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Appendix E1

Synthesis and Characterization of PEG-HAuNS and Dox@PEG-HAuNS

PEG-HAuNS were synthesized by the cobalt nanoparticle–mediated reduction of chlorauric acid followed by PEGylation as described previously (14). HAuNS were coated readily with MeO-PEG5000-SH (Fluka, Buchs, Switzerland) to yield PEG-HAuNS, whose hollow structure was confirmed with transmission electron microscopy. The PEG-HAuNS diameter was 51.6 nm as determined by dynamic light scattering. The absorption spectra showed that the plasma resonance peak for PEG-HAuNS was tuned to the near infrared region (approximately 800 nm). The conjugate remained stable for > 1 week at room temperature.

For Dox (Sigma-Aldrich, St. Louis, Mo) loading, free Dox (16 mg) in water (10 mL) was added to a 30-mL citrate solution of PEG-HAuNS (20 optical density), and the mixture was stirred at room temperature for 24 hours. The resulting Dox@PEG-HAuNS were purified by repeated centrifugation and washing as described previously (3–5). Consistent with previously reported data (5), the Dox payload of Dox@PEG-HAuNS was 60% by weight.

Dox@PEG-HAuNS were imaged by using a JEM 1010 transmission electron microscope (JEOL, Peabody, Mass) at an accelerating voltage of 80 kV. The Dox@PEG-HAuNS diameter was determined by means of dynamic light scattering by using a particle analyzer (Zeta Plus; Brookhaven Instruments, Holtsville, NY). The absorption spectrum was analyzed by using ultraviolet-visible spectroscopy. The Dox payload was analyzed as described previously (3).

^{64}Cu Radiolabeling

^{64}Cu-labeled PEG-HAuNS (PEG-[^{64}Cu]-HAuNS) were prepared as described previously (15). ^{64}Cu (obtained from the cyclotron and radiochemistry facility, Center for Advanced Biomedical Imaging, the University of Texas MD Anderson Cancer Center) was introduced to PEG-HAuNS by means of the radiometal chelator tetraazacyclododecane tetraacetic acid thioactamide . ^{64}Cu–tetraazacyclododecane tetraacetic acid thioacetamide was mixed with an aqueous solution of citric acid–stabilized HAuNS (400 μL, approximately 2×10^{13} particles) at room temperature for 4 hours to produce ^{64}Cu-labeled HAuNS. Then, 200 μL of mercaptopolyethylene glycol 5000-SH (5 mg/mL) was mixed with ^{64}Cu-labeled HAuNS at room temperature overnight to produce PEG-(^{64}Cu)-HAuNS. The radiolabeling efficiency was determined by using instant thin-layer chromatography. The overall efficiency of ^{64}Cu radiolabeling of PEG-HAuNS was greater than 96%, and PEG-(^{64}Cu)-HAuNS had a specific radioactivity of 690–750 MBq/nmol.