Supporting Information

Smart Conjugated Polymer Nanocarrier for Healthy Weight Loss by Negative-Feedback Regulation of Lipase Activity

*Yu-Lei Chen, Sha Zhu, Lei Zhang, Pei-Jian Feng, Xi-Kuang Yao, Cheng-Gen Qian, Can Zhang, Xi-Qun Jiang, and Qun-Dong Shen**

General materials and methods: All chemicals were purchased from Sigma-Aldrich unless otherwise specified. 2,7-Dibromo-9,9-bis(3'-((N,N-dimethyl)-N-ethylammonium) propyl) fluorene was purchased from Hanhong Chemical Co. (Shanghai, China). 2,7-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9,9-bis(6-bromohexyl)fluorene was purchased from Synwit Technology Co., Ltd. (Beijing, China). 5,7-Bis(5-bromo-2-thienyl)-2,3-dimethyl-thieno[3,4-b]pyrazine was purchased from Beijing Allmers Chemical S&T Co. Ltd. (Beijing, China). All organic solvents were purchased from Nanjing Chemical Works. Dulbecco's modified Eagles medium (DMEM, Gibco, USA) and fetal bovine serum (FBS) were purchased from Pufei Biotechnology Co., Ltd. (Nanjing, China) Trypsin, penicillin, streptomycin, non-essential amino acids (NEAA) and phosphate buffered saline (PBS) were from Hyclone (Waltham, USA). BCA Protein Assay Kit was from Beyotime Institute of Biotechnology. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) was purchased from the Sunshine Biotechnology Co., Ltd. (Nanjing).

^{1}H-NMR spectra were collected on a DRX-500 spectrometer. The molecular weight and molecular weight distribution were determined by gel permeation chromatography (GPC) using Waters 244 (Milford, MA, USA) with 0.03M LiBr-contained DMF as eluent.

Synthesis of BTTPF-Br: 2,7-Dibromo-9,9-bis(3'-((N,N-dimethyl)-N-ethylammonium) propyl) fluorene (0.0856 g), 2,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9,9-bis(6-bromo-hexyl)fluorene (0.1488 g), 5,7-bis(5-bromo-2-thienyl)-2,3-dimethyl-thieno[3,4-b]pyrazine (0.0402 g), and tetrakis-(triphenyl phosphine) palladium (0) (0.05 g) were dissolved in a degassed mixture of 40 mL of 2 mol/L K_2CO_3 aqueous solution and 40 mL of N,N-dimethylformamide. The mixture was stirred at 90 ^{o}C for 48 h under argon atmosphere. After cooling down to room temperature, the mixture was poured into 500 mL of acetone. The precipitate was collected by centrifugation, and then dissolved and dialyzed in distilled water

using a membrane with a cutoff molecular weight of 8000-14000 g/mol for 3 days. The precipitation was removed after centrifugation. The final product was gathered by rotary evaporation to afford 60.5 mg black powder. ^{1}H NMR (500 MHz, DMSO-d_6, ppm) 7.0-8.1 (m, Ar-H), 3.2-2.8 (m, $BrCH_2$, N-CH_3, N-CH_2, N=C-CH_3), 2.4-2.1 (m, $ArCH_2$), 1.2-0.7 (m, -CH_2-C**H**$_2$-CH_2-, CH_2-C**H**$_3$)

Synthesis of BTTPFN-OH: BTTPF-Br (0.0428 g) and diethanolamine (0.8 mg) were dissolved in a mixture of 10 mL aqueous solution and 10 mL tetrahydrofuran. The mixture was stirred at 25 ^{o}C for 48 h under argon atmosphere. The mixture was then dialyzed against distilled water for 3 days using a membrane with a cutoff molecular weight of 8000-14000 g/mol. Then the solvent was removed and the residue was vacuum dried overnight to yield BTTPF-OH. ^{1}H NMR (500 MHz, DMSO-d_6, ppm) 7.0-8.3 (m, Ar-H), 3.2-2.7 (m, O-CH_2, N-CH_3, N-CH_2, N=C-CH_3), 2.4-2.1 (m, $ArCH_2$), 1.2-0.7 (m, -CH_2-C**H**$_2$-CH_2-, CH_2-C**H**$_3$)

