Supporting Information

Smart Nanofibers with Photo-responsive Surface for Controlled Release

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Experimental Section

Materials

The monomers, glycidyl methacrylate (GMA, 97%) and 4-vinylbenzyl chloride (VBC, 90%), were purchased from Acros Organic Co. of Geel, Belgium. GMA and VBC were used after removal of inhibitors in a ready-to-use disposable inhibitors-removal column. *N,N*-Dicyclohexylcarbodimide (DCC), 4-dimethylaminopyridine (DMAP), and α-cyclodextrin were purchased from Aldrich Chemical Co. and were used as received. Sodium azide (99%), 5-flurouracil and chloro-acetic acid, azobisisobutyronitrile (AIBN) and other regents were purchased from Shanghai Chemical Reagent Manufacturing Co. The RAFT agent, 2-cyanoprop-2-yl-1-dithionaphthalate (CPDN), was synthesized according to procedures reported earlier [Zhu J. et. al. *Polymer*. **2002**, 43, 7037-7042]. The azobenzene, 4-propargyloxyazobenzene (PAB), was synthesized according to the procedures reported in the literature [Juan M. et. al. *Tetrahedron* **2008**, 64, 10919]. 5-Fluorouracil-1-acetic acid was prepared according to the method in the literature [Qu, J. M. et. al. *Acta Cryst.* **2006**, 62, 1504-1506].

Characterization

The chemical structures of P(VBC), PVBC-*b*-PGMA bolck copolymer and *a*-CD-5FU were characterized by ^{1}H NMR spectroscopy on a Brucker ARX 300 MHz spectrometer, using $CDCl_3$ or D_2O as the solvent in 1000 scans at a relaxation time of 2 s. Gel permeation chromatography (GPC) measurements were performed on an HP 1100 high pressure liquid chromatograph (HPLC), equipped with an HP 1047A

refractive index detector and Plgel MIXED-C 300 7.5 mm columns (packed with 5 μm gel particles). The column packing allowed the separation of polymers over a wide molecular weight range of 200-3,000,000. THF was used as the eluent at a low flow rate of 1 mL/min at 30 ^{o}C. Polystyrene standards were used as the references. Fourier transform infrared (FTIR) spectra were obtained on the MAGNA-IR 750 spectrometer of Nicolet Instrument Co. The sample was dispersed in a KBr disc. Mass spectrometry (MS) analysis was carried out on a Perkin-Elmer Sciex mass spectrometer. The absorption spectra were measured usingm a Hitachi U-4100 UV-vis spectrophotometer. Scanning electron microscopy (SEM) images were obtained from a Hitachi X-650 SEM at an accelerating voltage of 1-10 kV and object distance of 8 mm.

Synthesis of 4-propargyloxyazobenzene

An anhydrons aceton solution 30 mL of 1 g (5.044 mmol) 4-hydroxyazobenzene and 3.486 g (25.220 mmol) K_2CO_3 was stirred at room temperature for 30 min under nitrogen. Three gram (25.220 mmol) of propargyl bromide (80% w/w in toluene) was added and the mixture was stirred at 60 °C for 24 h. The solvent was removed in a rotary evaporator and the crude product was further purified by passing through a silica gel column using mixed diethyl ether/hexanes (1:1 in volume ratio) as eluent. Yield=90%; ^{1}H NMR (DMSO-d_6): 3.67(1H, ≡CH), 4.94 (2H, CH_2), 7.19-7.92 (9H, ArH). FTIR (KBr, cm^{-1}) : 3263,3070, 2921, 2858, 1600, 1581, 1496, 1238, 1142.

Synthesis of 5-fluorouracil-1-acetic acid

A mixture of 5-flurouracil (5.2 g), chloro-acetic acid (3.8 g), potassium hydroxide (4.48 g) and water (100 mL) was refluxed at 353 K for 2 h and then cooled to room temperature. After the pH of the mixture was adjusted to 2 with 2 M hydrochloric acid, the compound was obtained. (Yield=69%)

Synthesis of α-cyclodextrin-5- fluorouracil prodrug (α-CD-5Fu)

DCC (2.19 g, 10.6 mmol), DMAP (0.26 g, 2.12 mmol), and 5-fluorouracil-1-acetic acid (1 g, 5.3 mmol) were added to 20 mL of anhydrous DMF solution (0.52 g, 5.3 mmol) of α-cyclodextrin. After the mixture was stirred at 50 °C for 96 h, an excess amount of acetone was added, and the mixture was filtered. The precipitate was redissolved in anhydrous DMF, anhydrous ethanol was added, and the mixture was filtered. The process was repeated twice. The resulting solid was further purified by passing through a silica column using mixed 1-propanol/water/concentrated aqueous ammonia (10/2/1 in volume ratio) as eluent. The di- and monosubstituted α-cyclodextrin were then separated and pure disubstituted α-cyclodextrin was obtained as a colorless solid. Yield=53%; MS: $[M+Na]^+$=1162.93; FTIR (cm^{-1}) : $\nu_{(OH)}$=3438, $\nu_{(C=O)}$=1705.

