Figure S1

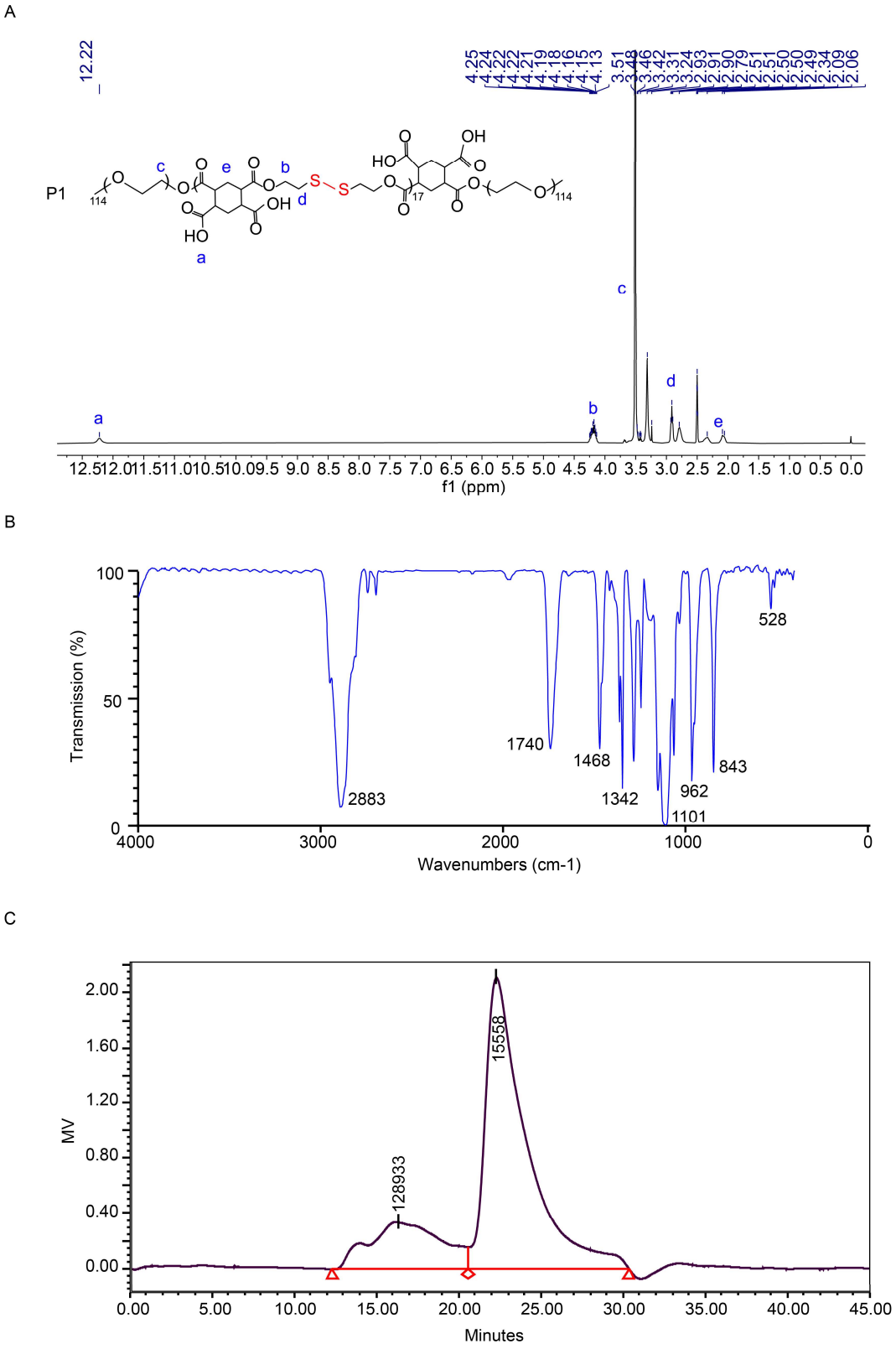

Figure S1. Characterization of P1 Polymer. The synthesized P1 polymer was characterized using ^1H NMR (A), FT-IR (B), and GPC (C) techniques. (A) The ^1H