Synthesis of BTTPFN-g-PCL: BTTPFN-OH was allowed to react with ε-caprolactone by ring-opening polymerization. Briefly, BTTPFN-g-PCL (0.0245 g), ε-caprolactone (1 mL), and stannous octoate (0.02 g) were degassed and stirred for 0.5h at room temperature. The mixture was washed by water and ethanol three times, and then was dried under vacuum overnight to obtain BTTPFN-g-PCL. ^{1}H NMR (500 MHz, DMSO-d_6): 7.0-8.2 (m, Ar-H), 4.0 (t, -O-CH_2-), 3.2-2.8 (m, N-CH_3, N-CH_2), 2.6 (s, N=C-CH_3), 2.3 (t, -CH_2-C=O), 1.5 (m, -CH_2-), 1.3 (m, -CH_2-); Mn = 193,000, PDI = 1.26.

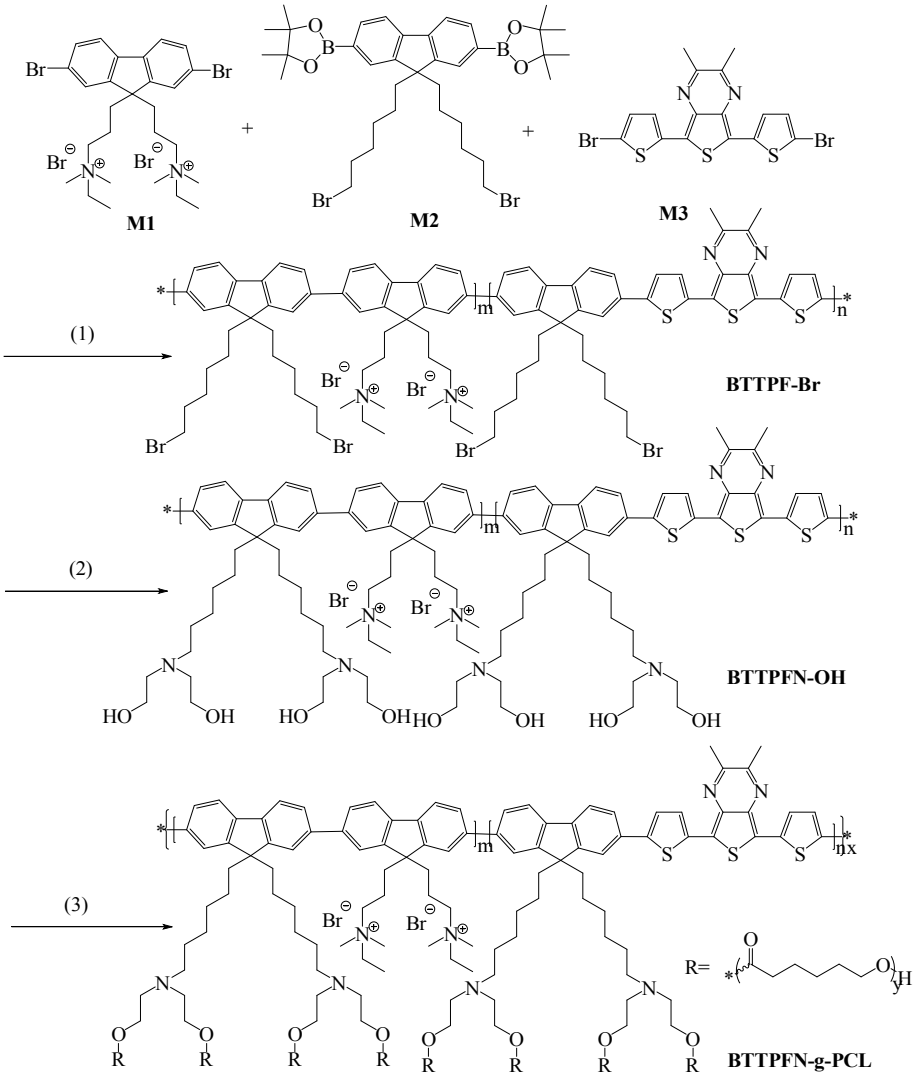

Figure S1. Synthesis procedure of BTTPFN-g-PCL.

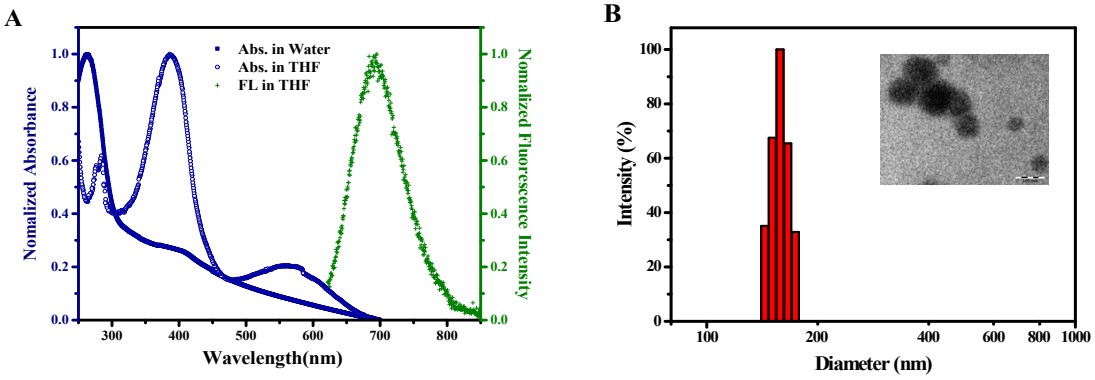

