Supporting Information:

Experimental Methods

Quantum Dot Synthesis

CdSe nanocrystals were synthesized[18] and water-solubilized with mercaptoacetic acid (MAA)[1] as previously described. Briefly, CdSe nanocrystals were synthesized by rapid injection of a precursor $Cd(CH_3)_2$/Se solution into high temperature TOPO solvent. The size of the particles was controlled by manipulating the TOPO impurities and the Oswald ripening process. The temperature was lowered to 70°C, methanol was added to precipitate the QDs, and then centrifuged. Excess TOPO was soluble in the methanol and was removed during the decantation process. These QDs were readily redissolved in chloroform. Finally, excess MAA was added to chloroform-soluble QDs to yield water-soluble particles for cellular studies.

Quantum Dot Surface Coating

ZnS. To increase the quantum yield and protect the CdSe surface, a capping layer of 1-2 monolayers of ZnS was deposited by the slow addition of a $Zn(CH_3CH_2)_2$/S solution at a temperature lower than for the synthesis of CdSe (270°C vs 360°C)[14,16,17]. After the final of addition of the $Zn(CH_3CH_2)_2$/S solution, the temperature was lowered, methanol was added, and the QDs redissolved in chloroform. The ZnS/CdSe QDs were water-solubilized with MAA.

Bovine Serum Albumin (BSA) coating. 1 mg/mL MAA-QDs were added to a 5% BSA solution in PBS. 50mM of 1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide-hydorchloride (EDAC)(Sigma) was added to cross-link the BSA with the QDs, via the formation of a peptide bond. Since this reaction is non-specific, BSA proteins are also cross-linked to each other on the surface of the QD. This forms a highly stable protein-shell on the surface of the particle. These QDs are single, as observed by their intermittent on/off behavior on an epifluorescence

microscope under Hg-lamp excitation. After conjugation, ultracentrifugation (45k RPM) was used to remove excess BSA from solution. Pelleted QDs were redissolved in small amounts of PBS.

Epidermal Growth Factor (EGF) coating. The procedure described in Akerman and coworkers was utilized to coat ZnS-capped CdSe with polyethylene glycol and EGF[6].

QD Processing and Characterization

TOPO oxidation of QD surface. Organic-soluble QDs were dissolved in tri-n-octylphosphine oxide (TOPO, Alfa Aesar) (heated to 60-70 °C to liquefy the TOPO) and exposed to air for 30 minutes, 2.5 hours and 12 hours. The oxidized QDs were then water-solubilized with MAA (as above).

Ultraviolet Exposure. Solutions of QDs in PBS were placed under a 100W longwave (365 nm) UV lamp (UVP) at a distance of approximately 10 cm for 1, 2, 4, and 8 hours. The spherical irradiation was 15mW/cm^2 as determined with a radiometer (Cole-Parmer). For CdSe and ZnS/CdSe, the QDs precipitated between 2 and 4 hours of UV exposure, due to photo-catalyzed disulfide bond formation and subsequent loss of MAA ligands. BSA coated QDs remained soluble after 8 hours of UV exposure.

Spectroscopy. Absorbance measurements were made with a SpectraMax Plus spectrophotometer (Molecular Devices). A PerkinElmer LS45 luminescence spectrometer was used for fluorescence measurements.

QD solution images. A 1.3 megapixel digital camera (Olympus) was used to capture the white light and UV light images in Figure 2A.

Inductively Coupled Plasma Optical Emission Spectroscopy (ICP/OES)

5% nitric acid was added to samples of 0.25 mg/mL QDs in media to precipitate the nanoparticles, but retain the free cadmium in solution for analysis. The samples were centrifuged at 15k RPM to remove the QDs, and the solution was further diluted with nitric acid. A Perkin-Elmer Optima 3000DV was used to measure the samples and Cd standards. Calibrated emission peaks at 228.8, 214.4 and 226.5 nm were averaged.

Hepatocyte Culture and Viability

Hepatocytes were isolated from 2-3 month old adult female Lewis rats (Charles River Laboratories) by collagenase perfusion as previously described[30]. Less than one hour after isolation, $5x10^5$ cells were seeded on 35mm wells coated with collagen I purified from rat tail tendons. Cultures were conducted at 37°C in DMEM with high glucose (Invitrogen), 10% fetal bovine serum, supplemented with 0.5 U/mL insulin, 7 ng/mL glucagon, 7.5 µg/mL hydrocortisone, 10 U/mL penicillin, and 10 µg/mL streptomycin. Twenty-four hours after seeding, spent media was removed and replaced with fresh media supplemented with QDs. After an additional 24 hours, the cultures were assayed for cell viability with MTT (Methylthiazolyldiphenyl-tetrazolium bromide, Sigma). The cells were washed with sterile PBS and a solution of 1mg/mL MTT in DMEM without phenol red was added. After one hour at 37°C, the media was removed and the purple precipitate was dissolved in 50% DMSO/isopropanol. The intensity of the purple color was measured as the absorbance at 570 nm minus background at 660 nm. Viability was determined by comparison to control cultures with no exposure to QDs.

Micropatterned Hepatocyte Co-Cultures and Biochemical Function

Hepatocyte/fibroblast co-cultures were conducted as described previously[29]. Briefly, photoresist patterns were generated by spin-coating of S1818 photoresist on clean 2" glass wafers (Erie Scientific), exposure to UV light through a mask with 100 μm diameter features and 250 μm spacing, and development. Collagen I was adsorbed onto exposed glass domains, and remaining photoresist was removed by lift-off in acetone. The micropatterned collagen domains were subsequently treated with 0.05% BSA to block non-specific cell adhesion. Fresh hepatocytes were loaded with EGF-QDs by incubation in suspension for one hour at 37°C in a 62.5 μg/mL solution of red EGF-QDs in media. QD-labeled hepatocytes were seeded on micropatterned substrates in serum-free media to form micropatterned hepatocyte colonies. 3T3 Fibroblasts (ATCC) were grown in DMEM with 10% bovine calf serum. The following day, $1.5x10^6$ 3T3 cells were seeded onto the micropatterned hepatocytes in fibroblast media, thereby producing micropatterned co-cultures.

Culture media was collected daily, stored at -20°C, and assayed for albumin secretion rates, a marker of liver-specific function, by ELISA with a horse radish peroxidase reporter conjugated to an anti-rat albumin antibody (Cappel Laboratories) using O-phenylenediamine (Sigma) as the chromogen.

Microscopy

Cell cultures were observed with an inverted microscope (Nikon TE200) by phase contrast microscopy or epifluorescence. Fluorescent images were acquired at λ_{ex} = 540/25 with λ_{em} = 630/60, captured by a CCD camera (CoolSnap HQ, Roper Scientific), and processed on MetaVue software (Universal Imaging).