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Supplementary Information

Materials: Selenium shots, cadmium oxide, TOP, TOPO, and oleic acid are obtained from Aldrich and used as supplied. CdSe QDs are synthesized as described below. CdSe/ZnS (655 nm emission) QDs are commercially obtained from Invitrogen. Lipids (1,2-dioleoyl-*sn*-glycero-3-phosphoethanolamine (DOPE), 1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine (DPPE) and 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[biotinyl(polyethylene glycol)-2000] (DSPE-PEG2000)) are obtained from Avanti Polar Lipids. ZnO nanopowder, $ZnSO_4$, $CdCl_2$, hexadecyl amine, and spectroscopic grade solvents are obtained from Wako and used as supplied. Heat-inactivated fetal bovine serum (FBS), tripsin, and phosphate buffered saline (PBS) are obtained from Sigma. Dulbecco's modified Eagle's medium (DMEM) is obtained from Gibco.

Preparation of quantum dots samples: Briefly, a mixture of cadmium oleate (1.2 ml, 1.2 M solution in oleic acid) and trioctylphosphine selenide [TOPSe, 1 ml, 1.36 M solution in trioctylphosphine (TOP)] is reacted at 120°C for 2 hours in the presence of hexadecyl amine (2 g, 8.3 mmol) and trioctylphosphine oxide (TOPO, 2 g, 5.2 mmol).[18] Cadmium oleate and TOPSe solutions are prepared by dissolving required amounts of CdO powder and Se shots in oleic acid and TOPO, respectively. CdSe QDs are purified by precipitation from a mixture (5:1 v/v) of methanol and *n*-butanol (*n*BuOH). Finally, the purified QD sample is suspended in TOPO and stored under N_2 gas at room temperature.

Aqueous CdSe QDs are prepared by the ligand (TOP/TOPO) exchange of organic CdSe QDs with dihydrolipoic acid (DHLA) by following the method reported by

Uyeda et al[34] with the following modifications to the original procedure. The organic CdSe QDs are first suspended in *n*BuOH and then diluted in ethanol at a volume ratio of 1:2 (*n*BuOH:EtOH). Excess amounts of lipoic acid (LA, 206 mg, 1 mmol) and sodium borohydride (227 mg, 6 mmol) are added to the organic QD solution. An equal volume (3 mL) of deionized (DI) water is added and the mixture is vortexed, sonicated, heated to 60°C, and stirred for 6 hours. The organic and aqueous phases are separated by adding chloroform and DI water at a volume ratio of 1:1. The aqueous layer is separated and dialyzed three times against a membrane for 2kDa molecular weight to remove excess ligands and ions.

For the preparation of QDs embedded in liposomes,[32,33] first CdSe/ZnS QDs suspended in decane are dried in a round bottom flask by purging nitrogen gas and further dried under reduced pressure to completely remove the solvent. In parallel, the lipid solution is prepared using 1,2-dioleoyl-*sn*-glycero-3-phosphoethanolamine (DOPE), 1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine (DPPE), and 1, 2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[biotinyl(polyethylene glycol)-2000] (DSPE-PEG2000) in molar ratios of 49.75:49.75:0.5 (DOPE:DPPE:DSPE-PEG2000) in chloroform. The lipid solution is added to the dried QDs and chloroform is removed by evaporation under reduced pressure to form a dry fluorescent lipid film on the bottom of the flask with QDs embedded in the lipid bilayer. The lipid film is hydrated using an aqueous solution consisting of 7.5 mg of glucose, 57 µL of rhodamine 123 dye solution (2.6 mM) and 1.443 ml DI water. The flask is vortexed followed by 10 minutes of sonication at 65°C to form

QD-embedded liposomes (QD-liposomes). The QD-liposome solution is sterilized by filtration through a 0.2 μm membrane filter before administering to cells for MTT assay or fluorescence microscopy.

