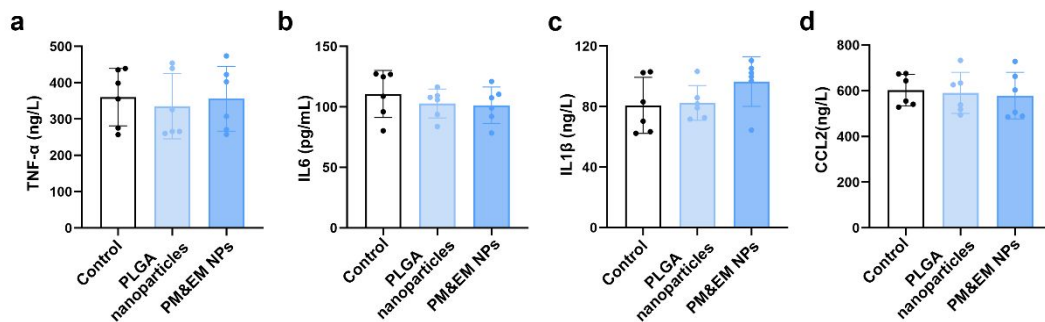


Figure S5 Mouse serum cytokines relevant to inflammation. (mean \pm SD, n = 6 independent experiments). one-way ANOVA, Tukey's multiple comparison test.

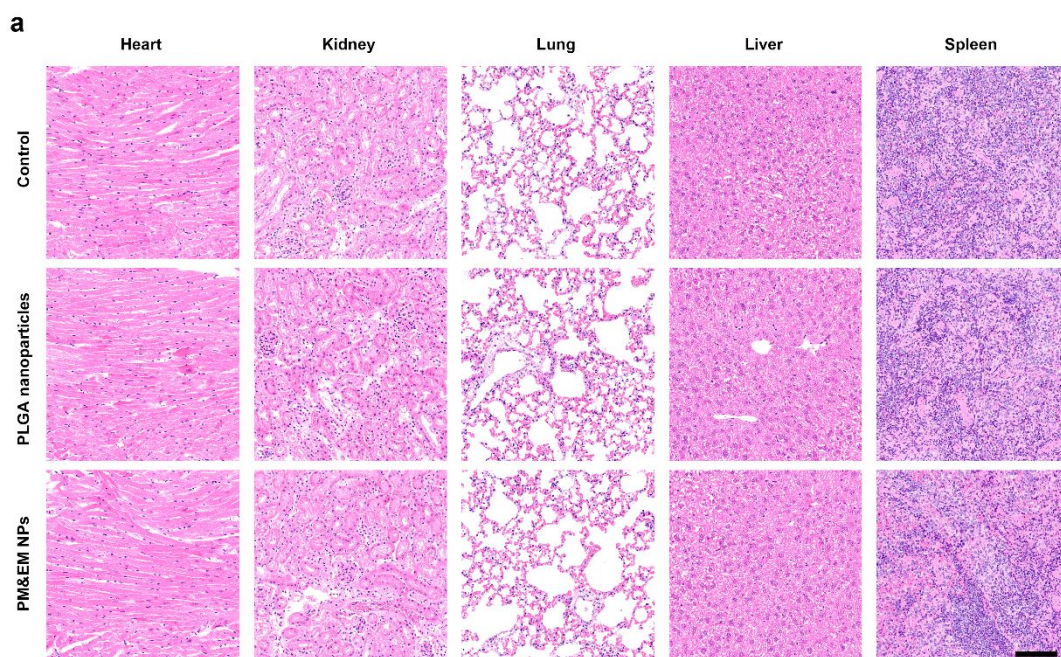


Figure S6 H&E staining of the main organs collected from the mice treated with PLGA nanoparticles and PM&EM NPs (scale bar = 100 μ m).

