Supporting Information

Thermosensitive Biodegradable Copper Sulfide Nanoparticles for Real-Time Multispectral Optoacoustic Tomography

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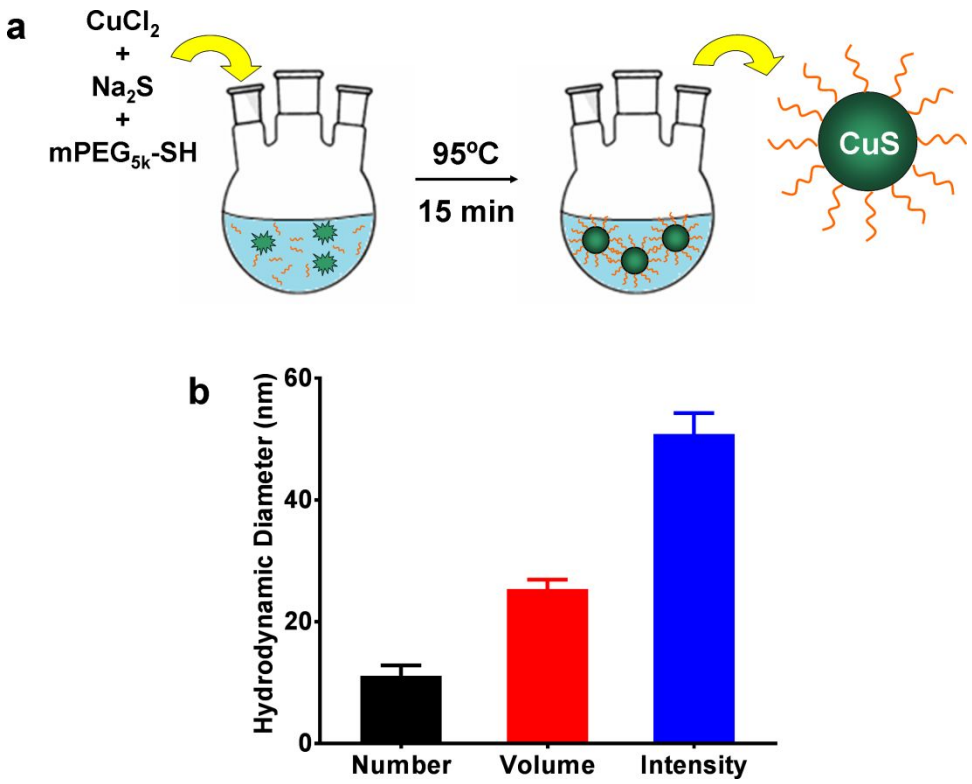

Figure S1. Synthesis and characterization of CuS-PEG nanoparticles. (**a**) Schematic illustration of the one-step synthesis of CuS-PEG nanoparticles. (**b**) Average hydrodynamic diameters of CuS-PEG nanoparticles with number, volume, and intensity size distribution.