NMR spectrum of P1 was recorded in DMSO-d6, with peaks corresponding to different functional groups highlighted in the figure. (B) The FT-IR spectrum of P1 further demonstrates the successful synthesis of the polymer through typical absorption bands. The peak at 1,750–1,735 cm^{-1} corresponds to the C=O stretching vibration from ester and amide groups, while the peak at 500–550 cm^{-1} indicates the presence of the disulfide (S–S) linkage. These key absorption bands confirm the incorporation of the functional groups in the polymer structure. (C) GPC analysis indicates a peak molecular weight (MP) of approximately 15,000 g/mol, confirming the uniformity and quality of the synthesized polymer.

Figure S2

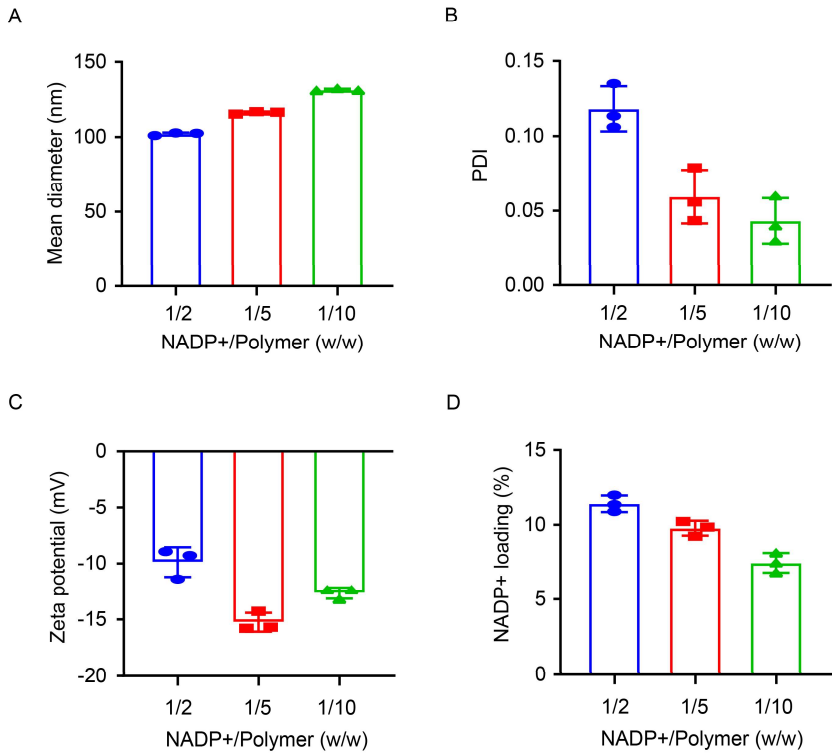

Figure S2. Formulation optimization of the nanoparticles. The size (A), PDI (B), zeta potential (C), and NADP+ loading (D) were assessed for various NADP+-to-polymer mass ratios.

Figure S3

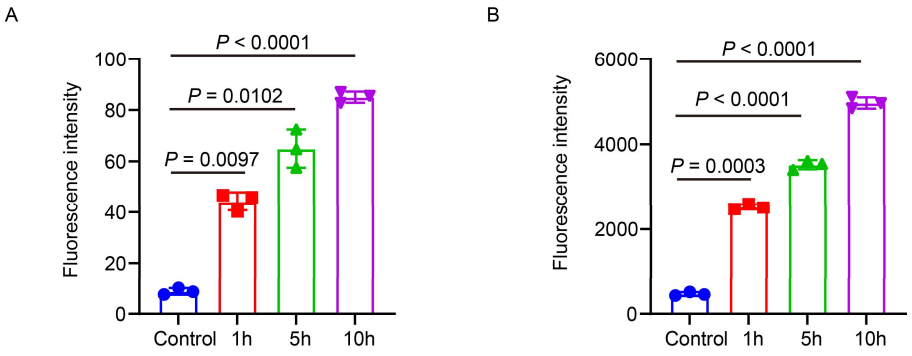

Figure S3. Cellular uptake of reduction-responsive nanoparticles encapsulating NADP+ and Rhodamine B. (A) Relative quantification of immunofluorescence results showing the levels of Rhodamine B in treated and control groups. Related to Figure 2B. (B) Quantitative analysis of flow cytometry results displaying the levels of Rhodamine B in treated and control groups. Related to Figure 2C.