Solar simulated UV-irradiation of engineered nanomaterials: Solar simulated UV irradiation is performed using a 75 W Xenon lamp equipped with a band-pass filter to allow UV-radiation (330 to 400 nm) to pass through. The distance from the lamp to the sample is fixed at 7 cm to simulate the intensity of solar UV radiation at sea level. Photoetching experiments are conducted to measure the amount of zinc and cadmium ions leaching that occurs during the simulated solar UV irradiation. In the photoetching experiments, aqueous solutions of ZnO nanoparticles (1 mM) or CdSe QDs (57 μM) are irradiated with ultraviolet light for intervals of 3, 6, and 9 hours. After each irradiation interval, the sample is loaded in a dialysis cassette for 2 kDa molecular weight cutoff, and dialyzed overnight by immersing in DI water under vigorous stirring. Concentrations of Cd^{2+} and Zn^{2+} produced as a result of photoirradiation are estimated from the ions released into DI water and the dilution factor. In separate experiments, 5 mL nanoparticle samples are exposed to solar simulated UV light and 1 ml samples are collected after each irradiation interval. The samples are filtered through a 0.2 μm filter, and stored in a dark bottle for detecting the concentration of ions produced and evaluating the cytotoxic effects of the leached ions.

Cell culture and cell viability assay: We used human lung epithelial adenocarcinoma cells (H1650) for evaluating the intracellular delivery of nanoparticles using liposomes as well as the cytotoxicity of metal ions leached out during the photoirradiation of CdSe QDs and ZnO nanoparticles. H1650 cells are cultured up to

~ 60 % confluence in DMEM medium supplemented with 10% heat-inactivated fatal bovine serum (FBS). For fluorescence imaging, H1650 cells are cultured up to 80% confluence, supplemented with a mixture of 1.8 mL phosphate buffered saline (PBS) and 0.2 ml of QD-liposome solution, and incubated at 37°C for 1 h. The cells are washed 3 times with PBS before adding the cell culture medium and observing by fluorescence microscopy.

The protocol for 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay is supplied by the manufacturer. Briefly, H1650 cells are seeded onto 96 well plates and cultured up to 100% confluence. Cells are washed with PBS and the medium is replaced with a medium containing liposomes, QD-liposome, Cd^{2+}, Zn^{2+}, CdSe QDs, ZnO nanoparticles, or the photo-irradiated CdSe QDs or ZnO nanopowder. The cells are incubated with the nanoparticles or ions for 4 or 72 h and then washed with PBS, the medium is replaced with medium containing MTT, and the cells are incubated overnight. Subsequently, the cells are treated with the lysis buffer provided in the MTT assay kit and incubated overnight. The optical density of purple formazan formed as a result of the reduction of MTT by the NADP/H-dependent oxidoreductase enzymes in the cytosol is estimated using a microplate reader.

Comet genotoxicity assay: Reagents including the lysis solution, alkaline unwinding solution, alkaline electrophoresis solution and staining solution are prepared according to the protocol for comet assay provided by the manufacturer. H1650 cells cultured up to 100% confluence in the presence or absence of Cd^{2+} or Zn^{2+} are harvested by tripsinizing and centrifugation. Low molecular weight agarose (LMAgarose) is heated at 95 ^{o}C and successively stabilized at 37 ^{o}C for 20 min. The

cell pellets are suspended separately in 500 μL PBS, mixed with LMAgarose at a 1:10 ratio, and immediately pipetted onto the comet slide glass. The agarose coated slides are allowed to gel in the dark at 4°C for 15 minutes, followed by soaking in chilled lysis solution for 30 min. The slides are then soaked in an alkaline chromosome/DNA unwinding solution for 30 minutes at room temperature in the dark. The slides are placed in the pre-chilled alkaline electrophoresis solution in an electrophoresis apparatus and gel electrophoresis is performed by applying 21 volts for 45 minutes. Slides are then immersed twice in DI water for 5 min and then in 70% ethanol before drying at 44°C for 15 minutes. DNA in the slides are stained with Syto16 dye by pipetting 10 μM dye solution onto the dried agarose. The stained slides are placed in the refrigerator for 5 minutes, excess dye solution is pipetted out and the slides are dried at room temperature in the dark. Samples are stored in a dessicator until imaging by fluorescence microscopy. Comets are observed by fluorescence microscopy and scored using a computer-aided software scoring program (Comet Assay Software Project, CASP 1.2.2).[50]

Scanning electron microscopy characterization: ZnO nanopowder and QD-embedded liposomes are characterized by field emission scanning electron microscopy (FESEM). QD-embedded liposomes are prepared as above and an additional amount of glucose is added to stabilize the QD-liposomes (5:1 mass ratio of glucose:lipid). The liposome solution is frozen overnight at -80°C, and the frozen solution is immediately freeze-dried for several hours until completely dried. The sample is deposited on a copper tape substrate and imaged using FESEM. ZnO nanopowder samples for