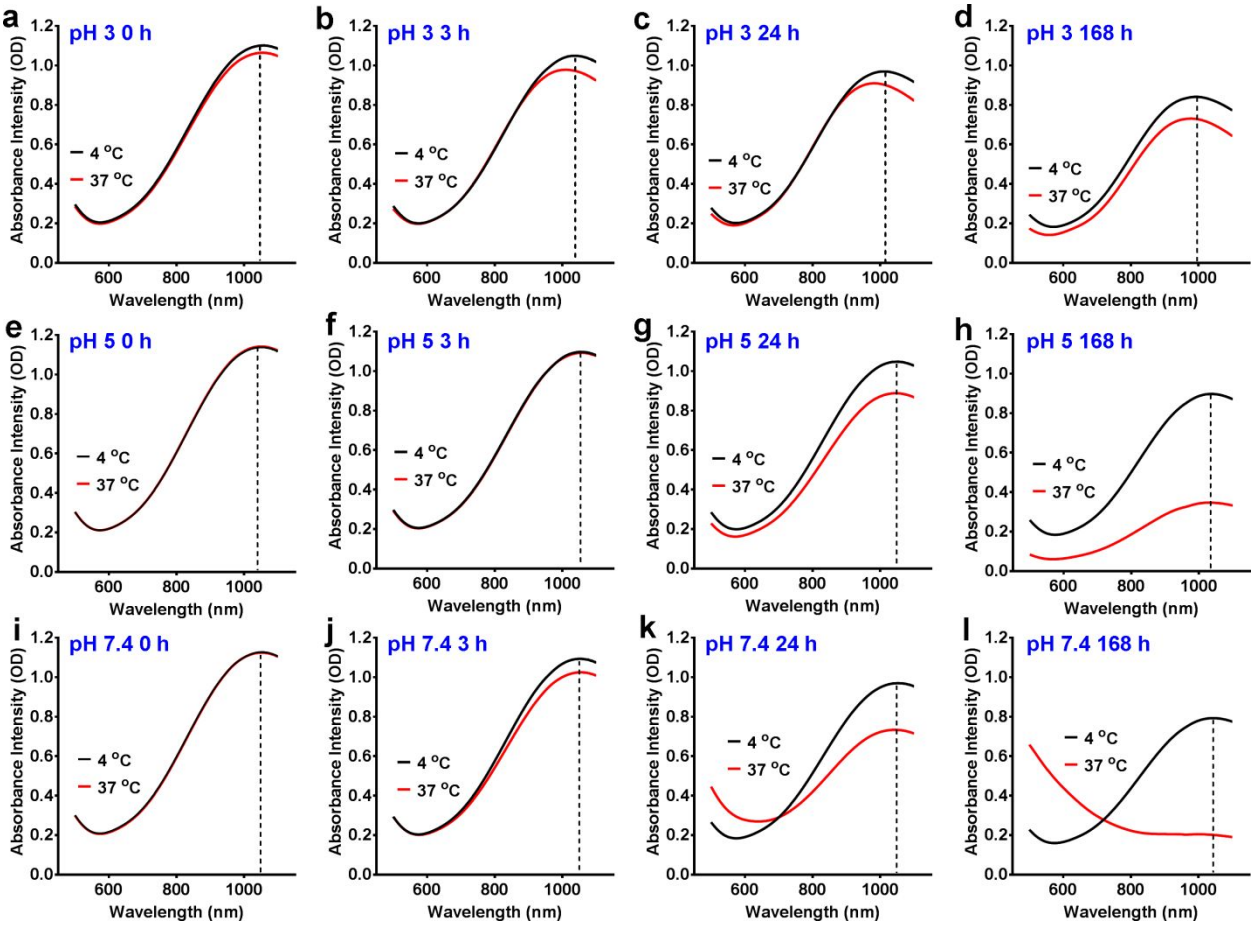

Figure S2. (**a-l**) Comparison of absorbance profiles of CuS-PEG nanoparticles incubated at 4 ºC and 37 ºC under different conditions.