Figure S4

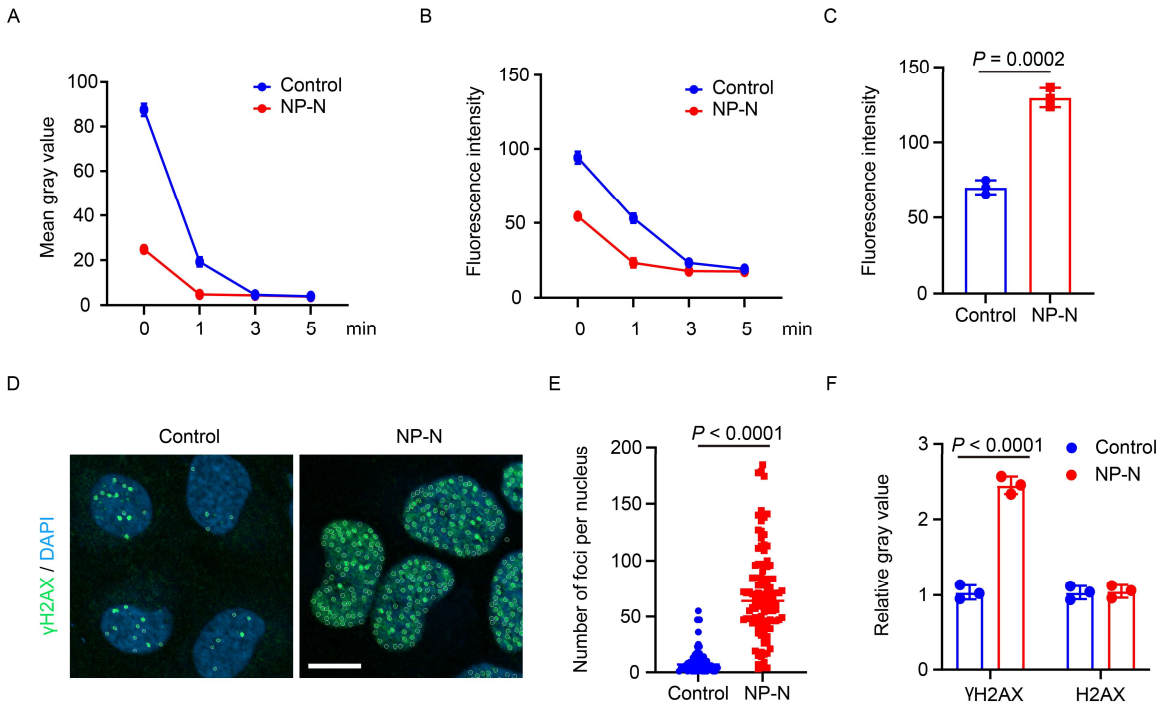

Figure S4. Inhibition of PARylation by nanoparticles loaded with NADP+. (A) Relative quantification of dot bolt results showing the levels of PAR after MMS treatment. Related to Figure 3A. (B) Relative quantification of immunofluorescence results showing the levels of PAR after MMS treatment. Related to Figure 3B. (C) Relative quantification of immunofluorescence results showing the levels of γH2AX in treated and control groups. Related to Figure 3C. (D) γH2AX foci observed after MMS treatment. White circles indicate the foci. Related to Figure 3C. Bar, 5 μm. (E) Quantification of the number of γH2AX foci in treated and control groups. Related to Figure 3C. (F) Relative quantification of western bolt results displaying the levels of γH2AX and H2AX in treated and control groups. Related to Figure 3D.

