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SUPPORTING INFORMATION

Modular Poly(ethylene glycol) Ligands for Biocompatible Semiconductor and Gold Nanocrystals with Extended pH and Ionic Stability

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Synthesis of N_3–PEG600–N_3. Poly(ethylene glycol) (MW ~600 Da) (53.2 g, ~$8.87x10^{-2}$ mol), THF (100 mL) and methanesulfonyl chloride (23.3 g, 0.20 mol) were placed in a 500 mL round-bottom flask, purged with N_2 and cooled to ~0 °C using an ice bath. Triethylamine (30.3 mL, 0.22 mol) was added dropwise to the reaction while the mixture was stirred. The reaction mixture was gradually warmed to room temperature and stirred overnight. The mixture was then diluted with H_2O (100 mL) and $NaHCO_3$ (6.3 g, $7.5x10^{-2}$ mol) was added to basify the solution. Sodium azide (15.7 g, 0.24 mol) was added and the biphasic reaction mixture was heated to distill off the THF, and refluxed for 7 hours. After cooling, the reaction mixture was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and the solvent evaporated to obtain the crude product. Finally, the product was purified by silica gel column chromatography using 15:1(v/v) CH_2Cl_2:MeOH as the eluent (~76 % yield), which was a viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 3.62-3.71 (m), 3.39 (t, 4H, J = 5.2 Hz)

Synthesis of NH_2–PEG600–N_3. N_3–PEG600–N_3 (10.0 g, ~$1.5x10^{-2}$ mol) was diluted in 1 M HCl (25mL) in a 500mL round bottom flask, cooled to 0 °C and stirred under N_2. Triphenylphosphine (4.5 g, $1.7x10^{-2}$ mol) dissolved in ethyl acetate (125 mL) was added dropwise into the reaction. The reaction was then warmed up to room temperature, and stirred overnight. The biphasic mixture was separated to retain the aqueous layer and discard the ethyl acetate. The aqueous layer, which contains the product, was washed with ethyl acetate to remove a fast moving by-product (as shown by TLC). Then, the aqueous layer was basified with KOH (10 g, 0.11 mol) and extracted with ethyl

acetate. The later ethyl acetate layers were dried over Na_2SO_4 and the solvent evaporated to obtain the product (~74 % yield) , which was a viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 3.59-3.70 (m), 3.51 (t, 2H, *J* = 5.2 Hz), 3.39(t, 2H, *J* = 5.2 Hz), 2.87 (t, 2H, *J* = 5.2 Hz)

Synthesis of TA–PEG600–N_3. NH_2–PEG600–N_3 (6.73 g, $1.08x10^{-2}$ mol), 4-(*N*,*N*-dimethylamino) pyridine (0.41 g, $2.39x10^{-3}$ mol), *N*,*N*'-dicyclohexylcarbodiimide (1.65 g, $1.14x10^{-2}$ mol) and 100mL CH_2Cl_2 were placed in a 250 mL round-bottom flask, and stirred under N_2 at 0 °C using an ice bath. Thioctic acid (2.34 g, $1.13x10^{-2}$ mol) was mixed with 30 mL of CH_2Cl_2 and added into the reaction dropwise. The reaction was stirred for 2 hours at 0 °C, warmed up to room temperature, and stirred overnight. The mixture was filtered through celite, rinsed with ethyl acetate, and the solvent was evaporated from the filtrate. After evaporating the solvent, the crude product was chromatographed on silica gel with CH_2Cl_2 as the eluent to remove a fast moving by-product. Following the removal of the fast moving band, the eluent was changed to 20:1(v/v) CH_2Cl_2:MeOH to obtain the product (~93 % yield) , which is a yellow viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 6.22 (s, 1H), 3.62-3.71 (m), 3.55 (m, 4H), 3.46 (t, 4H, *J* = 5.2 Hz), 3.40 (t, 4H, *J* = 5.0 Hz), 3.08-3.22 (m, 2H), 2.42-2.52 (m, 1H), 2.20 (t, 2H, *J* = 7.2 Hz), 1.86-1.96 (m, 1H), 1.59-1.78 (m, 4H), 1.40-1.55 (m, 2H)

Synthesis of TA–PEG600–NH_2. TA–PEG600–N_3 (5.0 g, $6.16x10^{-3}$ mol) was dissolved in THF (60 mL) in a 250 mL round bottom flask and stirred under N_2. Triphenylphosphine (3.15 g, $1.2x10^{-2}$ mol) was added at room temperature under N_2. After 30 minutes of stirring, H_2O (3 mL, 0.16 mol) was added and the reaction was stirred overnight. The solvent was evaporated using a rotorvap, and the contents transferred into a separatory funnel. A mixture of 1 M HCl (70 mL) and ethyl acetate (50 mL) was added into the separatory funnel. The organic layer was separated and the aqueous layer was washed with ethyl acetate several more times. Na_2CO_3 was added until the aqueous layer was basified, then the product was extracted with CH_2Cl_2 and dried over Na_2SO_4. The product obtained by extraction is sufficiently pure as determined by NMR, but further purification can be done by column chromatography using 5:1 (v/v) CH_2Cl_2:MeOH (~85 % yield). The product obtained in this reaction was also yellow viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 6.22 (br s, 1H), 3.58-3.70 (m), 3.56 (t, 2H, *J* = 4.8 Hz), 3.45 (m, 2H), 3.08-3.22 (m, 2H),

