Supporting Information

Triangular-shaped homologous heterostructure as photocatalytic H_2S scavenger and macrophage modulator for Rheumatoid Arthritis therapy

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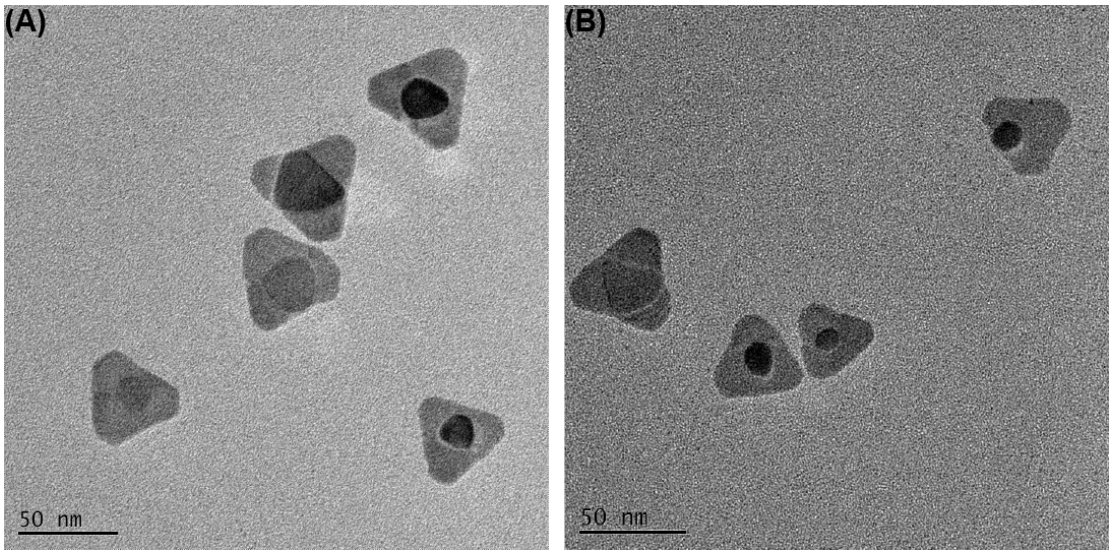

Fig. S1 TEM image of (A) Ag/Ag_2S-PEG-FA NTs and (B) Ag/Ag_2S-PEG-FA/RSV NTs.

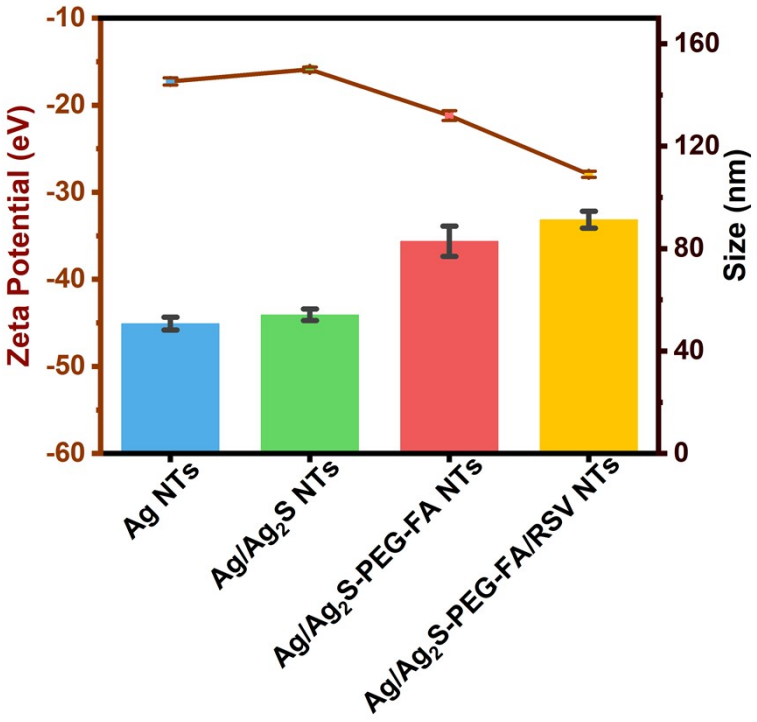

Fig. S2 Zeta potential and particle size of Ag NTs, Ag/Ag_2S NTs, Ag/Ag_2S-PEG-FA NTs, Ag/Ag_2S-PEG-FA/RSV NTs.