Figure S5

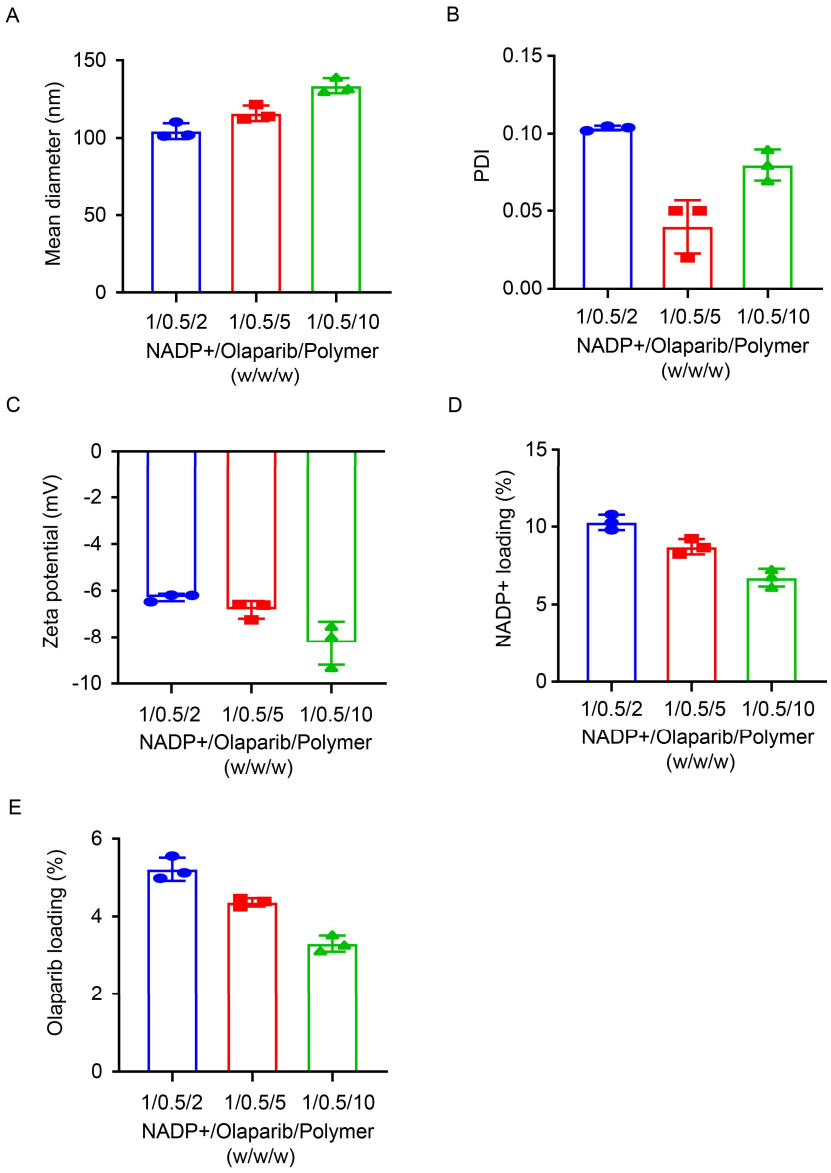

Figure S5. Formulation optimization of the nanoparticles. The size (A), PDI (B), zeta potential (C), NADP+ loading (D), and Olaparib loading (E) were assessed for various NADP+-Olaparib-polymer mass ratios.