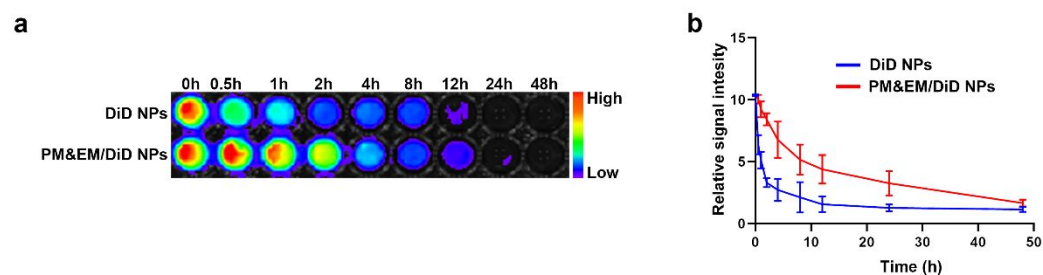


Figure S7 (a) and (b) Relative fluorescence intensity of DiD NPs and PM&EM/DiD NPs in blood. (mean \pm SD, n = 3).

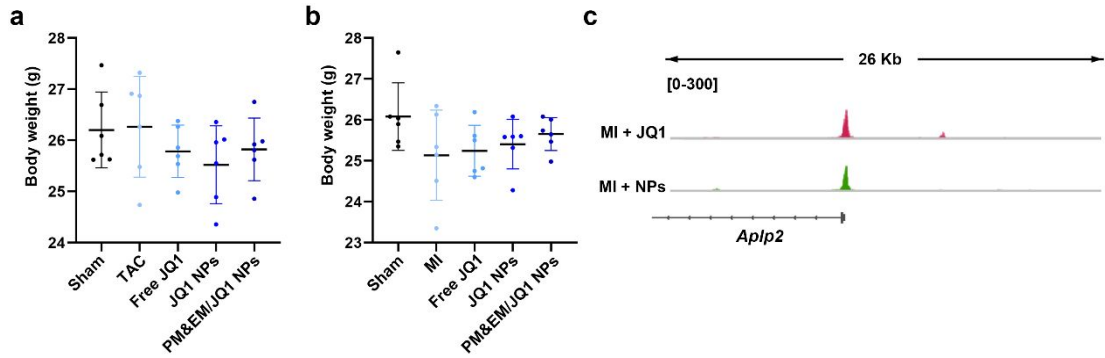


Figure S8 The body weights of the mice for both TAC (a) and MI (b) experiments (mean \pm SD, $n = 6$). (c) ATAC-seq from the fibrosis sites of MI mouse with free JQ1 and PM&EM/JQ1 NPs therapy at the *Apfp2* locus.