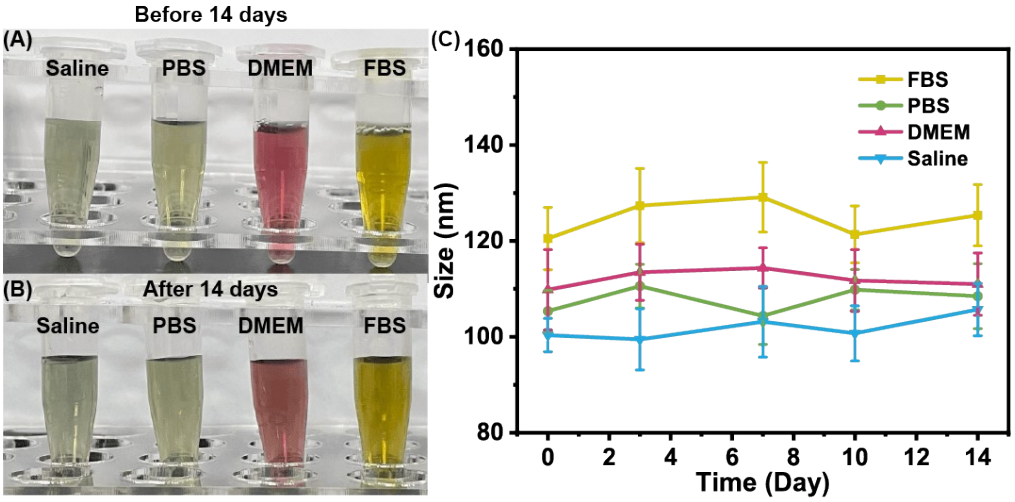

Fig. S3 (A) Digital photos of Ag/Ag_2S-PEG-FA/RSV NTs in Saline (0.9%), PBS, pure fetal bovine serum (FBS) and Dulbecco's Modified Eagle's Medium (DMEM) before 14 days. (B) Digital photos of Ag/Ag_2S-PEG-FA/RSV NTs in Saline (0.9%), PBS, FBS and DMEM after 14 days. (C) Variation of the hydrodynamic size of Ag/Ag_2S-PEG-FA/RSV NTs dispersed in various media measured by the DLS method.

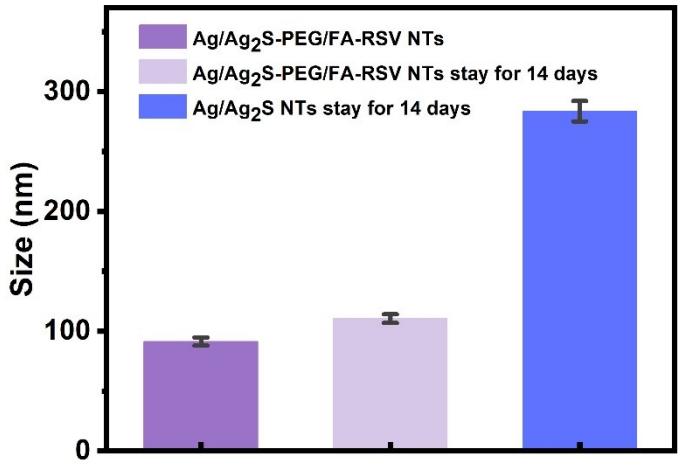

Fig. S4 The particle size of Ag/Ag_2S-PEG-FA/RSV NTs, Ag/Ag_2S NTs and Ag/Ag_2S-PEG-FA NTs stay for 14 days.

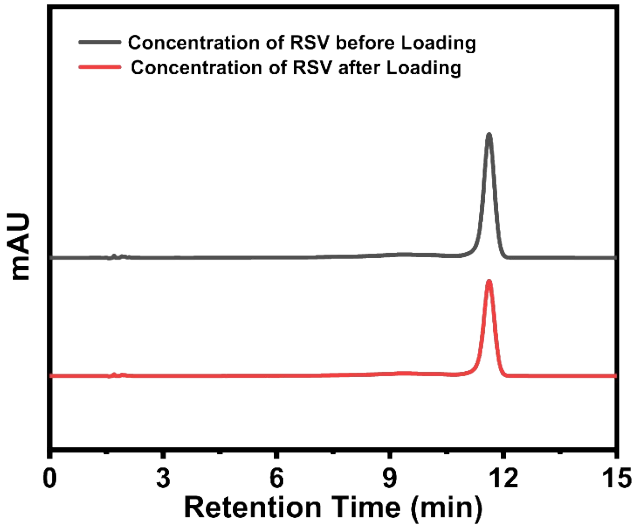

Fig. S5 HPLC spectrum for RSV loading.

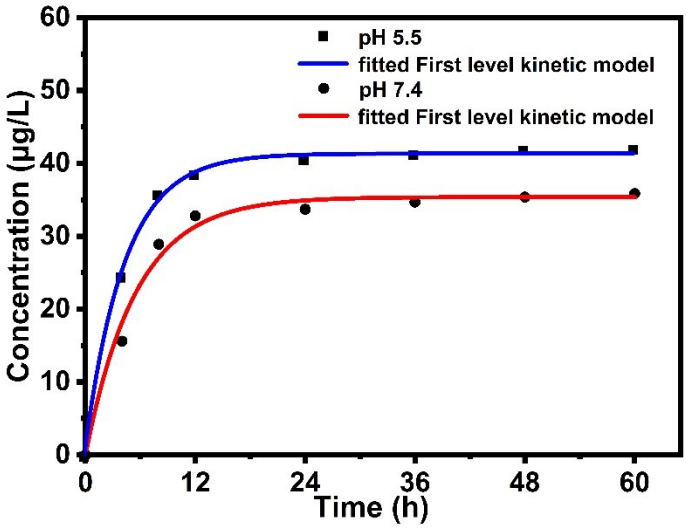

Fig. S6 RSV cumulative releasing profile at pH 5.5 and pH 7.4.