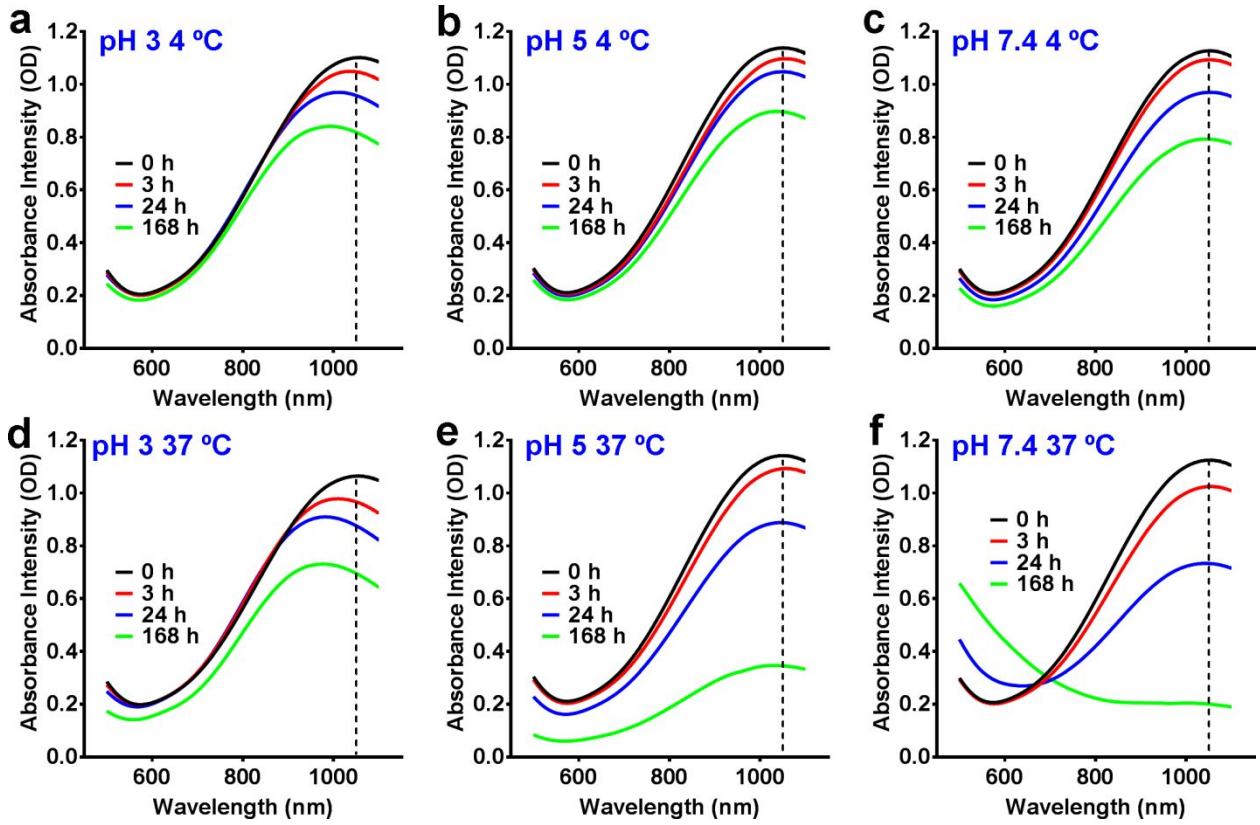

Figure S3. (**a-f**) Comparison of absorbance profiles of CuS-PEG nanoparticles incubated for 0, 3, 24, and 168 h under different conditions.

