## **Supporting Information**

## Activation of the PPARγ/NF-κB pathway by A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP via scavenging reactive oxygen species to alleviate hepatic ischemia-reperfusion injury

Dong Mo,<sup>af</sup> Wei Cui,<sup>a</sup> Linxin Chen,<sup>a</sup> Juanjuan Meng,<sup>a</sup> Yuting Sun,<sup>g</sup> Kaiyong Cai,<sup>d</sup> Jixi Zhang,<sup>\*d</sup> Jianrong Zhang,<sup>\*c</sup> Kui Wang <sup>\*de</sup>, and Xiaohe Luo <sup>\*ab</sup>

<sup>a</sup> Department of Central Laboratory, Chongqing University Three Gorges Hospital, School of Medicine, Chongqing University, Chongqing, 40400, China.

<sup>b</sup> Department of Laboratory Medicine, Chongqing University Three Gorges Hospital, School of Medicine, Chongqing University, Chongqing, 40400, China.

<sup>c</sup> Department of Cardiovascular Surgery, Chongqing University Three Gorges Hospital, School of Medicine, Chongqing University, Chongqing, 40400, China.

<sup>d</sup> Key Laboratory of Biorheological Science and Technology, Ministry of Education, College of Bioengineering, Chongqing University, No. 174 Shazheng Road, Chongqing 400044, China.

<sup>e</sup> Department of Pharmacy, The Second Affiliated Hospital of Army Medical University, Chongqing 400037, China.

<sup>f</sup> State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Collaborative Innovation Center of Biotherapy, Chengdu, 610041, China.

<sup>g</sup> College of Biosystems Engineering and Food Science, Zhejiang University, Hangzhou, 310058, China.

\* Corresponding authors:
E-mail: jixizhang@cqu.edu.cn(J. Zhang)
E-mail: jianrongzhang@cqu.edu.cn (J. Zhang);
E-mail: kuiwang@cqu.edu.cn (K. Wang);
E-mail: xiaoheluo@cqu.edu.cn (X. Luo).

## Characterization

Transmission electron microscopy (TEM) images were performed on a JEM 2010 (JEOL, Japan) instrument at 200 kV acceleration to investigate the size, morphology and integrity of NPs. Samples were dried on carbon-coated Cu grids before characterization. The bulk and surface chemical compositions of samples were analyzed with high-angle annular dark-field imaging, scanning transmission electron microscopy (HAADF-STEM) and elemental mapping images using a JEM-6700F instrument (JEOL, Japan). Powder X-ray diffraction (XRD) measurements were obtained using a Bruker D8 (Germany) Advance X-Ray powder diffractometer (40 kV, 40 mA, CuKal radiation of  $\lambda = 1.54059$  Å) with a scan speed of 2°/min and a step size of 0.02°. Nitrogen sorption isotherms were measured through an ASAP 2010 analyzer (Micrometrics, USA). XPS analysis was determined using an Axis Ultra spectrometer (Kratos, UK) with Al Ka excitation radiation at ca. 5  $\times$  10<sup>-9</sup> Pa. Fourier transform infrared (FTIR) spectra were recorded on a Spectrum 100 infrared spectrophotometer (PerkinElmer, USA) at a test range of 400-4,000 cm<sup>-1</sup> with KBr pellet. UV-vis absorption was recorded on a UV-Vis spectrofluorometer (NanoDrop One, Thermo). Fluorescence spectra were recorded on a fluorescence spectrophotometer (RF-6000, Shimadzu, Japan) using a xenon lamp as an excitation source.

Antibody name	Dilution ratio	kD	Source	Brand	Catalog No.
β-actin	1:1000	41.6	Mouse	ZSGB-BIO	TA-09
Caspase-3	1:1000	35/19/17	Rabbit	Cell Signaling Technology	14220
Bax	1:500	23	Mouse	SANTA CRUZ BIOTECHNOLOGY	sc-7480
Bcl-2	1:1000	26	Rabbit	abcam	ab59348
TNF-α	1:500	17/26	Mouse	SANTA CRUZ BIOTECHNOLOGY	sc-52746
IL-6	1:500	21	Mouse	SANTA CRUZ BIOTECHNOLOGY	sc-32296
IL-1β	1:1000	31	Mouse	Cell Signaling Technology	12242S
PPARγ	1:1000	57	Rabbit	Cell Signaling Technology	24358
NF-κB	1:1000	61	Rabbit	BEIJING BIOSYNTHESIS BIOTECHNOLOGY	bs-0465R
p-NF-κB	1:1000	65	Rabbit	Cell Signaling Technology	3033S
Ι-κΒ-α	1:1000	39	Rabbit	Cell Signaling Technology	4812S
p-I-κB-α	1:1000	40	Mouse	Cell Signaling Technology	9246S
F4/80	1:1000	65-250	Rabbit	Cell Signaling Technology	70076S

 Table S1 the antibodies used in the present study.



**Fig. S1.** TEM image of Fe<sub>3</sub>O<sub>4</sub> (a) and MPDA NPs (b), DLS size distribution (c) and Zeta potential (d) of MPDA, A-MPDA, A-MPDA@Fe<sub>3</sub>O<sub>4</sub>, and A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPs in water.



24 h. (b) DLS size distribution of A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPs in different dispersing solvents for 24 h.



**Fig. S3.** High-resolution X-ray photoelectron spectra of C1s in MPDA (a) and A-MPDA NPs (b); (c) High-resolution XPS spectra of Fe 2p in A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP.



Fig. S4. Fourier transform infrared spectroscopy (FT-IR) of Fe<sub>3</sub>O<sub>4</sub>, A-MPDA, and A-MPDA@Fe<sub>3</sub>O<sub>4</sub> NPs.



**Fig. S5.** (a) scavenging efficiencies of  $H_2O_2$  with MPDA, A-MPDA,  $Fe_3O_4$  and A-MPDA@Fe\_3O\_4@PVP NPs; (b) scavenging efficiencies of  $H_2O_2$  exposed to different concentrations of A-MPDA@Fe\_3O\_4@PVP NPs, respectively, and the corresponding absorbance of each system and decomposition rate of A-MPDA@Fe\_3O\_4@PVP NPs toward  $H_2O_2$  (c).



Fig. S6. O2 bubbles observation of A-MPDA@Fe3O4@PVP NPs (2 mg·mL<sup>-1</sup>) solution after addition of 200 mM H2O2.



Fig. S7. Representative intracellular ROS staining of untreated and different concentration of A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPs-treated L02 cells with  $H_2O_2$  treatment (200  $\mu$ M). Scale bar: 300  $\mu$ m.



**Fig. S8.** Representative intracellular ROS staining of untreated and different concentration of A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPstreated L02 cells with LPS treatment (20 μg·mL<sup>-1</sup>). Scale bar: 300 μm.



Fig. S9. Flow cytometry analysis of representative intracellular ROS staining of different nanoparticles -treated cells with LPS treatment.





Fig. S11 In vivo biocompatibility of A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPs. (a) Serum levels as part ALT, AST. n=5 per group; (b) Representative H&E staining images of the main organs at 0.5, 3, 7, and 30 days after intravenous injection of 5 mg·kg<sup>-1</sup> A-MPDA@Fe<sub>3</sub>O<sub>4</sub>@PVP NPs on healthy mice. Scale bar: 200 μm



Fig. S12. Change in serum ALP a) and TBIL b) levels from various groups of mice (n = 4).