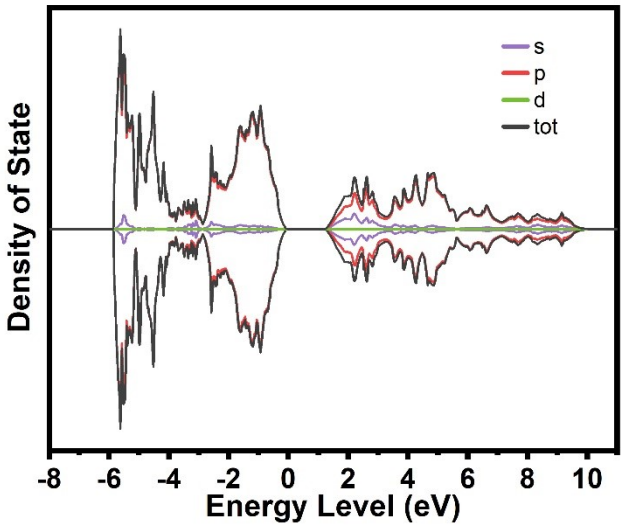

Fig. S7 Theoretical calculations of Density of state (DOS) of Ag_2S.

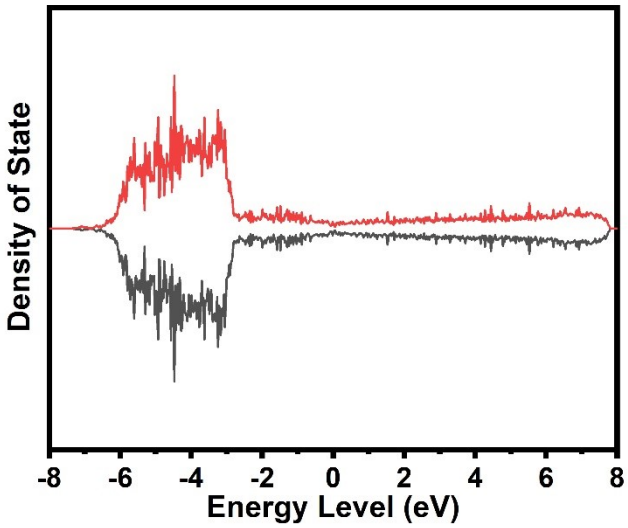

Fig. S8 Theoretical calculations of DOS of Ag.

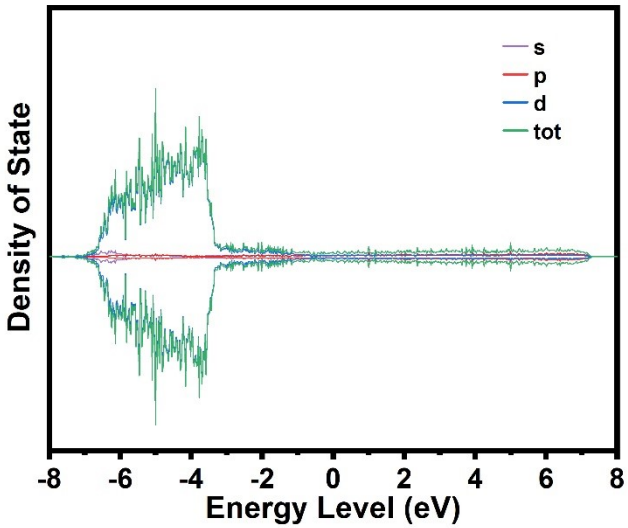

Fig. S9 Theoretical calculations of DOS of Ag/Ag_2S.

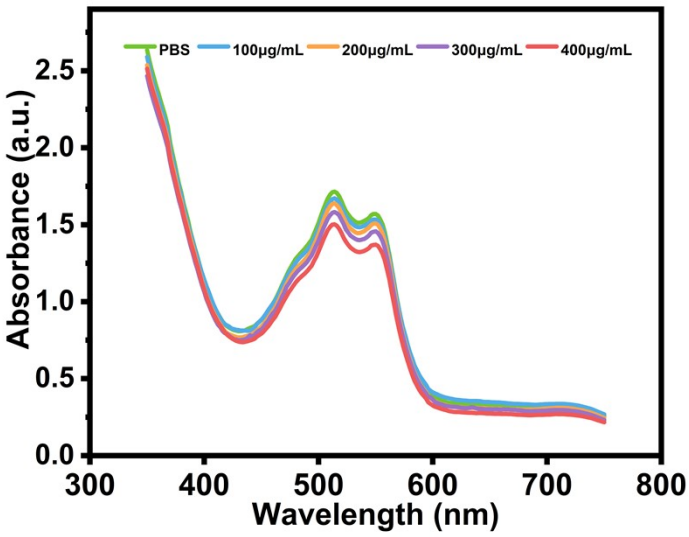

Fig. S10 H_2S scavenging of Ag/Ag_2S-PEG-FA/RSV NTs with different concentration under NIR-II irradiation. (PBS, 100 μg/mL, 200 μg/mL, 300 μg/mL, 400 μg/mL).

