Supporting Information

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SI Methods: Polymer Synthesis

Carboxylated PDLLA (PDLLA-COOH) Synthesis. LA and HDA were purified by recrystallization from ethyl acetate and toluene, respectively. After placing 5 g (34.7 mmol) of D,L-lactide and 180 mg (1 mmol) of HDA in two-necked rbf connected with Dean stark and reflux condenser, 80 ml of anhydrous toluene was added. By heating the flask at 110°C, 30 ml toluene containing little water could be removed. $Sn(Oct)_2$ (5 mg) dissolved in anhydrous toluene was added and the temperature was elevated up to 130°C, which removed another 30 ml toluene. The reaction was carried out for 24 h. After removing toluene, the product was dissolved in dichloromethane (DCM) (25 ml) and precipitated against excess *n*-hexane twice. White powder of PDLLA-COOH was obtained by vacuum drying with P_2O_5 for 2 days. The number average molecular weight (Mn = 5,000) was determined by ^{1}H-NMR.

MPEG-PDLLA Synthesis. To prepare various diblock copolymers with an identical PDLLA block, MPEG-PDLLA was synthesized by coupling between α-amino-methoxy PEG (MPEG-NH_2, MW 5000) and PDLLA-COOH. After dissolving 0.5 g (0.1 mmol) of MPEG-NH_2, 0.5 g (0.1 mmol) of PDLLA-COOH, 25 mg (0.12 mmol) of DCC, 11.5 mg (0.1 mmol) of NHS, and 25 μl of TEA in 20 ml of DCM, the reaction was performed at room temperature for 2 days. The reaction was stopped by one drop of water. Impurities were removed by filtration, and the filtrate was precipitated against excess diethyl ether twice. After drying under vacuum with P_2O_5 for 2 days, white powder of MPEG-PDLLA (5,000:5,000) was vacuum-sealed with silica gel and stored at −70°C for further experiment.

FITC-PEG-PDLLA Synthesis. After dissolving 0.4 g (0.067 mmol) of H_2N-PEG-NH_2 (MW 6,000), 50 μl of TEA, and 5 μl of DBDL in 5 ml of anhydrous dimethyl sulfoxide (DMSO) and 30 mg (0.077 mmol) of FITC in 1 ml of anhydrous DMSO, two solutions were mixed. Reaction was carried out at 80°C for 4 h. The reaction mixture was cooled down to room temperature and directly poured into a dialysis bag (MWCO 3500, Spectra/Por RC). DMSO and unreacted FITC were removed against excess deionized water for 2 days. FITC-PEG-NH_2 was purified by cation exchange column chromatography (CM Sephadex G-25, 1.5 × 30 cm column). Elution was performed with a linear NaCl gradient from 0 to 1 M (citrate buffer, pH 5.0). Fractions were collected, concentrated, and dialyzed against deionized water for 2 days. Yellow-orange powder was obtained by lyophilization. FITC-PEG-PDLLA (6,000:5,000) was then synthesized with FITC-PEG-NH_2 and PDLLA-COOH by the same method as for the MPEG-PDLLA synthesis.

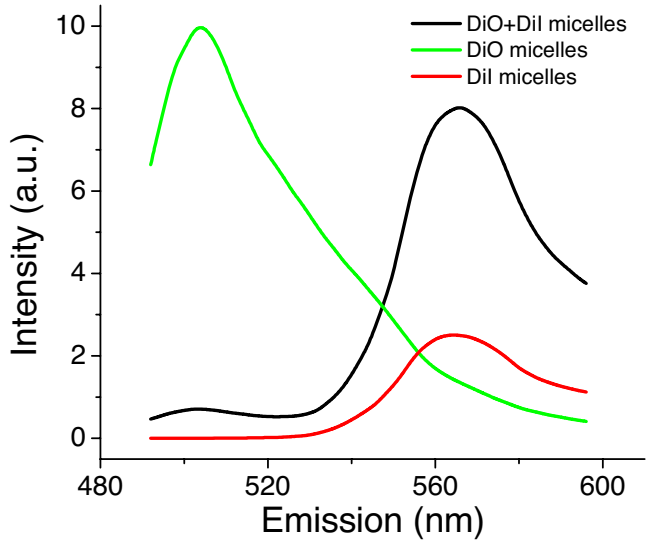

Fig. S1. Fluorescence spectra of FRET micelles (0.75% DiI and 0.75% DiO, black curve), 0.75% DiO micelles (green curve), and 0.75% DiI micelles (red curve) with 484-nm excitation.