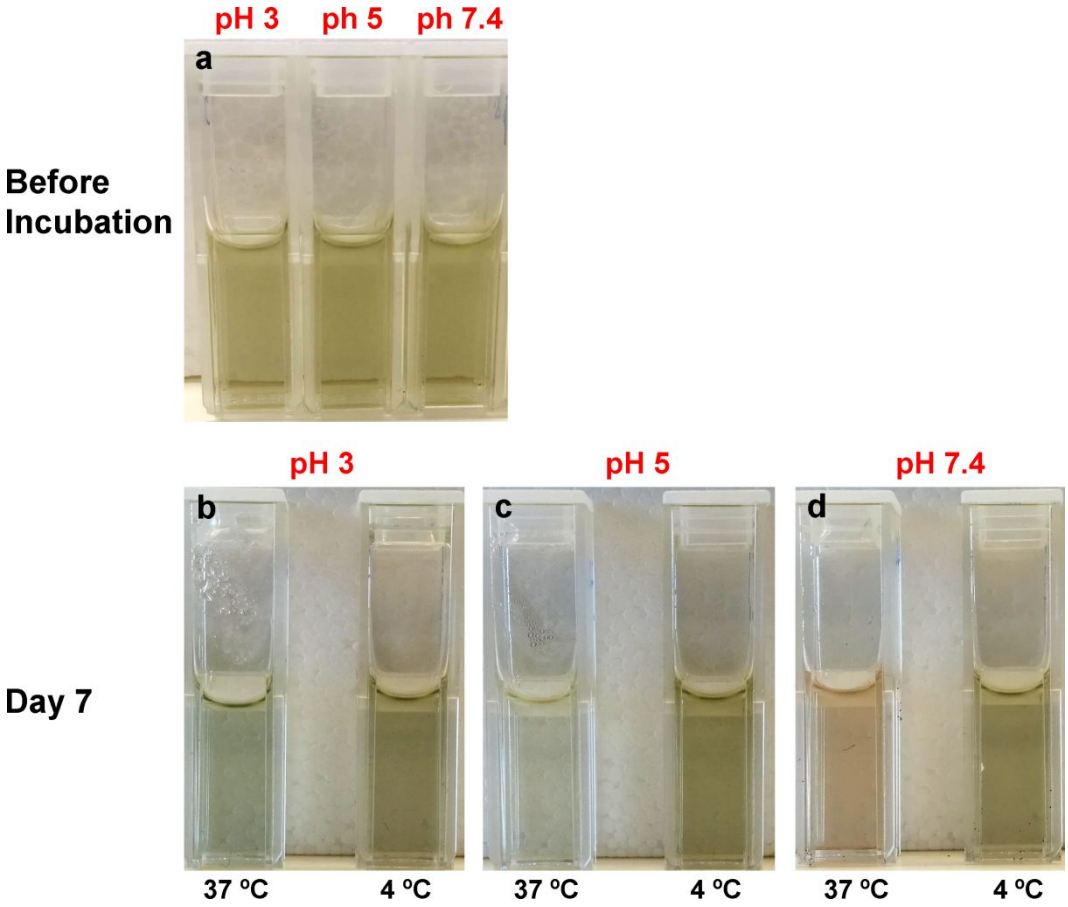

Figure S4. The photographs of CuS-PEG nanoparticles before incubation (**a**) or after 7 days incubation at different conditions (**b-d**).

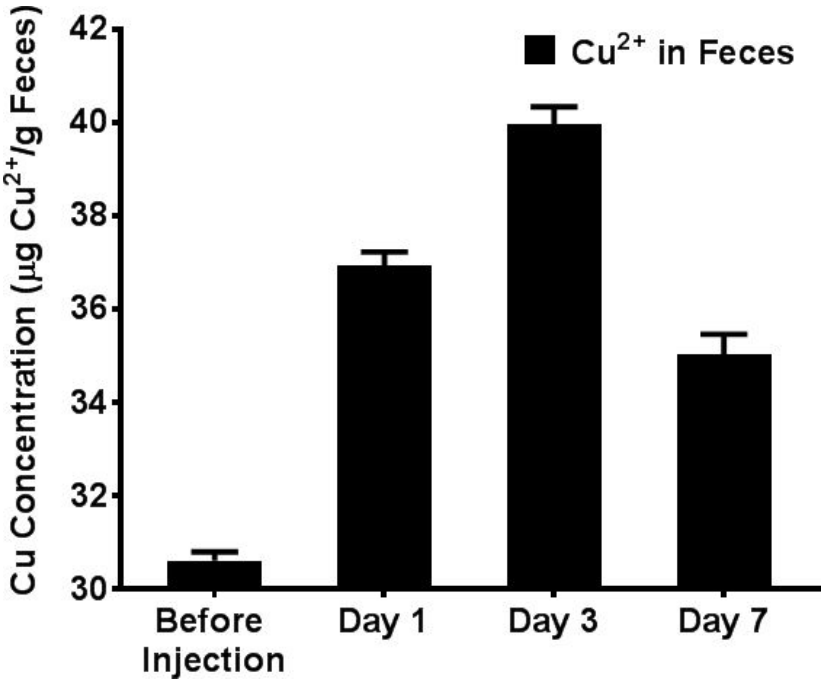

Figure S5. ICP-OES analysis of Cu elemental concentration in mouse feces collected at different time points after i.v. injection of CuS-PEG nanoparticles (n = 3).