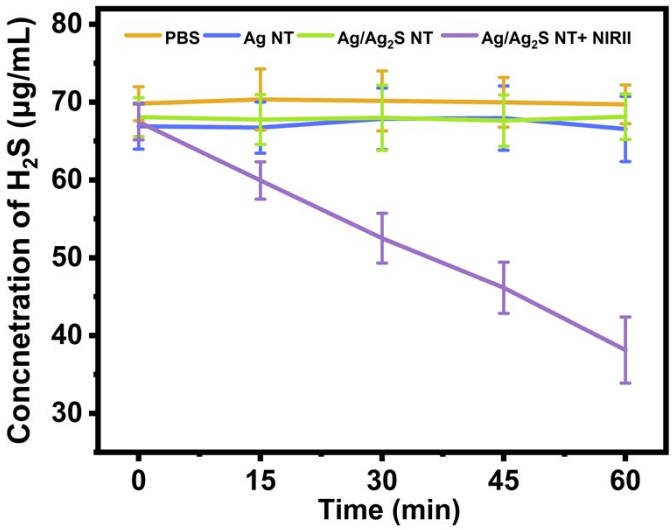

Fig. S11 H_2S scavenging of Ag NTs, Ag/Ag_2S NTs and Ag/Ag_2S NTs under NIR-Ⅱ irradiation.

Fig. S12 Image of O_2 generation catalyzed by Ag/Ag_2S-PEG-FA/RSV NTs.

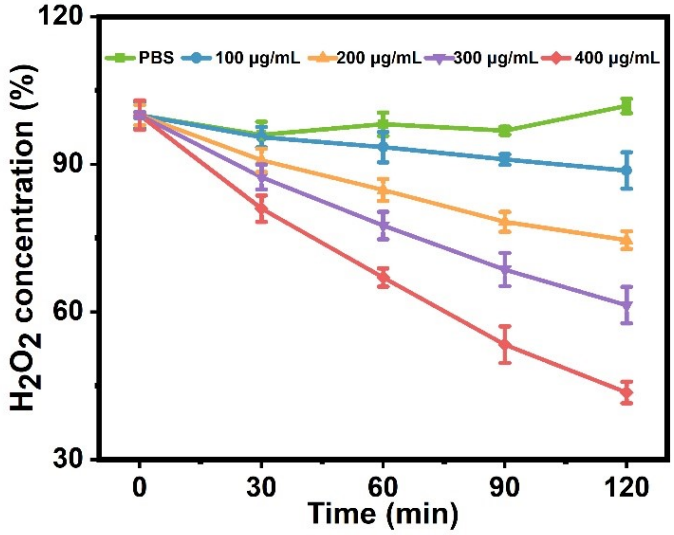

Fig. S13 H_2O_2 scavenging catalyzed by Ag/Ag_2S-PEG-FA/RSV NTs with different concentration (PBS, 100 μg/mL, 200 μg/mL, 300 μg/mL, 400 μg/mL).