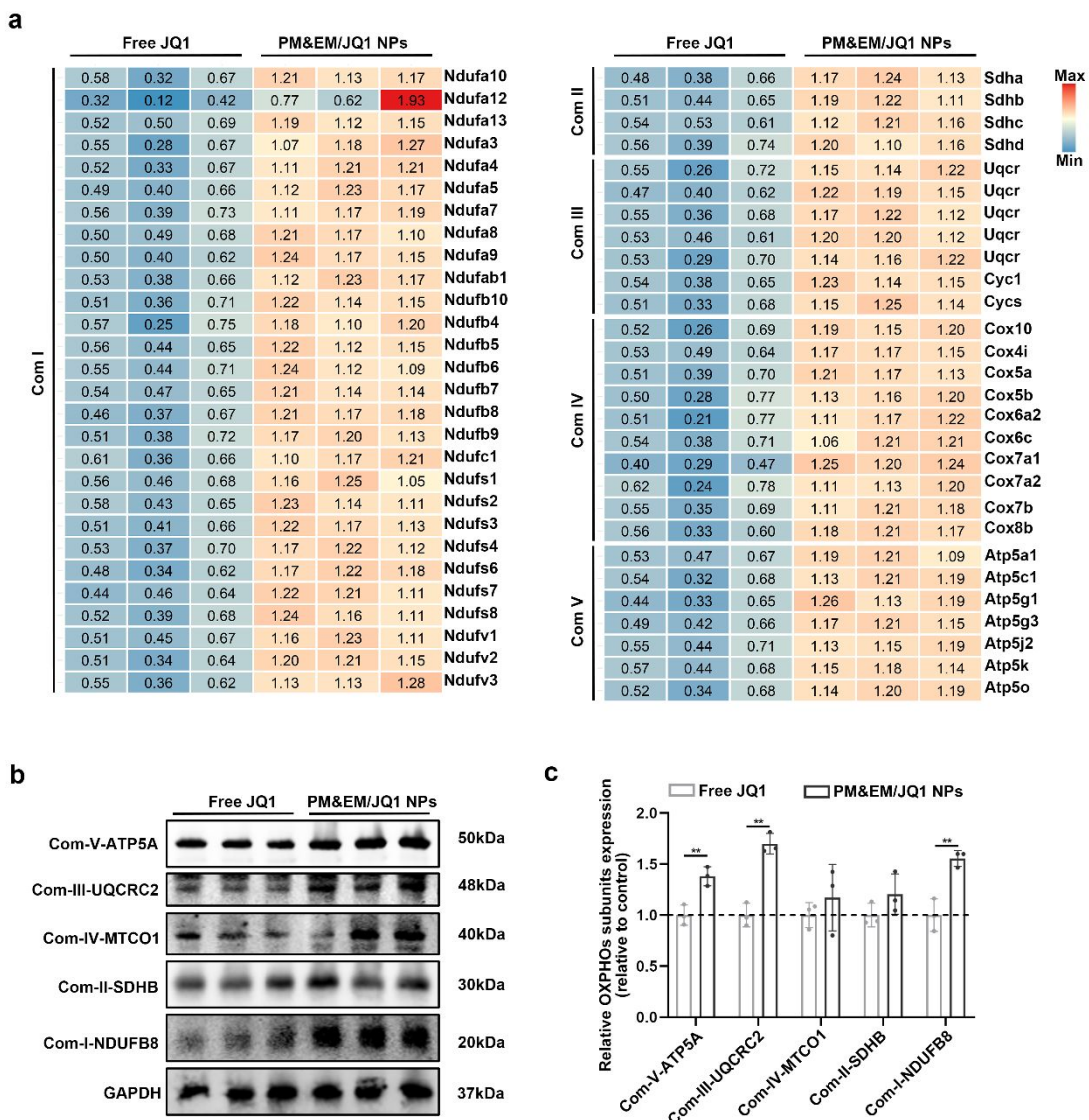


Figure S9 (a) Heatmap demonstrating mean normalized expression of transcripts encoding the subunits of the mitochondrial respiratory chain. (b) and (c) Western blots of oxidative phosphorylation (OXPHOS) complexes in Free JQ1 and PM&EM/JQ1 NPs group. (mean \pm SD, $n = 3$ independent experiments). $**p < 0.01$, one-way ANOVA, Tukey's multiple comparison test

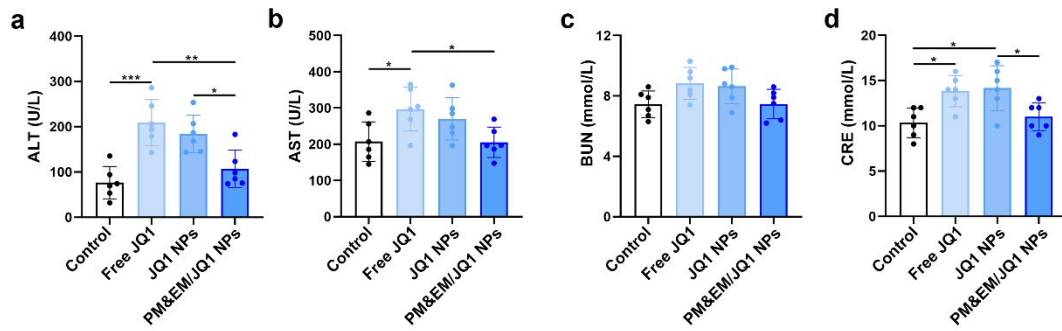


Figure S10 Biochemical markers relevant to hepatic and kidney function (mean \pm SD, $n = 6$ independent experiments). * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$, one-way ANOVA, Tukey's multiple comparison test.