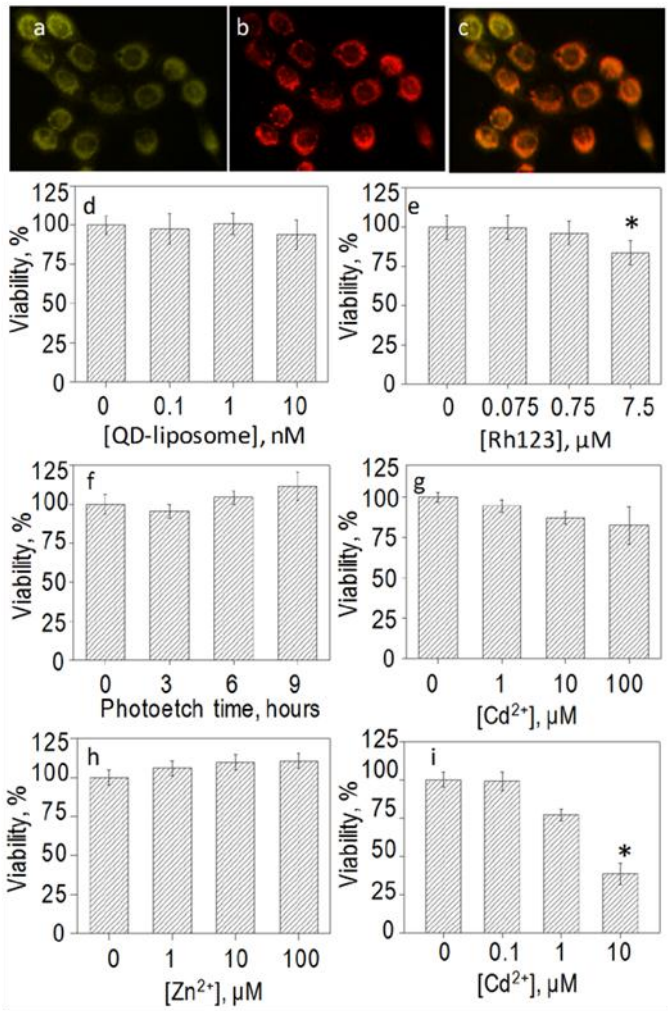
FESEM imaging are prepared by suspending 1 mg powder in 10 mL deionized water, placing drops on copper tapes and drying overnight under vacuum.

Steady-state absorption and fluorescence spectroscopy: Absorption and fluorescence spectra are recorded using a Hitachi-4100 spectrophotometer. Estimates of CdSe QD concentration are made using the Beer-Lambert relationship;[19] concentration of CdSe QDs in the as purified sample is calculated from the optical density corresponding to the band-edge absorption (See Supplementary Information). Fluorescence spectra are recorded using a Hitachi-4500 spectrofluorometer. Samples for fluorescence measurements are excited at 415 nm. Fluorescence detection of Cd^{2+} and Zn^{2+} are carried out using solutions of tetracarboxyphenylporphyrin (20 nM in 5% K_2CO_3 solution) or the commercial Measure iT Pb/Cd sensor dye by adding 50 μL solutions of $ZnSO_4$ or $CdCl_2$ or photoetched CdSe QDs or ZnO nanopowder (concentrations of standards, $ZnSO_4$ and $CdCl_2$, ranged from 100 uM to 1 mM).

Fluorescence microscopy: Fluorescence images of liposomes and QD-embedded cells are obtained in an inverted optical microscope (Olympus IX70) equipped with an objective lens (Olympus PUlanApo, 60X), band-pass filters for QDs and rhodamine 123 dye, and a standard Olympus CCD camera or an Andoor EMCCD camera. The excitation light source used is 532 nm cw laser (200 W/cm^2) from a 532 nm diode pumped Nd:YVO_4 laser (Spectra Physics Millennia IIs).

Atomic force microscopy (AFM) imaging: Samples for AFM imaging are prepared by using colloidal solutions of CdSe QDs or ZnO nanoparticles, depositing the solutions onto freshly cleaved mica sheets and drying in air. AFM images are taken with an MFP-3D AFM (Asylum Research, Santa Barbara, USA) equipped with reflective

aluminum-coated ultra-sharp (radius of curvature ~ 10 nm) silicon nanoprobes (Olympus, Japan). The cantilevers used are 160 μm long, and have spring constants of ca 42 N/m and resonance frequencies of ca 360 kHz. Tapping mode AFM images are recorded in air, and the average diameters of the particles are estimated from the height image.