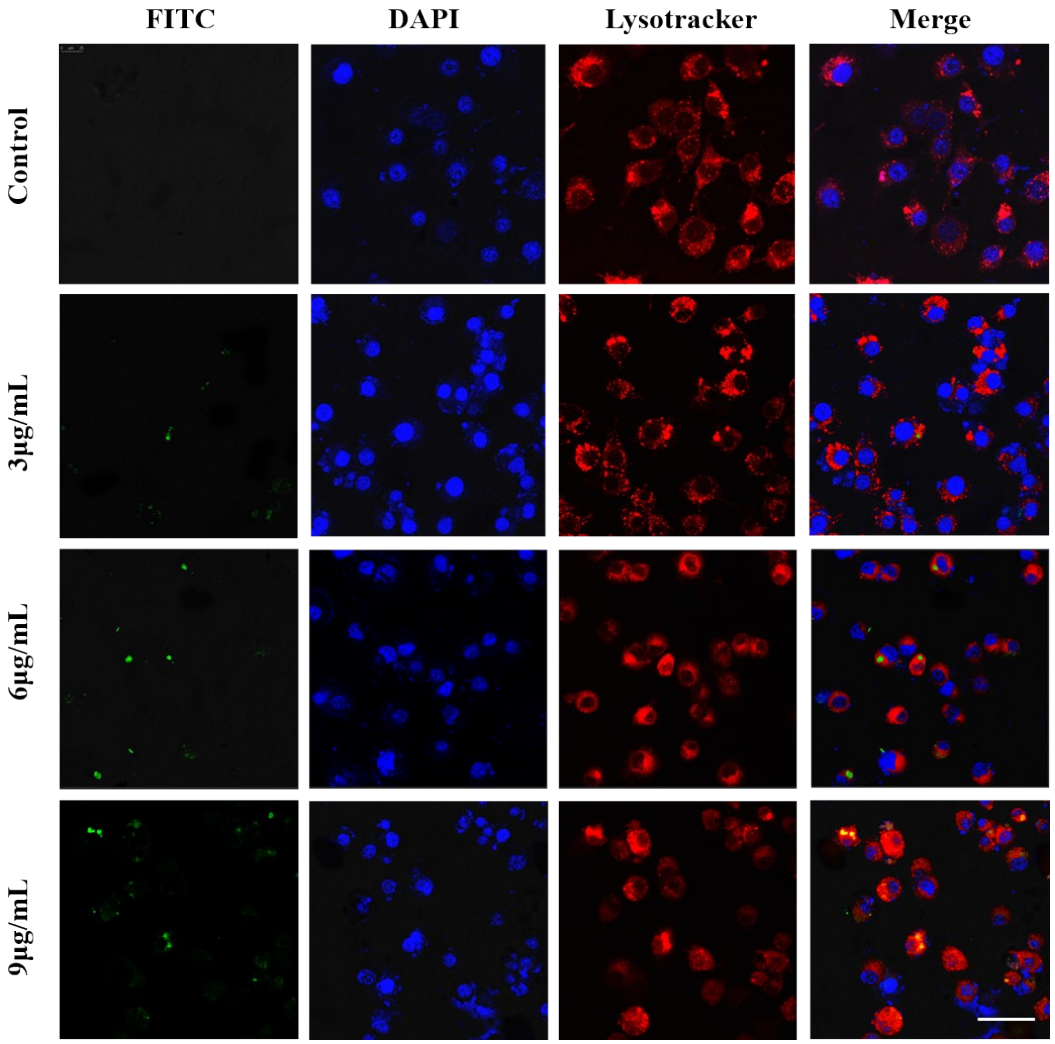

Fig. S14 CLSM images of cellular uptake of Ag/Ag_2S-PEG-FA/RSV NTs with different concentrations (3, 6, 9 μg/mL).

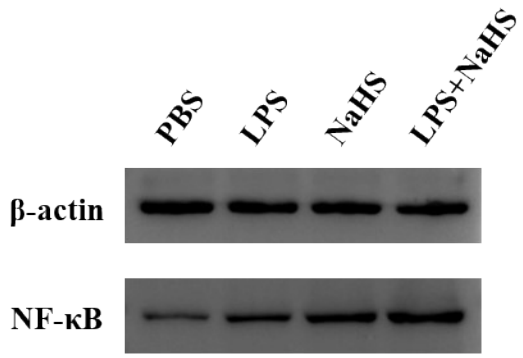

Fig. S15 Western blot analysis of protein expression of NF-κB in RAW 264.7 incubated with different stimuli formulation. (LPS 100ng/mL, NaHS 400 ng/mL and LPS/ NaHS)

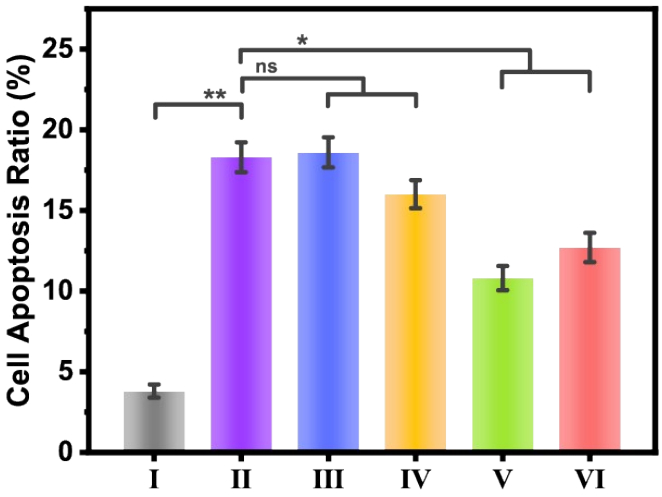

Fig. S16 Quantitative analysis of apoptotic cell ratios in RAW264.7 cells after different treatments. Data are shown as the mean ± SD (n=3). *p<0.05, **p<0.01, ***p<0.001.