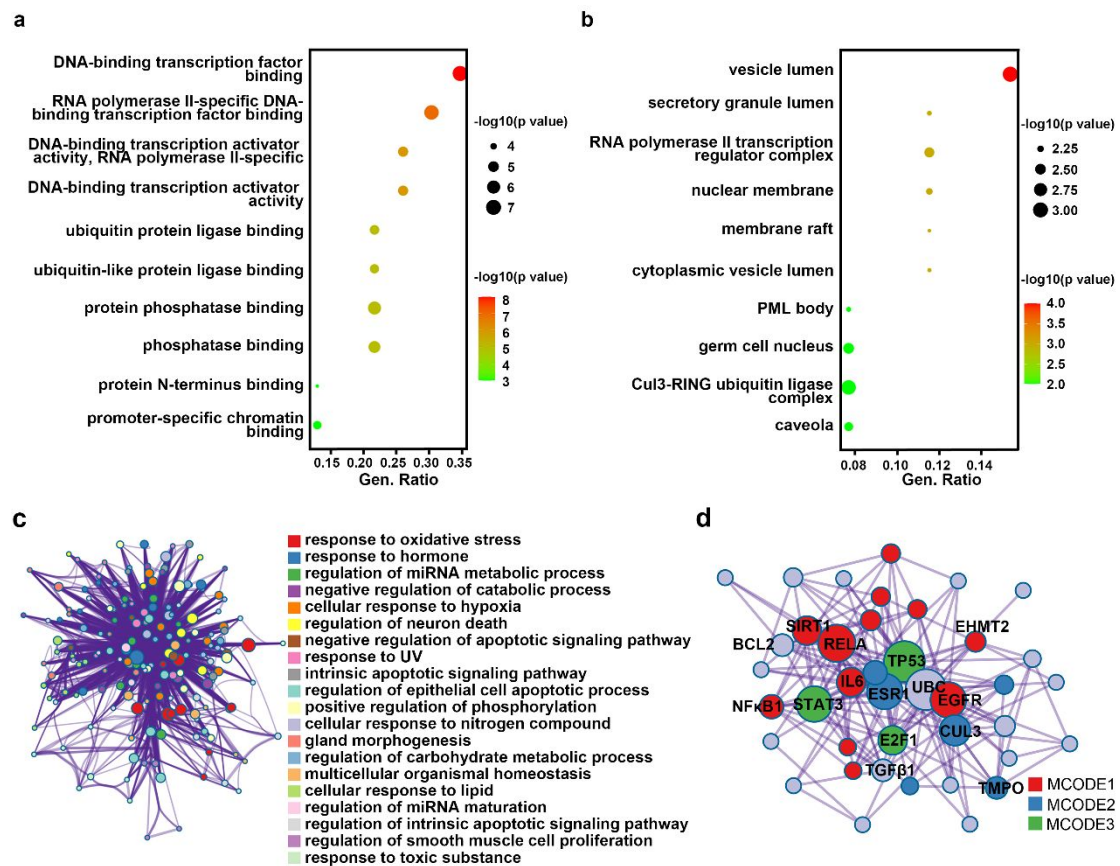


Figure S11 a and b GO pathway enrichment analysis (Molecular Function, MF and Cellular Component, CC) of the common gene from different groups by R. **c** GO pathway enrichment analysis of the common gene from different groups by Metascape. **d** The key regulatory molecules of the significant enrichment pathways.