Figure S6

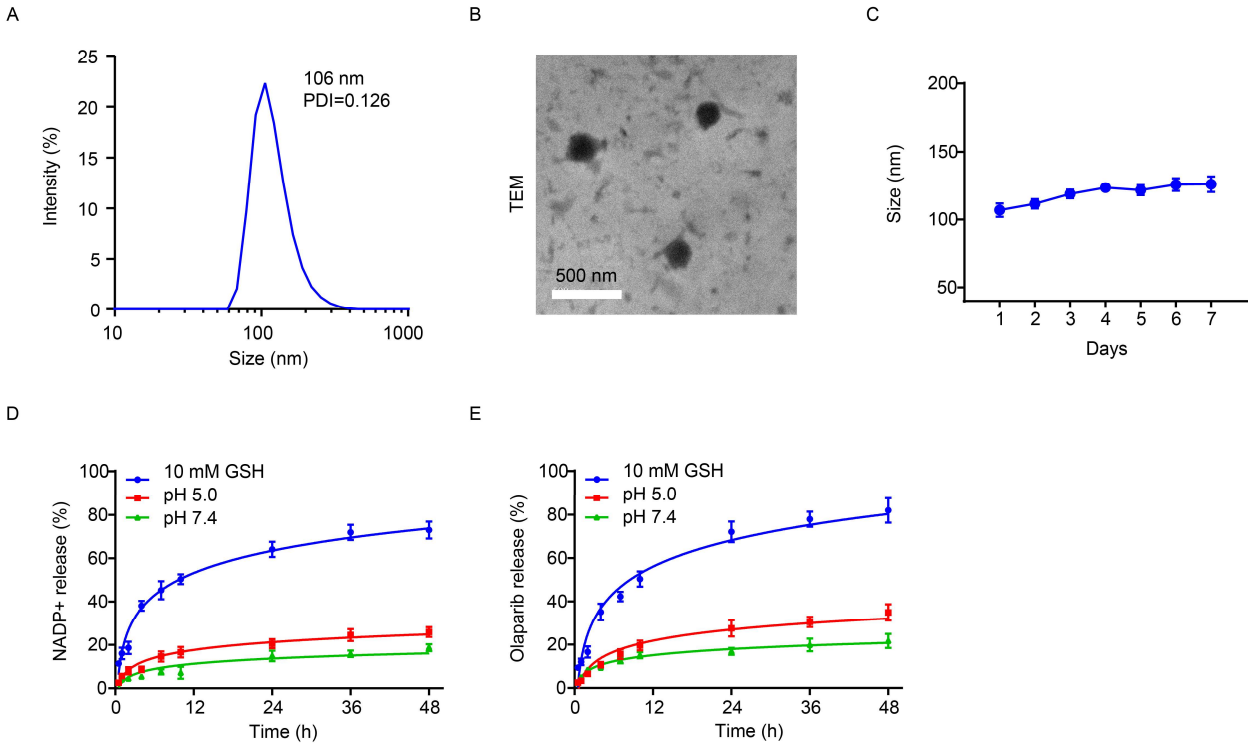

Figure S6. Synthesis and characterization of reduction-responsive nanoparticles encapsulating NADP+ and Olaparib (NP-N&O). (A) Representative dynamic light scattering (DLS) results for NP-N&O. (B) Representative transmission electron microscopy (TEM) images of NP-N&O. Scale bar, 500 nm. (C) Particle size of NP-N&O after 7 days of incubation in PBS. (D, E) The NADP+ release (D) and Olaparib release (E) profile of NP-N&O under various conditions (10 mM GSH, pH = 5.0, and pH = 7.4).