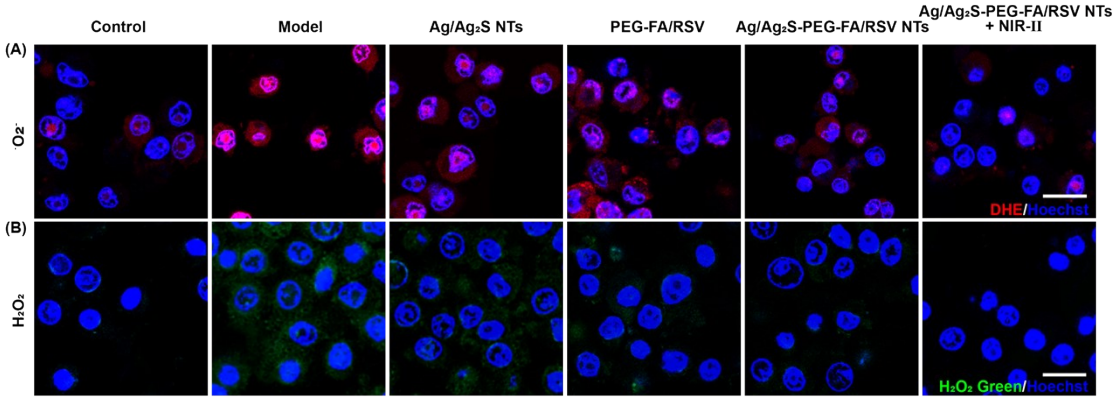

Fig. S17 CLSM image of intracellular (A) $^{\bullet}O_2^-$ and (B) H_2O_2 after various treatment formulation. I: Control, II: Model (LPS 100 ng/mL, NaHS 400 ng/mL), III: Ag/Ag_2S NTs (100 μg/mL), IV: PEG-FA/RSV (100 ng/mL), V: Ag/Ag_2S-PEG-FA/RSV NTs (100 μg/mL) and VI: Ag/Ag_2S-PEG-FA/RSV NTs (100 μg/mL) + NIR-II (980nm 0.6 W, 1 min). Scale bar: 25 μm.

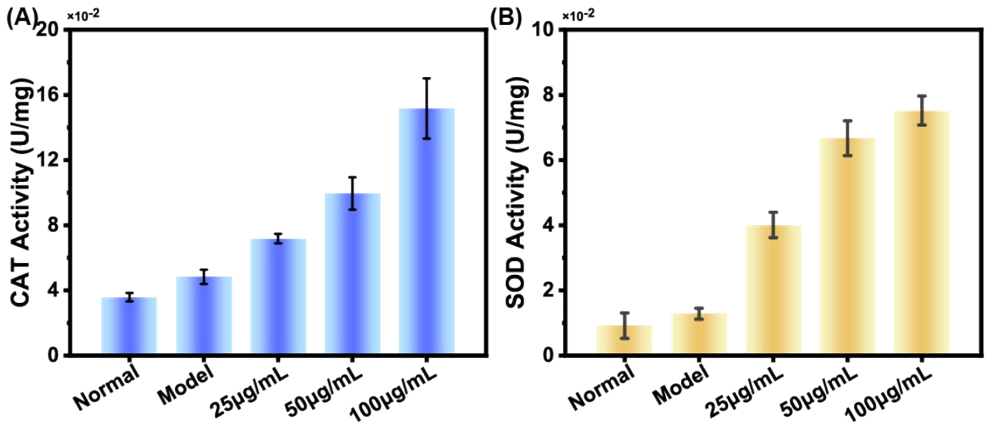

Fig. S18 In vitro SOD and CAT activity of macrophage treated with Ag/Ag_2S-PEG-FA/RSV NTs. Data are shown as the mean ± SD (n = 3). *p < 0.05, **p < 0.01, ***p < 0.001.

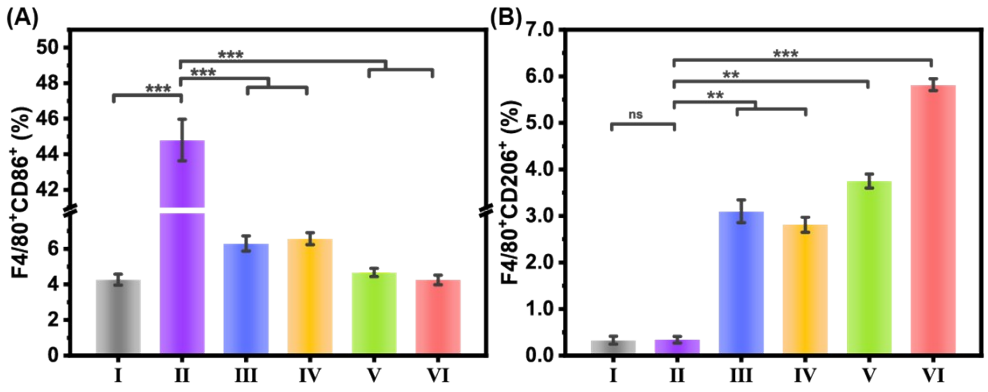

Fig. S19 Quantitative analysis of (A) F4/ 80$^+$CD86$^+$ and (B) F4/80$^+$CD206$^+$ in RAW264.7 cells in flow cytometry analysis. The data are representative of three independent experiments. Data are shown as the mean ± SD (n=3). *p<0.05, **p<0.01, ***p<0.001.