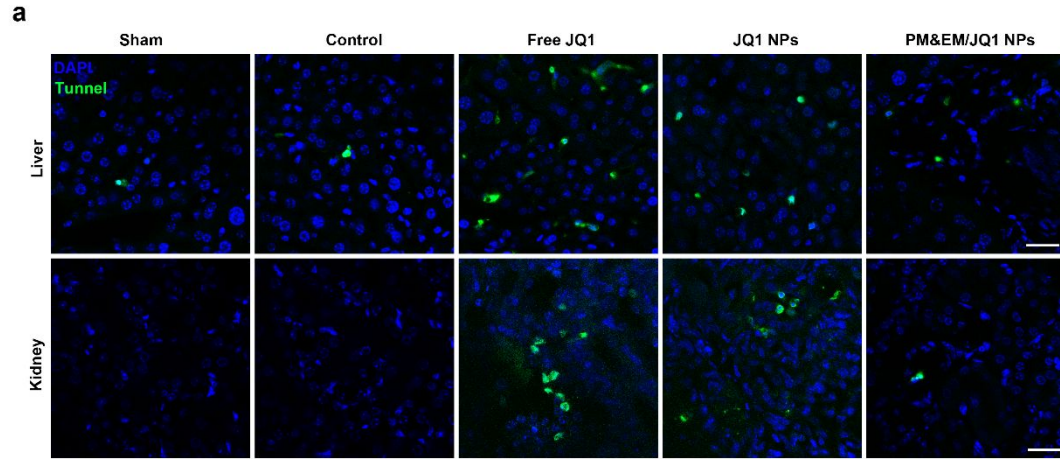


Figure S12 Representative cross sections from liver and kidney stained with TUNNEL staining, scale bar = 20 μm .

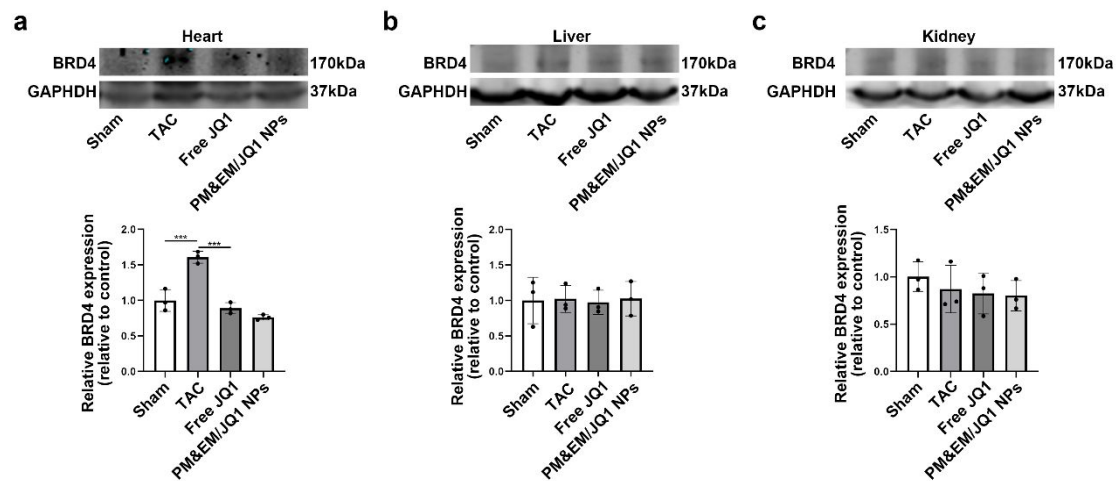


Figure S13 Western blots of BRD4 in TAC, Free JQ1 and PM&EM/JQ1 NPs-treated mouse heart (a), liver (b) and kidney (c). (mean \pm SD, $n = 3$ independent experiments). *** $p < 0.001$, one-way ANOVA, Tukey's multiple comparison test.

JQ1	PLGA monomer	PLGA nanoparticles	JQ1 NPs	PM&EM NPs	PM&EM/JQ1 NPs

Table S1. Illustrated explanations of the main abbreviations.

BRD4	bromodomain-containing protein 4
MI	myocardial infarction
BET	bromodomain and extraterminal domain
PM&EM	platelet membrane- erythrocytes membrane complex
FRET	Förster resonance energy transfer
DLS	Dynamic light scattering
TEM	Transmission electron microscopy
CLSM	confocal laser scanning microscopy
PCA	Principal component analysis
LE	loading rate
EE	encapsulation rate
FBS	fetal bovine serum
FC	flow cytometry
ECs	endothelial cells
SMCs	smooth muscle cells
CCK-8	Cell Counting Kit-8
ALT	Alanine Transaminase
AST	Aspartate Aminotransferase
BUN	blood urea nitrogen
CRE	creatinine
TAC	transverse aortic constriction
MPS	mononuclear phagocyte system
ROS	reactive oxygen species

Table S2. Abbreviations in this manuscript.