Figure S7

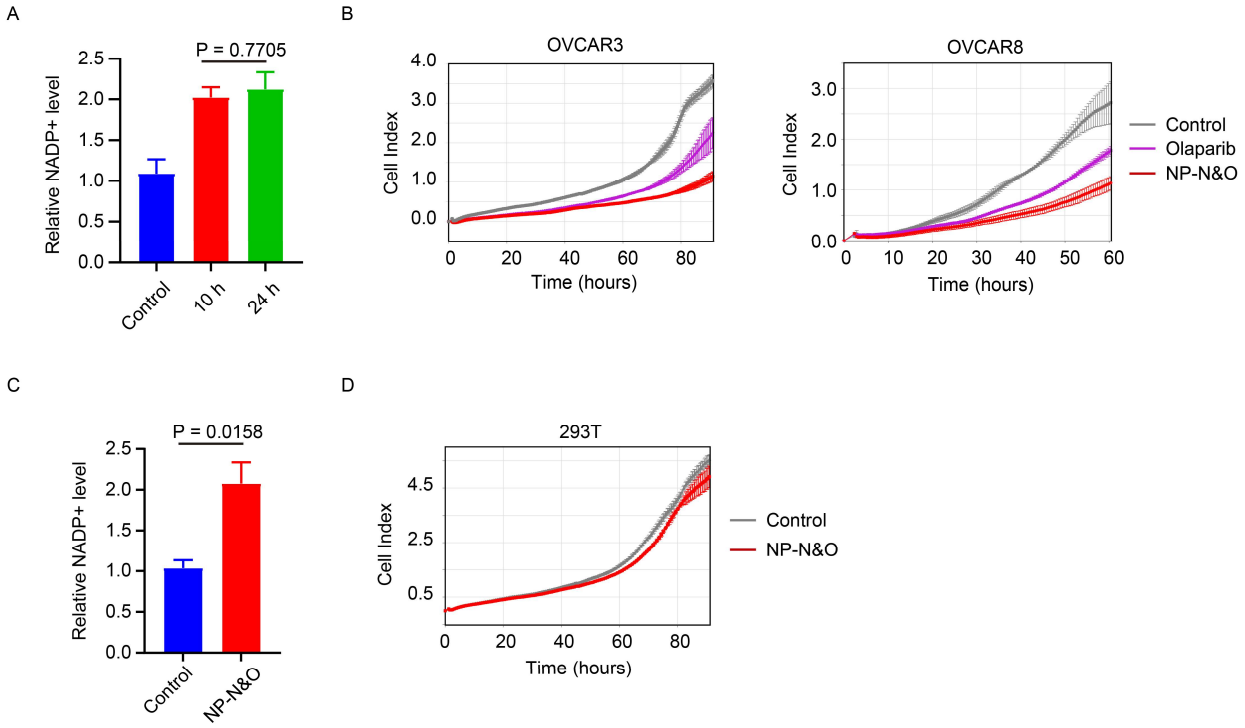

Figure S7. Effects of Nanoparticles loaded with NADP+ and Olaparib on different cell lines. (A) The relative NADP+ levels in HeLa cells were measured after incubation with NP-N at different time points: 10 and 24 h. The cells were treated with NP-N with the NADP+ at 20 μM in the culture medium at 37 °C for the respective time durations. Untreated cells were used as a control. (B) Real-time cell proliferation assay of OVCAR3 and OVCAR8 cells treated with Olaparib and NP-N&O with the Olaparib at 10 μM in the culture medium at 37 °C for the indicated times. (C) The relative NADP+ levels in 293T cells were measured after incubation with NP-N&O at 24 h. The cells were treated with NP-N&O with the NADP+ at 20 μM in the culture medium. Untreated cells were used as a control. (D) Real-time cell proliferation assay of 293T cells treated with NP-N&O with the Olaparib at 10 μM in the culture medium at 37 °C for the indicated times.