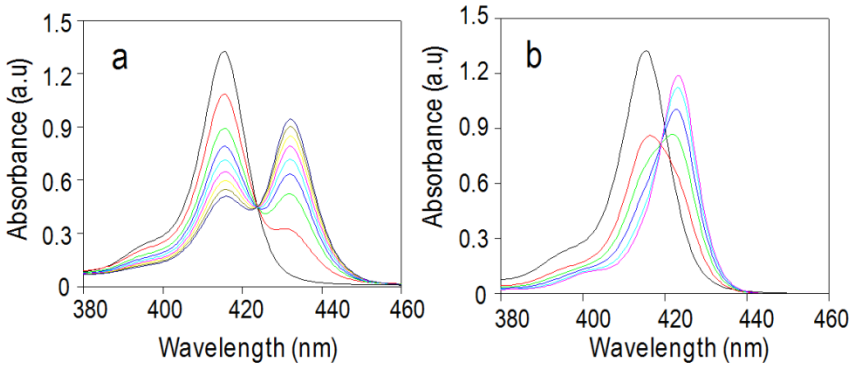


Supplemetary Figure 1. (a-c) Fluorescence microscopy images of H1650 cells labeled with CdSe/ZnS quantum dots- and rhoramine 123 (Rh123)- encompassed liposomes: (a) fluorescence signal collected through a band pass filter for Rh123, (b) fluorescence signal collected through a 620 nm long pass filter for CdSe/ZnS QDs, and (c) overlay image of ‘a’ and ‘b’. (d-i) MTT cytotoxicity assay of H1650 cells

treated with (d) QD-liposome, (e) Rh123, (f) photoirradiated CdSe QD solutions (4 h), (g) $CdCl_2$ solutions (4 h), (h) $ZnSO_4$ solutions (72 h), and $CdCl_2$ solutions (72 h).

UV-VIS-Spectroscopy of TCPP, TCPP-Zn, and TCPP-Cd complexes

UV-VIS absorption spectroscopy measurements are recorded for the complexes formed from TCPP with Zn and Cd. Such measurements show that the absorption peak of TCPP is redshifted by 8 nn and 17 nm upon addition of either zinc or cadmium ions as shown below.



Supplementary Figure 2. UV-VIS absorption spectroscopy measurements of TCPP after addition of A.) $CdCl_2$ and B.) $ZnSO_4$.

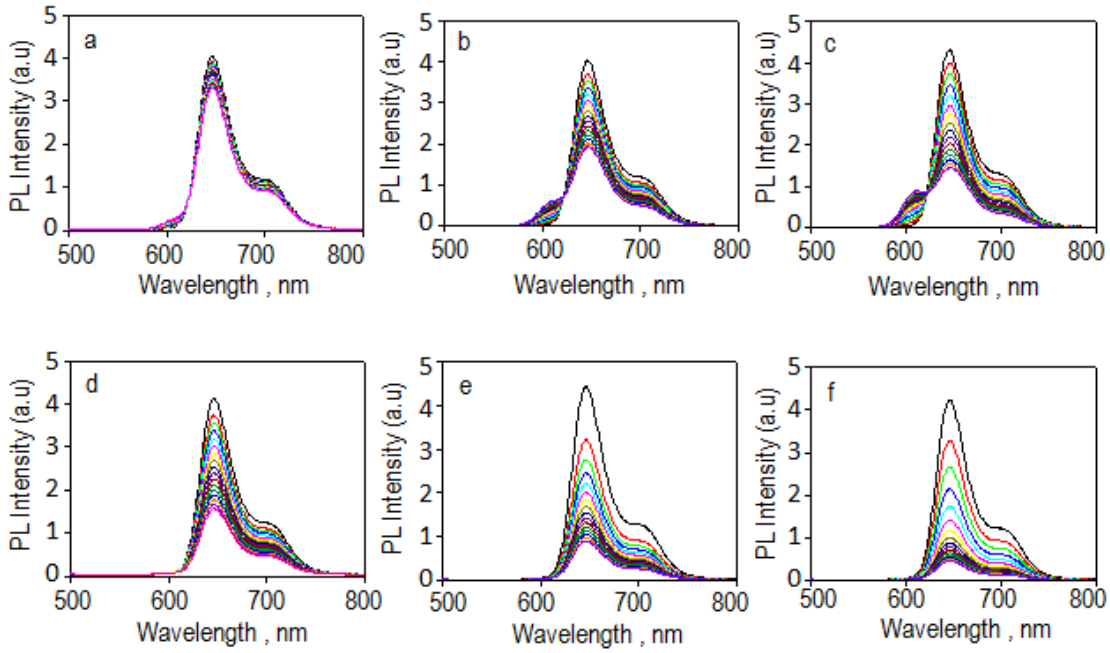
Fluorescence quenching of TCPP with $ZnSO_4$ and $CdCl_2$