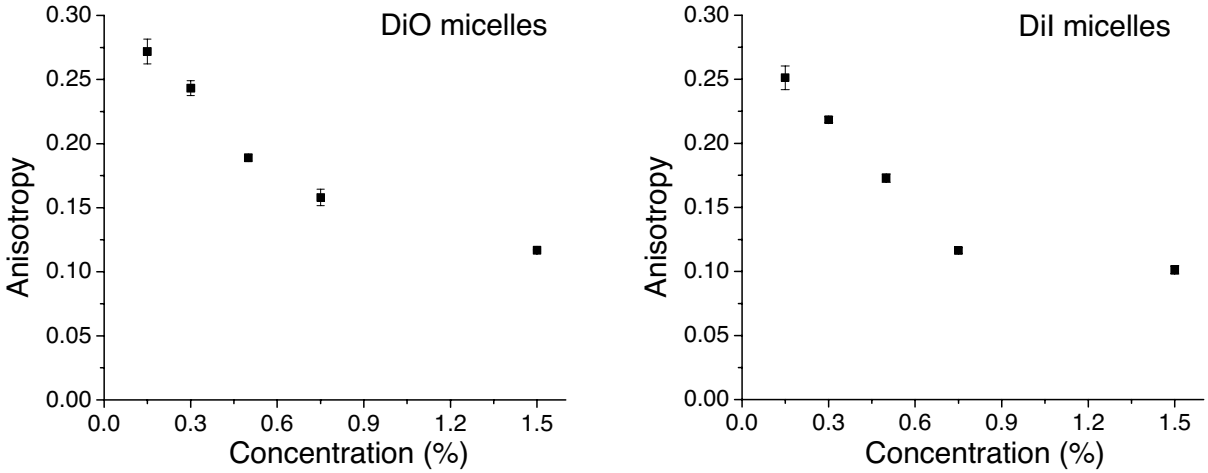

Fig. S2. Concentration-dependent homo-FRET between DiO or DiI detected by anisotropy measurement of DiO or DiI fluorescence. 0.15%, 0.3%, 0.5%, 0.75%, and 1.5% DiO or DiI were loaded into PEG-PDLLA micelles. Micelles were diluted 10 times by water for anisotropy measurement.