2.94 (t, 2H, *J* = 5.2 Hz), 2.42-2.52 (m, 1H), 2.19 (t, 2H, *J* = 7.2 Hz), 1.86-1.96 (m, 1H), 1.59-1.78 (m, 4H), 1.40-1.55 (m, 2H)

Synthesis of TA–PEG600–COOH. TA–PEG600–NH_2 (1.06 g, ~1.36x10^{-3} mol), succinic anhydride (0.273 g, 2.73 x10^{-3} mol), CH_2Cl_2 (10 mL) and triethylamine (0.38 mL, 2.7 x10^{-3} mol) were stirred overnight at room temperature under N_2. The reaction mixture was then diluted with 1 M HCl solution (60 mL) and the product was extracted with CH_2Cl_2. The organic layers were combined, filtered, and the solvent was evaporated to obtain the product (~85 % yield), which was a yellow viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 6.75-6.95 (br s, 1H), 6.1-6.3 (br s, 1H), 3.58-3.70 (m), 3.56 (t, 4H, *J* = 4.8 Hz), 3.45 (m, 4H), 3.08-3.22 (m, 2H), 2.67 (m, 2H), 2.55 (m, 2H), 2.42-2.52 (m, 1H), 2.20 (t, 2H, *J* = 7.2 Hz), 1.86-1.96 (m, 1H), 1.59-1.78 (m, 4H), 1.40-1.55 (m, 2H)

Synthesis of DHLA-PEG600-NH_2 (5). TA–PEG600–NH_2 (0.58 g, 7.4x10^{-4} mol), and ethanol (10 mL) was stirred under N_2 and cooled to ~0 °C using an ice bath. $NaBH_4$ (8.4x10^{-2} g, 2.2x10^{-3} mol) was dissolved in H_2O (5 mL) and added dropwise into the reaction. It was stirred for 2 hours, warmed up to room temperature, and stirred overnight. The ethanol was evaporated from the reaction mixture. The mixture was then diluted with brine (10 mL) and extracted with CH_2Cl_2. The organic layers were dried over Na_2SO_4 to obtain the product (~93 % yield), which was a colorless viscous oil at room temperature. ^{1}H NMR (400 MHz, in $CDCl_3$): δ 6.35-6.45 (br s, 1H), 3.58-3.70 (m), 3.56 (t, 2H, *J* = 4.8 Hz), 3.51 (t, 2H, *J* = 4.8 Hz), 3.46 (m, 2H), 2.92 (m, 1H), 2.85 (t, 1H, *J* = 5.2 Hz), 2.62-2.78 (m, 2H), 2.20 (t, 2H, *J* = 7.6 Hz), 1.86-1.96 (m, 1H), 1.59-1.78 (m, 4H), 1.40-1.55 (m, 2H)

Synthesis of DHLA-PEG600-COOH (6). TA–PEG600–COOH (1.75 g, 2.22x10^{-3} mol), ethanol (20 mL) and H_2O (5 mL) was stirred under N_2 and cooled to ~0 °C using an ice bath. $NaBH_4$ (0.35 g, 9.25x10^{-3} mol) was dissolved in H_2O (7 mL) and added dropwise into the reaction. It was stirred for 2 hours, warmed up to room temperature, and stirred overnight. The ethanol was evaporated from the reaction mixture, which was then acidified to pH~2 using a 1 M HCl solution, and extracted with CH_2Cl_2. The organic layers were dried over Na_2SO_4 and the solvent evaporated to obtain the desired product (~95 % yield), which was a colorless viscous oil at room temperature. ^{1}H

NMR (400 MHz, in $CDCl_3$): δ 6.75-6.95 (br s, 1H), 6.1-6.3 (br s, 1H), 3.58-3.70 (m), 3.54 (m, 4H), 3.45 (m, 4H), 2.92 (m, 1H), 2.62-2.79 (m, 4H), 2.55 (m, 2H), 2.20 (t, 2H, J = 7.4 Hz), 1.86-1.96 (m, 1H), 1.40-1.80 (m, 7H), 1.36 (t, 1H, J = 8.0 Hz), 1.31 (d, 1H, J = 7.6 Hz)