Figure S8

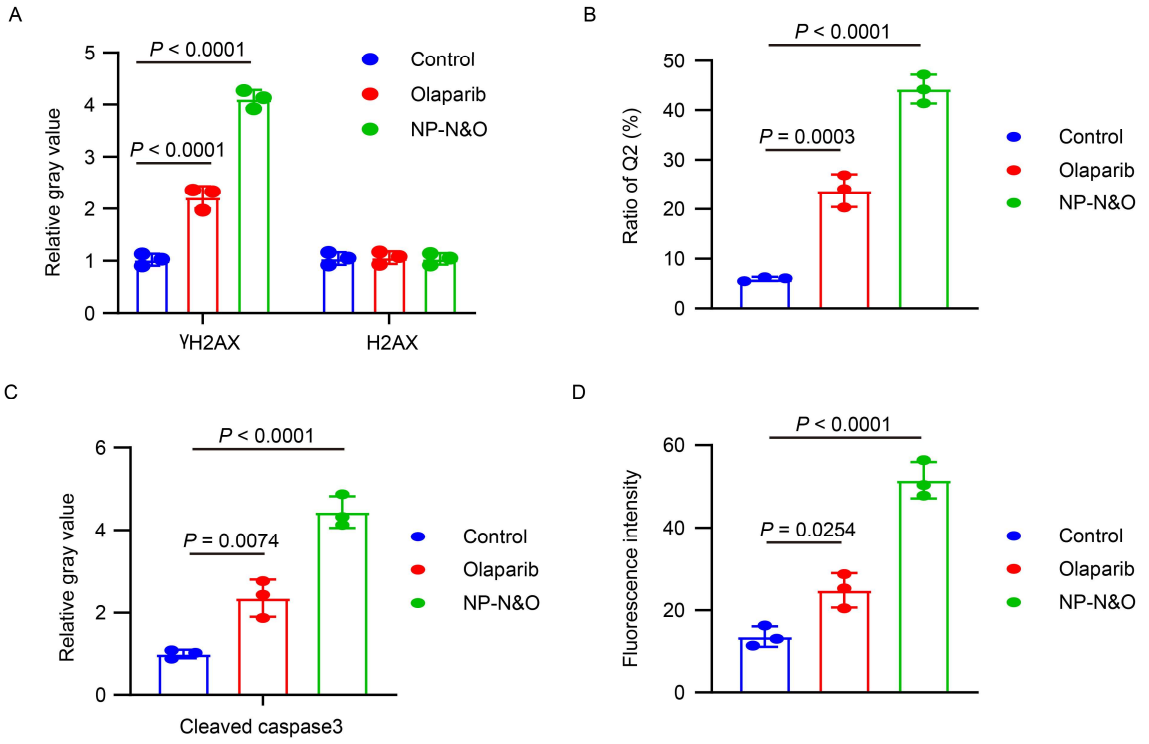

Figure S8. Effects of Nanoparticles loaded with NADP+ and Olaparib on cancer cells. (A) Relative quantification of western bolt results displaying the levels of γH2AX and H2AX in treated and control groups. Related to Figure 5A. (B) Quantitative analysis of flow cytometry results displaying the ratio of Q2 in treated and control groups. Related to Figure 5B-D. (C) Relative quantification of western bolt results displaying the levels of cleaved caspase3 in treated and control groups. Related to Figure 5E. (D) Relative quantification of immunofluorescence results showing the levels of active apoptosis in treated and control groups. Related to Figure 5F.

Figure S9

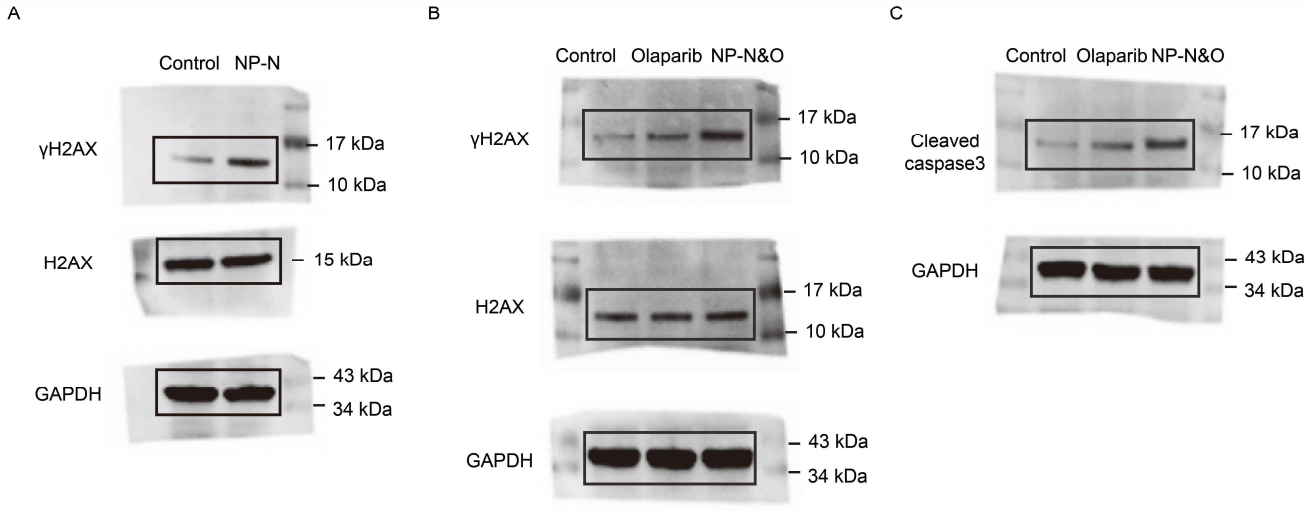

Figure S9. Uncropped Western Blot image with molecular weight markers indicated, related to Figure 3D (A), Figure 5A (B) and Figure 5E (C).