Fluorescence quenching of TCPP after addition of 100, 400, and 700 μM solutions of $ZnSO_4$ and $CdCl_2$ are shown in Supplementary Figure 3. These results are used to in Stern-Volmer plots to calculate the concentrations of Zn and Cd ions released during photoirradiation.

Table 1. CdSe Concentration using UV-VIS Absorption Spectroscopy

Time	First low energy peak, (E_{1S}), Absorbance	$\Delta E_{1S,HWHM}$	Size	Molar Absorptivity	CdSe Concentration

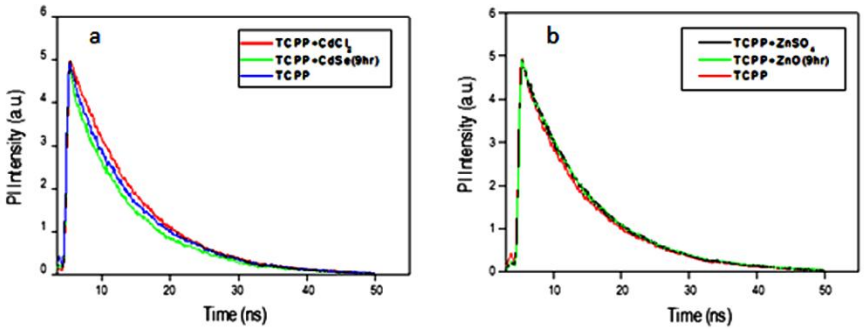
0 hours	0.0546 (520 nm, 2.384 eV)	0.26 eV	2.69nm	165740	57.06 µM
3 hours	0.0533 (519 nm, 2.389 eV)	0.256 eV	2.67 nm	165304	55.07 µM
6 hours	0.0513 (520 nm, 2.384 eV)	0.253 eV	2.69 nm	165740	52.18 µM
9 hours	0.0535 (518.5 nm, 2.39 eV)	0.254 eV	2.67 nm	165092	54.95 µM



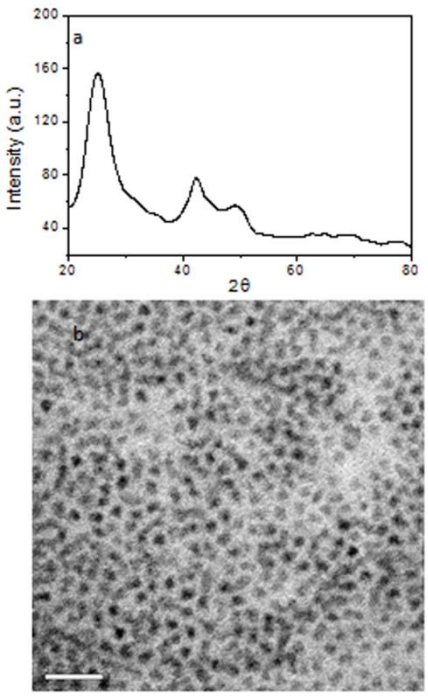
Supplementary Figure 3. Fluorescence quenching of TCPP after the addition of (A-C) 100, 400, and 700 uM solutions of $ZnSO_4$ and (D-F) 100, 400, 700 uM solutions of $CdCl_2$.

Fluorescence Lifetime of TCPP, TCPP-Cd and TCPP-Zn complexes

Fluorescence lifetime measurements are recorded of TCPP before and after addition of cadmium or zinc ions from $CdCl_2$ and $ZnSO_4$ or from photoirradiated CdSe and ZnO.



Supplementary Figure 4. Fluorescence lifetime measurements of TCPP after addition of A.) Cd ions from $CdCl_2$ or photoetched CdSe (9hrs) or B.) Zn ions from $ZnSO_4$ or photoetched ZnO (9hrs).



Supplementary Figure 5. (A) XRD data and (B) TEM image of QDs.