Supplementary Information

Synthesis of Phenylboronic Ester-linked PEG-lipid Conjugate for ROS-responsive drug delivery

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**Synthesis of mPEG<sub>2k</sub>-COOH.** To a solution of PEG<sub>2000</sub> (20.0 g, 10 mmol) and succinic anhydride (5 g, 50 mmol) in 120 mL of methylene dichloride was added DMAP (0.244 g, 2 mmol). The reaction mixture was allowed to stir at room temperature for 48 h. Subsequently, the mixture was concentrated by rotary evaporation and precipitated into excess cold ethyl ether. The white solid was obtained after filtration and dried under reduced pressure. Yield 18.16 g (86.5%). The structure of mPEG<sub>2k</sub>-COOH was characterized by <sup>1</sup>H NMR (300 MHz). The <sup>1</sup>H NMR confirmed the successful synthesis of mPEG<sub>2k</sub>-COOH (Figure 1a).

**Synthesis of propargyl isocyanoacetamide.** A mixture of propargylamine (2.43 g, 44 mmol) and isocyanoacetic acid ethyl ester (4.98 g, 44 mmol) was stirred at room temperature overnight. The reaction mixture was dissolved in THF and precipitated in n-hexane for three times. The product was dried under vacuum overnight to give propargyl isocyanoacetamide (4.7 g, 87%). The structure of propargyl isocyanoacetamide was characterized by <sup>1</sup>H NMR (300 MHz) and <sup>13</sup>C NMR (300 MHz). The <sup>1</sup>H NMR and <sup>13</sup>C NMR confirmed the successful synthesis of propargyl isocyanoacetamide (Figure S1).

**Synthesis of 3-azido-1,2-propanediol.** 3-chloro-1,2-propanediol (6.61 g, 59.8 mmol), sodium azide (6.2 g, 99.9 mmol) and water (25 mL) were added to a 100 mL flask. The mixture was stirred at 80 °C for 48 h. After cooling to room temperature, 50 mL of saturated NaCl aqueous solution was added. The mixture was then extracted with dichloromethane (3 × 80 mL), and wash twice using saturated NaCl aqueous solution. The organic mixture was dried over anhydrous sodium sulfate overnight and concentrated on a rotary evaporator. The obtained residues were dried under vacuum overnight to give colorless oil in 85% yield (Figure S5).

**Synthesis of 3-azido-1,2-propanediol distearate (N<sub>3</sub>-DSA).** A mixture of 3-azido-1,2-propanediol (1.5 g, 12.8 mmol), stearic acid (9.09 g, 30 mol), DMAP (2.44 g, 20 mmol) and DEC·HCl (7.68 g, 40 mmol) in 200 mL of dichloromethane were placed in a round-bottom flask. The reaction mixture was allowed to stir at room temperature for 48 h. Then the solution was sequentially washed with saturated NaCl aqueous solution, dilute hydrochloric acid, and saturated NaCl aqueous solution. The organic mixture was dried over anhydrous magnesium sulfate overnight and concentrated on a rotary evaporator. Then the excess stearic acid was removed by passing through an alkaline Al<sub>2</sub>O<sub>3</sub> column. The obtained residues were dried under vacuum overnight to give white solid in 44.5% yield (Figure S6).

**CMC of mPEG<sub>2k</sub>-PBPE-SA.** Fluorescence spectra were recorded on Photon Technology International (PTI) Fluorescence Master System with Felix 4.1.0 software using pyrene as a probe at room temperature. The final concentration of pyrene in different mPEG<sub>2k</sub>-PBPE-SA micelle solutions (1.65 × 10<sup>-6</sup> to 0.29 mg mL<sup>-1</sup>) was 1.0 × 10<sup>-6</sup> mol L<sup>-1</sup>. The excitation spectra were cored from 280 to 360 nm and the emission wavelength at 393 nm was applied for the measurements.
Figure S1. (a) $^1$H NMR and (b) $^{13}$C NMR spectrum of propargyl isocyanoacetamide in DMDO-$d_6$. 
Figure S2. MALDI-TOF MS of mPEG$_{2k}$-PBPE-alkynyl.

mPEG$_{2k}$-PBPE-alkynyl

$M_n=2436$, $\mathcal{D}=1.005$

Figure S3. MALDI-TOF MS of mPEG$_{2k}$-COOH.

mPEG$_{2k}$-COOH

$M_n=2073$, $\mathcal{D}=1.005$
Figure S4. In situ $^1$H NMR spectra of mPEG$_{2k}$-PBPE-alkynyl oxidized by H$_2$O$_2$ in D$_2$O, with the H$_2$O$_2$/PBPE molar ratio of (a) 5: 1 ([H$_2$O$_2$]/[PBPE] = 5.0) (b) 10: 1 ([H$_2$O$_2$]/[PBPE] = 10.0) (c) 20 : 1 ([H$_2$O$_2$]/[PBPE] = 20.0) (d) without H$_2$O$_2$. 
Figure S5. $^1$H NMR spectrum of 3-azido-1,2-propanediol in D$_2$O.

Figure S6. $^1$H NMR spectrum of N$_3$-DSA in CDCl$_3$. 
Figure S7. FTIR spectra of mPEG$_{2k}$-PBPE-alkynyl, N$_3$-DSA and mPEG$_{2k}$-PBPE-DSA.

Figure S8. CMC of mPEG$_{2k}$-PBPE-DSA micelles.
Figure S9. DLS size profiles of mPEG<sub>2k</sub>-PBPE-DSA NPs in (a) normal saline solution and (b) aqueous medium containing 10% fetal bovine serum at 37 °C.

Figure S10. DLS size profiles for various concentrations of mPEG<sub>2k</sub>-PBPE-DSA NPs, which were prepared by series dilution of mPEG<sub>2k</sub>-PBPE-DSA NPs solution from the concentration of 0.20 mg mL<sup>-1</sup>. The diluted solutions were aged for 24 h before DLS characterization.