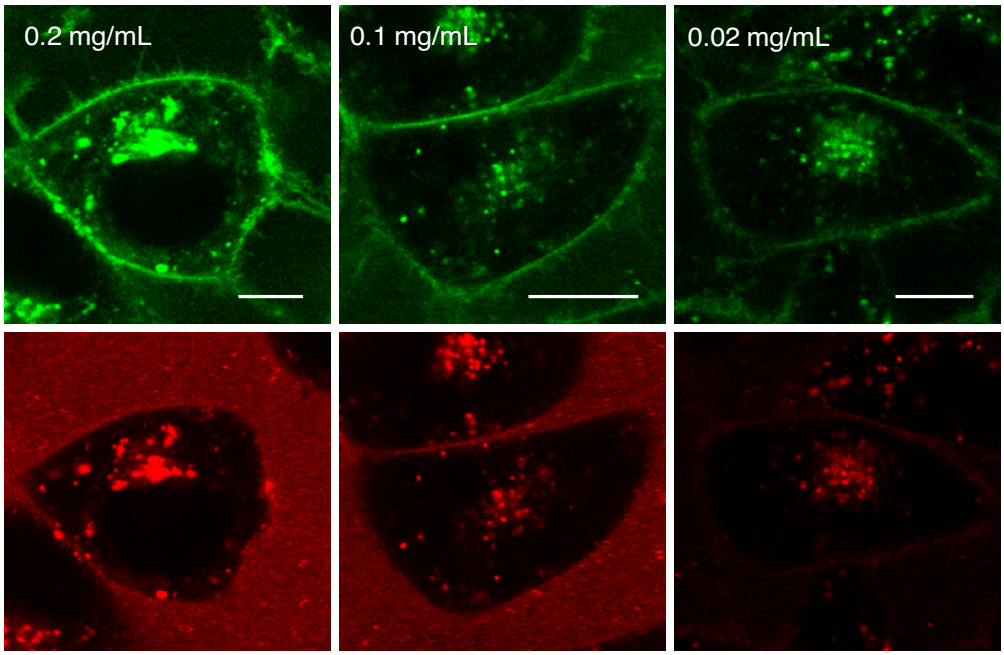

Fig. S3. DiO (green) and DiI (red) were released from micelles to cell membrane in KB cells incubated with 0.2, 0.1, and 0.02 mg/ml FRET micelles. Images were acquired at 2 h. (Scale bars: 10 μm.) The excitation wavelength was 488 nm.

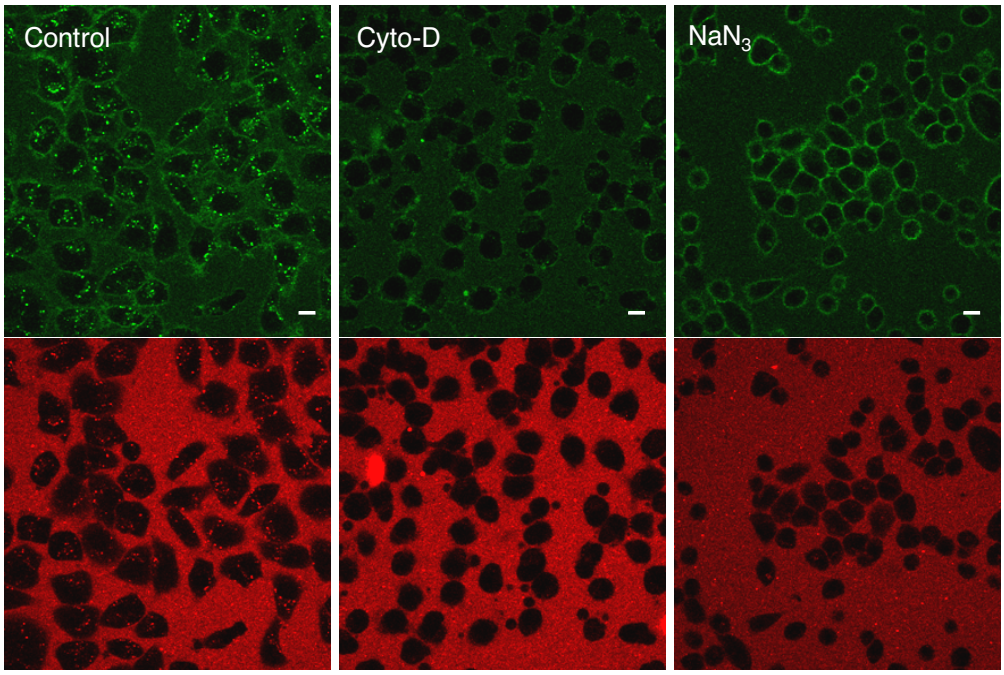

Fig. S4. Inhibition of endocytosis did not block the transfer of core-loaded molecules to plasma membrane but stopped their internalization into cells. KB cells were pretreated with either 10 μM cytochalasin D (Cyto-D) for 30 min at 37°C to inhibit the activity of actin microfilaments or 0.1% NaN_3 for 1 h at 4°C for energy depletion. The cells were then incubated with 0.2 mg/ml FRET micelles for 30 min at 37°C before imaging. The same experiment was carried out on normal KB cells as control. The excitation wavelength was 488 nm. Green and red represent the signal from DiO and DiI, respectively. (Scale bars: 10 μm.)

