Supporting Information

**In vivo Delivery of Nuclear Targeted Drugs for Lung Cancer Using Novel Synthesis and Functionalization of Iron Oxide Nanocrystals**

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Figure S1-S8
Figure S1. The hydrodynamic size distribution measured by dynamic light scattering shows a narrow size distribution with an average diameter of 65.7 ± 0.92 nm.

Figure S2. The EDS analysis of PEG-DOX-γ-Fe₂O₃-NC showed a strong signal from Fe and the presence of C, N and O due to DOX and PEG.
Figure S3. FTIR spectra of PEG, DOX and PEG-DOX-γ-Fe$_2$O$_3$-NC.

Figure S4. (A) The established standard curve of DOX at about 480 nm by UV-VIS absorption spectra; (B) UV-VIS absorption spectrum of DOX in supernatant.
Figure S5. Prussian blue staining A) Control and B) cells were incubated with 25 µg/mL PEG-DOX-γ-Fe₂O₃-NC for 24 hr, and stained with 2 mL of Prussian blue solution at 37°C for 30 min. A blue area or spot was observed in almost every cell (indicated by arrows).

Figure S6. Confocal microscopy image of A549 cells treated with PEG-DOX-γ-Fe₂O₃-NC. No DOX signal was obtained within 0 hr, but DOX was concentrated in the core within 3 hr, and evenly distributed DOX was also displayed around the core. Note: DOX (red) in cell.
Figure S7. Transmission electron microscopy of A549 cells showed the internalization of PEG-DOX-γ-Fe₂O₃-NC after 6 hr of incubation in the nuclei. Note: The red arrow represents the collection of nanocrystals.

Figure S8. Pharmacokinetics and biodistribution of DOX formulations in vivo. (a) In vivo DOX pharmacokinetics after i.v. injection of free PEG-DOX-γ-Fe₂O₃-NC and in to Sprague-Dawley rat. (b) Average semiquantitative signals of major organs and tumor after i.v. injection. Data are presented as mean ± SD (n = 3; *P < 0.05, ***P < 0.001).