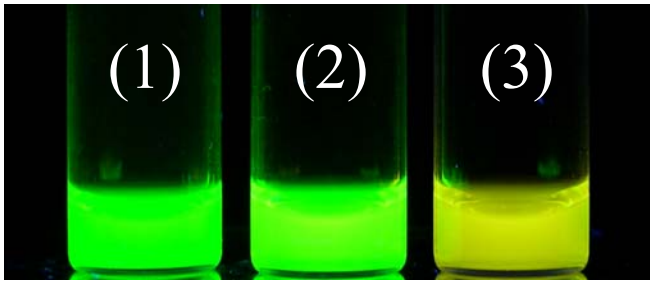

Figure S1: Luminescence of DHLA-PEG-OCH_3 cap-exchanged CdSe/ZnS QDs in DI water excited with a hand-held UV lamp at 365nm. (1) DHLA-PEG550-OCH_3-552QDs (2) DHLA-PEG750-OCH_3-552QDs (3) DHLA-PEG750-OCH_3-*578QDs*

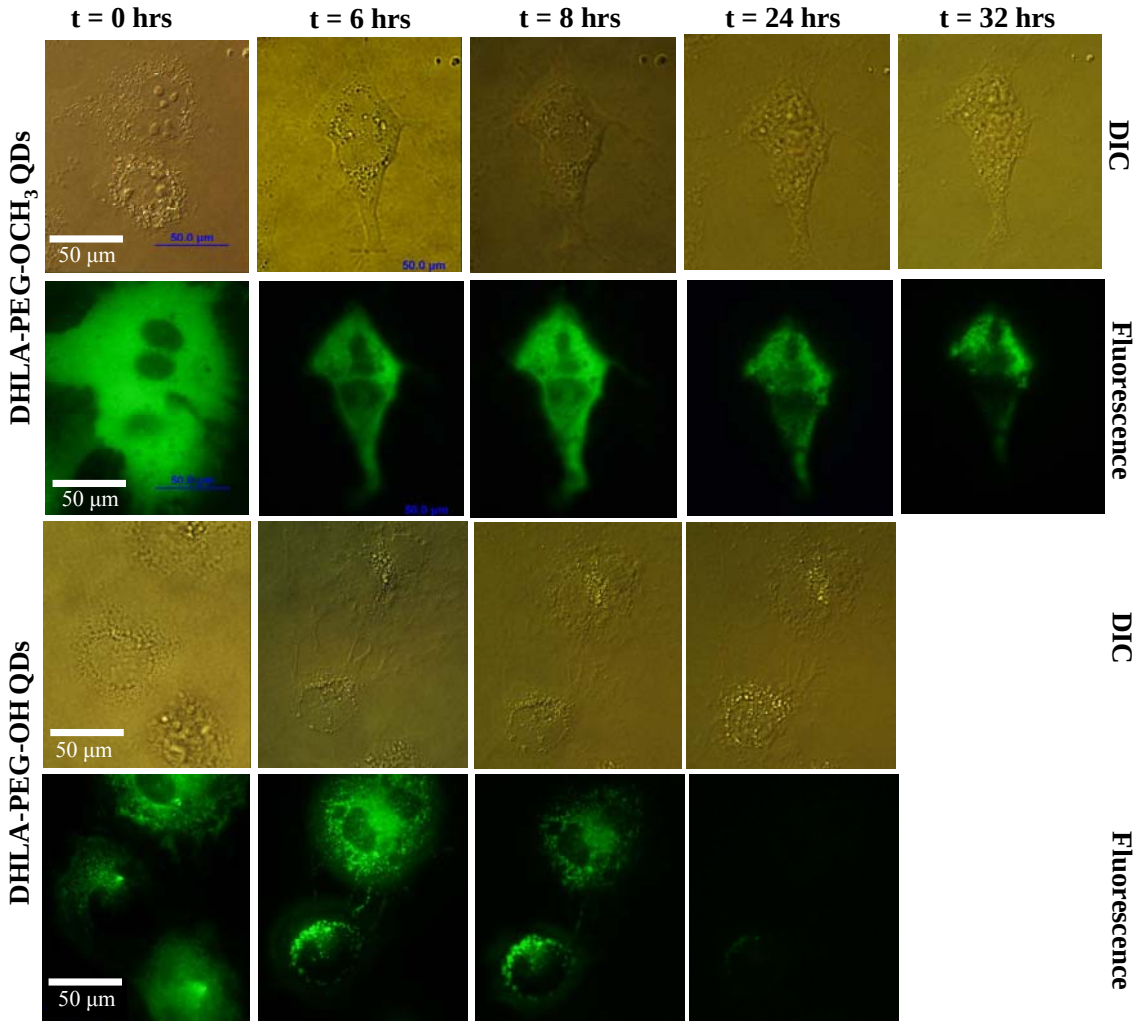

Figure S2: Additional micrographs of COS-1 cells injected with 552 nm emitting QDs capped with DHLA-PEG750-OCH_3 (top) and DHLA-PEG600-OH (bottom) and monitored over 32 hours after microinjection. Following microinjection, cells were stored at 37 ˚C in Ringer's solution. Images of the DHLA-PEG600-OH injected cells were not taken at t = 32 hours, because the QD emission has faded.