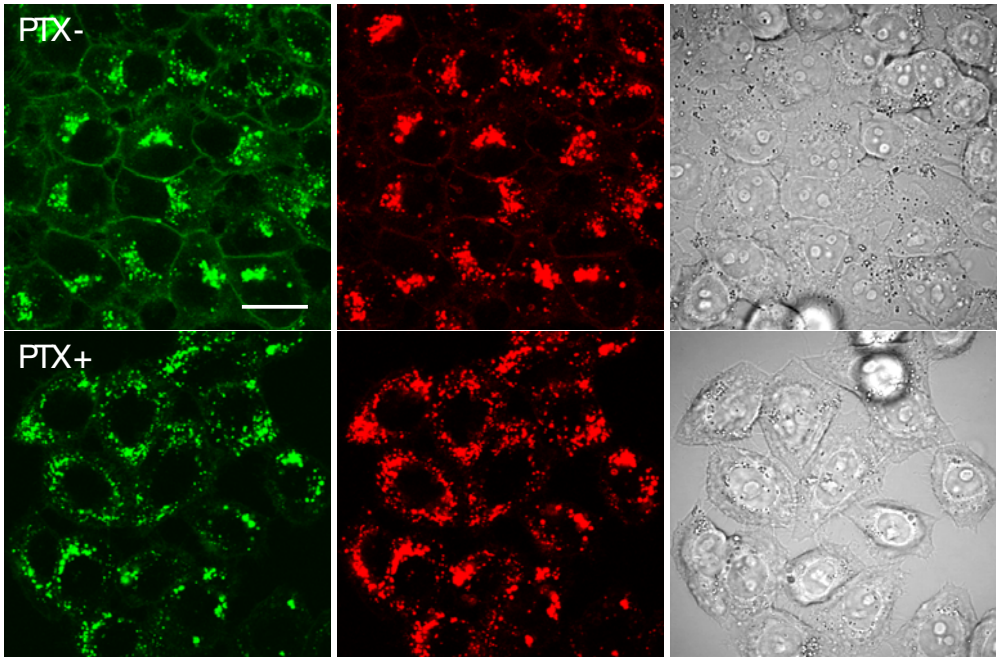

Fig. S5. Distributions of DiI-containing (red) and DiO-containing (green) endosomes in KB cells treated with FRET micelles and PTX-loaded FRET micelles for 2 h. (Scale bar: 20 μm.) The excitation wavelength was 488 nm. Transmission images of KB cells are provided in gray. In all KB cells treated with PTX-loaded FRET micelles, fluorescent endosomes were scattered into the whole cytosol, in contrast to the perinuclear accumulation in cells treated with FRET micelles.

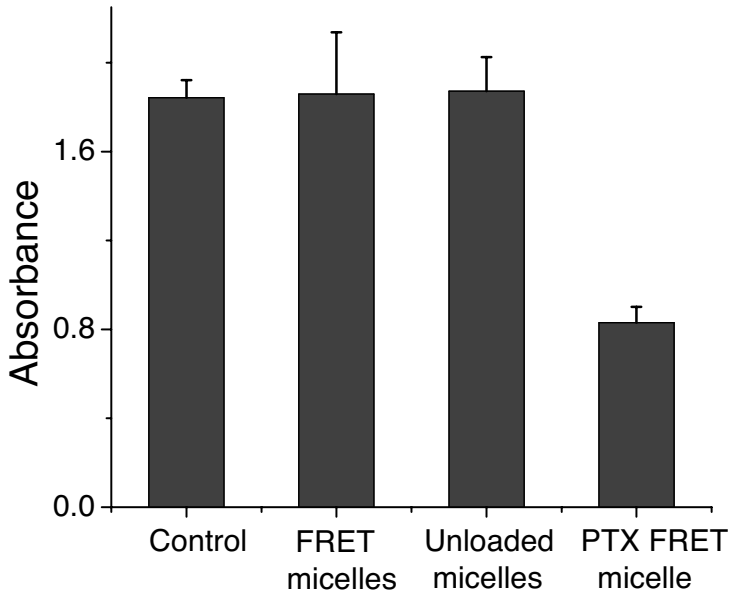

Fig. S6. MTT assay showed no cytotoxicity of FRET micelles and unloaded micelles, and high cytotoxicity of PTX-loaded FRET micelles. KB cells were treated with 100 μl of different micelles for 2 h at 0.2 mg/ml polymer concentration. Control KB cells were treated with 100 μl of deionized water for 2 h. After a 24-h incubation, the MTT assay was preformed to evaluate the cytotoxicity. Absorbance was measured at 540 nm by following the manufacturer's guide.