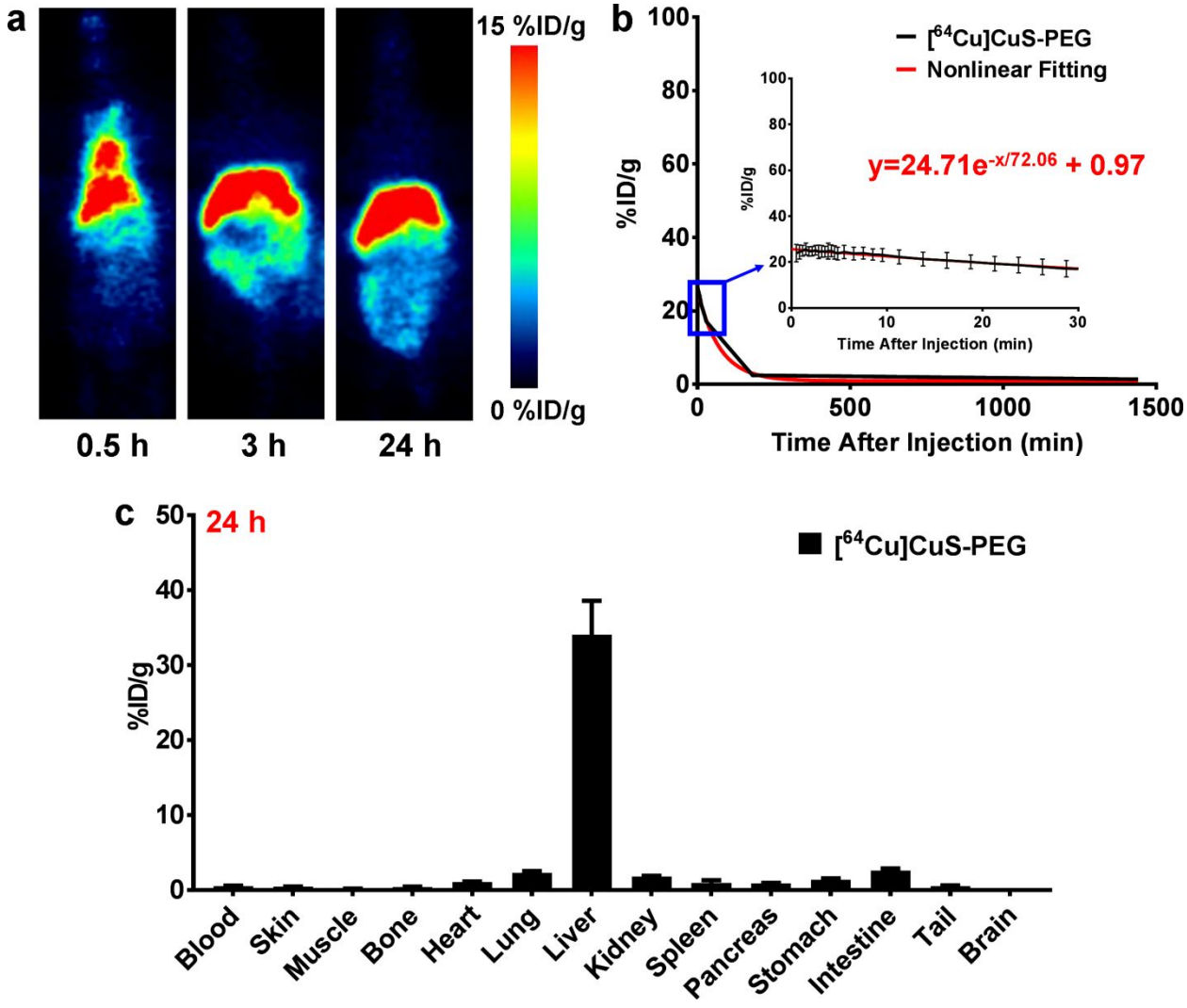

Figure S6. Serial *in vivo* PET images (**a**), region of interest (ROI) analysis of the blood uptake with nonlinear fitting (**b**) and *ex vivo* biodistribution studies (**c**) after i.v. injection of intrinsically radiolabeled CuS-PEG nanoparticles ([^{64}Cu]CuS-PEG) (n = 4). Dynamic scans were performed for the first 30 min immediately after injection of [^{64}Cu]CuS-PEG. Static scans were performed at 3 h and 24 h p.i.. The blood uptake was measured by ROI analysis of heart on PET images.