Table S1 Primer sequences used for real-time PCR *in vitro*.

Gene	Forward Primer	Reverse Primer
IL-6	5'- GCCCACCAAGAACGATAGTCAA - 3'	5'- TCCTCTGTGAAGTCTCCTCTCC - 3'
ARG-1	5'- AGTCTGGCAGTTGGAAGCAT - 3'	5'- GGAGTGTTGATGTCAGTGTGAG - 3'
IL-10	5'- GCTGGACAACATACTGCTAACC - 3'	5'- ATCATTTCCGATAAGGCTTGGC - 3'
iNOS	5'- CGAGACGGATAGGCAGAGATTG - 3'	5'- ACTCTTCAAGCACCTCCAGGAA - 3'
IL-1β	5'- ACTACAGGCTCCGAGATGAACA - 3'	5'- TTGTCGTTGCTTGGTTCTCCTT - 3'
CD206	5'- GGACTCTGGATTGGACTCAACA - 3'	5'- TGATGATGGACTTCCTGGTAGC - 3'

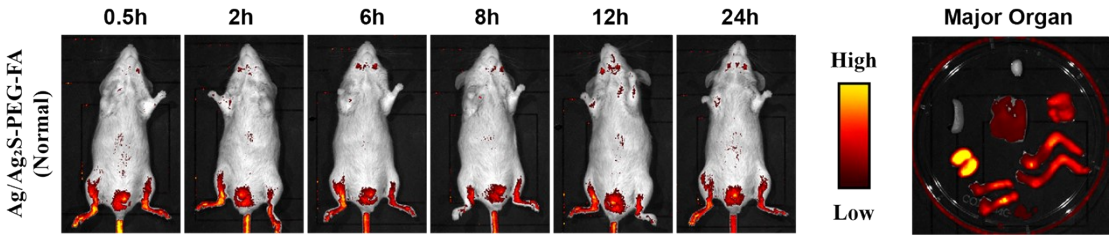

Fig. S20 Representative images of FITC labeled Ag/Ag_2S-PEG-FA/RSV NTs fluorescence distribution in normal mice and major organs at different times (0.5, 2, 4, 6, 8, 12, 24 h).

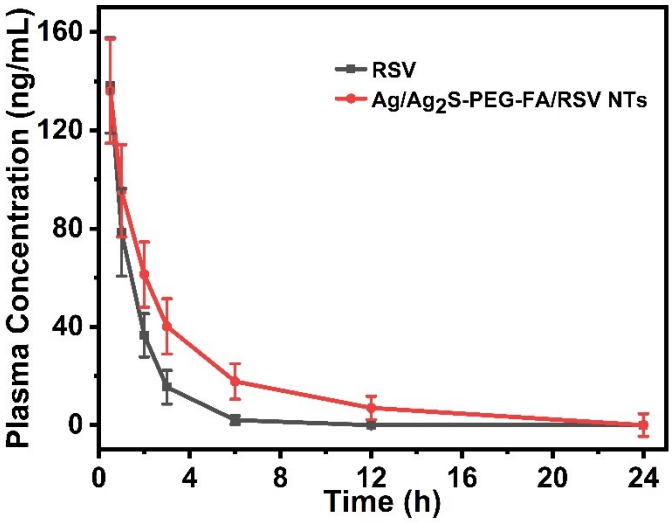

Fig. S21 Pharmacokinetics profile of free RSV and Ag/Ag_2S-PEG-FA/RSV NTs. Data are shown as the mean ± SD (n=3). *p<0.05, **p<0.01, ***p<0.001.

Table S2 Primer sequences used for real-time PCR *in vivo*.

Gene	Forward Primer	Reverse Primer
TNF-α	5'- CGTGGAACTGGCAGAAGAGG - 3'	5'- TCAGTAGACAGAAGAGCGTGGT - 3'
ARG-1	5'- AGTCTGGCAGTTGGAAGCAT - 3'	5'- GGAGTGTTGATGTCAGTGTGAG - 3'
IL-10	5'- GCTGGACAACATACTGCTAACC - 3'	5'- ATCATTTCCGATAAGGCTTGGC - 3'
iNOS	5'- CGAGACGGATAGGCAGAGATTG - 3'	5'- ACTCTTCAAGCACCTCCAGGAA - 3'