Figure S2. A) Normalized UV/Vis absorption spectra of BTTPFN-g-PCL in water and in THF and PL spectrum of BTTPFN-g-PCL in THF. B) The size distribution of the nanocarrier in water. Inset: TEM image. Scale bar, 100nm.

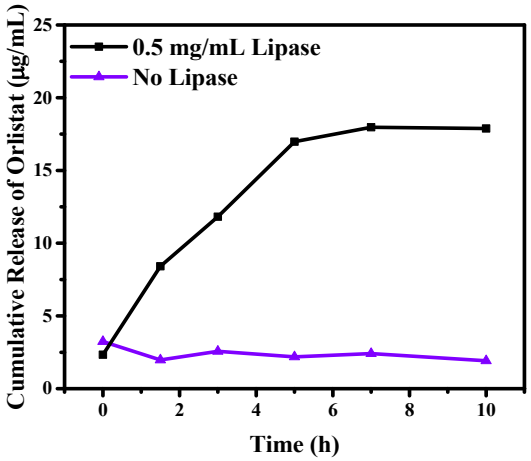

Figure S3. *In vitro* accumulated drug release of the nanocarrier in different lipase concentrations at pH=3 and 37 °C.

Table S1. Body mass index (BMI), liver weight, and fat pad weight of mice.

	Control	Free drug	Nanocarrier
BMI (g cm^{-2})	0.483 ± 0.003	0.439 ± 0.013	0.376 ± 0.025
Liver (g)	1.96 ± 0.12	1.59 ± 0.14	1.45 ± 0.14
Subcutaneous fat pad (g)	1.57 ± 0.14	0.98 ± 0.14	0.47 ± 0.08
Epididymal fat pad (g)	1.33 ± 0.10	0.95 ± 0.19	0.69 ± 0.17
Abdominal fat pad (g)	2.74 ± 0.52	1.48 ± 0.40	0.76 ± 0.04