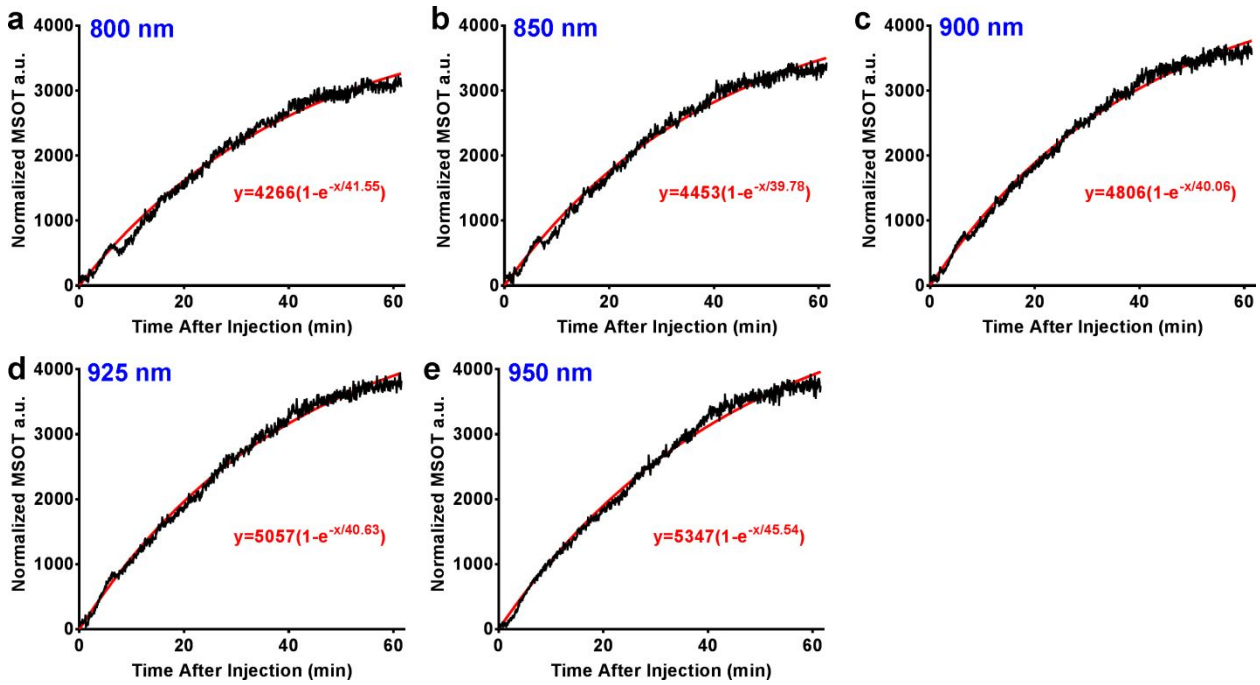

Figure S7. In situ tumor MSOT intensity profiles with nonlinear fitting using the equation of one-phase exponential association $y = y_{max} \bullet (1\text{-}e^{-x/\tau})$, where y represents normalized MSOT absorbance intensity (a.u.) and x represents the time after injection (min), at 800 nm (**a**), 850 nm (**b**), 900 nm (**c**), 920 nm (**d**), and 950 nm (**e**).