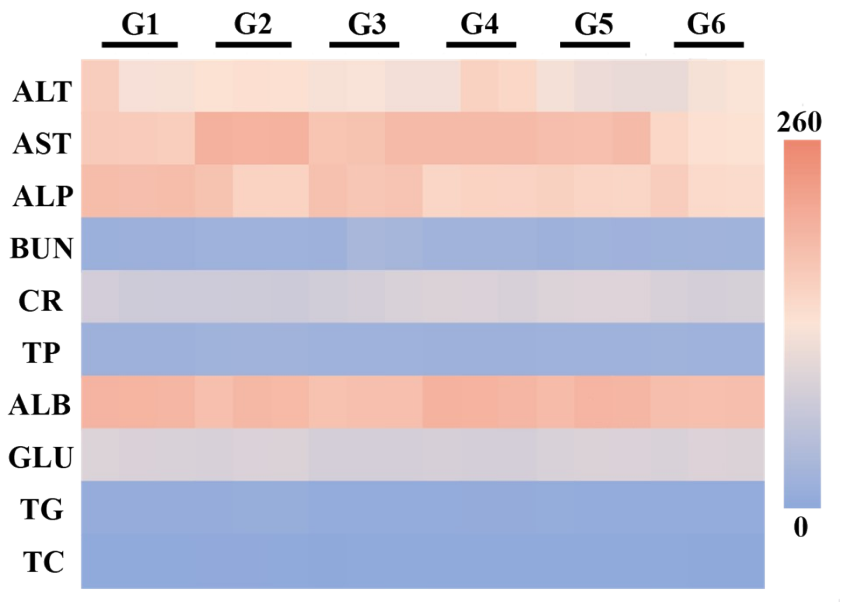

Fig. S22 Serum biochemical analysis of mice after various treatments. G1: Control, G2: Model, G3: Ag/Ag_2S NTs, G4: PEG-FA/RSV, G5: Ag/Ag_2S-PEG-FA/RSV NTs, G6: Ag/Ag_2S-PEG-FA/RSV NTs + 980 nm NIR-II irradiation.

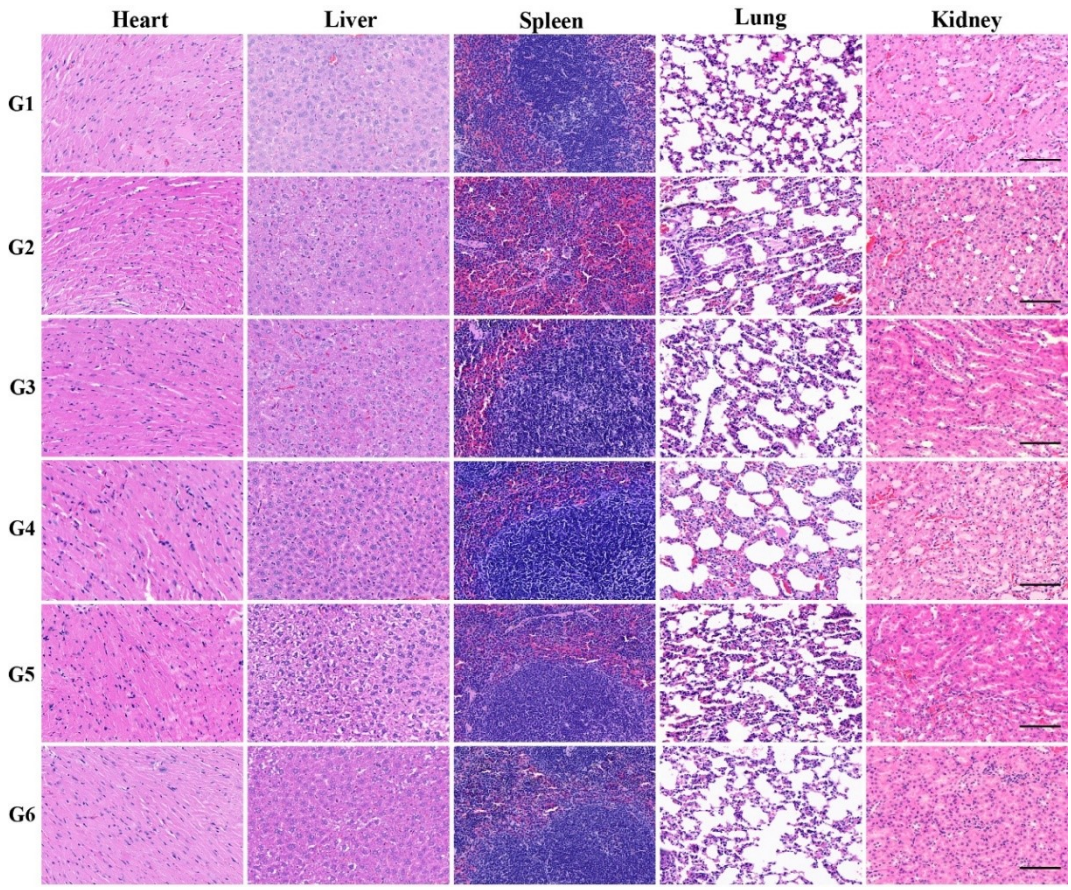

Fig. S23 Histopathological analysis of major organs after different treatments by staining with hematoxylin and eosin (H&E). Scale bar = 100 μm.