Preparation of VBC polymer (PVBC) by RAFT polymerization

VBC (3 mL, 21 mmol), AIBN (20 mg, 0.12 mmol), and CPDN (0.12 g, 0.44 mmol) and 2 mL of tetrahydrofuran were introduced into a 10 mL dry glass tube. The

solution was degassed with argon for 20 min. After that, the tube was sealed and stirred at 80 °C in an oil bath for 16 h. The reaction mixture was diluted with THF, and poured into an excess volume of methanol to precipitate the polymer. After drying under reduced pressure at room temperature over night, about 2.9 g of light-red powder was obtained. (M_n=11300 g/mol, PDI=1.22)

Preparation of PVBC-*block*-poly(glycidyl methacryalte) (PVBC-*b*-PGMA) copolymer.

GMA (2 mL, 14.0 mmol), AIBN (10 mg, 0.06 mmol), and PVBC (1.4 g) were dissolved in 2.0 mL of THF in a 10 mL dry glass tube under stirring. The homogeneous solution was purged with argon for 20 min. Polymerization was carried out at 60 °C for 8 h. At the end of the polymerization, the reaction mixture was diluted with THF, and precipitated into a large volume of methanol. The block copolymer, PVBC-*b*-PGMA, was dried under the reduced pressure at room temperature for at least 24 h. About 2.8 g of the copolymer were obtained. (M_n=17900 g/mol, PDI=1.27)

Electrospinning of PVBC-*b*-PGMA

The PVBC-*b*-PGMA copolymer was dissolved in THF to concentrations of 0.15 g/mL, 0.2 g/mL, 0.25 g/mL, respectively. In an electrospinning unit, the PVBC-*b*-PGMA solution was fed at a constant rate of 1.8 mL/h to a syringe by a digitally controlled micro-pump. The tip of the syringe was connected to a high-voltage supply (Tianjing

Dongwen High Voltage Electronics, Inc.). Electrospinning was carried out at an electrical potential of 18 kV using a needle with an inner diameter of about 0.6 mm. The distance between the tip of the needle and the grounded collector was fixed at about 10 cm. The electrospinning was carried out at room temperature. The nanofibers so-obtained were dried under reduced pressure overnight.

Immobilization of the azobenzene groups on the surface of PVBC-*b*-PGMA nanofibers

About 3.0 g of NaN_3 was dissolved in 80 mL of mixed solution of dimethylformaimide (DMF) and water (1:1, v:v). About 100 mg of the PVBC-*b*-PGMA nanofibers were immersed the solution at room temperature for 48 h. The nanofibers were removed from the solution and rinsed thrice with a large amount of distilled water. After drying under reduced pressure for 24 h, nanofibers with azide groups on the surface and crosslinked structure were obtained. The azobenzene (AB) groups were immobilized on the surface of crosslinked nanofibers via the 'Click Chemistry'. 4-Propargyloxyazobenzene (1.12 g, 4.7 mmol), $CuSO_4$ (12.5 mg, 0.05 mmol), sodium ascorbate (49.5 mg, 0.25 mmol) and 20 mL of THF were introduced into a 50 mL round-bottom flask. Then, 50 mg of crosslinked nanofibers were added into the solution carefully. The reaction was carried out at room temperature for 18 h. Then, the nanofibers were removed from solution and washed with distilled water. The crosslinked functional nanofibers ($CNF_{PVBC\text{-}b\text{-}PGMA}AB$) were obtained after drying under reduced pressure.

Loading of α-CD-5Fu prodrug on the surface of $CNF_{PVBC\text{-}b\text{-}PGMA}$-AB

The *α*-CD-5FU solution was prepared by dissolving 0.104 g (0.1 mmol) of α-CD-5FU in 100 mL deionized water. Then, 40 mg of $CNF_{PVBC\text{-}b\text{-}PGMA}$-AB was added carefully. After that, the solution was stirred in the dark overnight. The nanofibers were subsequently removed from solution, washed with distilled water and dried for 24 h under vacuum. Coupling of *α*-CD-5FU to the nanofibers was confirmed by XPS.

Photo-controlled release of prodrug from α-CD-5FU loaded $CNF_{PVBC\text{-}b\text{-}PGMA}$-AB

α-CD-5FU loaded nanofibers (10 mg) were immersed directly in 20 mL of water in a Pyrex tube. The tube was equipped with a magnetic stirring bar, and irradiated at λ=365 nm under continuous stirring. During the irradiation process, the samples for the UV-absorption spectroscopy measurement were prepared by collecting 50 μl of the solution at different UV exposure periods, followed by diluting them to 1 mL using deionized water. The release of α-CD-5FU was characterized via the change of the maximum UV absorbance at 260 nm. Since the absorption strength was proportional to the concentrations of α-CD-5FU, the amount of α-CD-5FU was determined by comparing to a calibration curve recorded at 0.1 μg/mL of α-CD-5FU aqueous solution after multiplication of dilution factors.

Dissociation of *a*-CD-5FU

The dissociation of *a*-CD-5FU was carried out in 15 ml of NaOH solution of pH 8.1 for one h at about 40 ^{o}C. After that, the solution PH was adjusted to 7 by addition of HCl solution (1 mol/L). The dissociation of *a*-CD-5FU was characterized by high performance liquid chromatography (HPLC) equipped with a Hitachi-Merck L6200 intelligent pump and a Hitachi-Merck UV-detector operating at 275 nm. The composition of dissociated *a*-CD-5FU and the degree of the dissociation were determined from the retention time and area ratio of peak components.

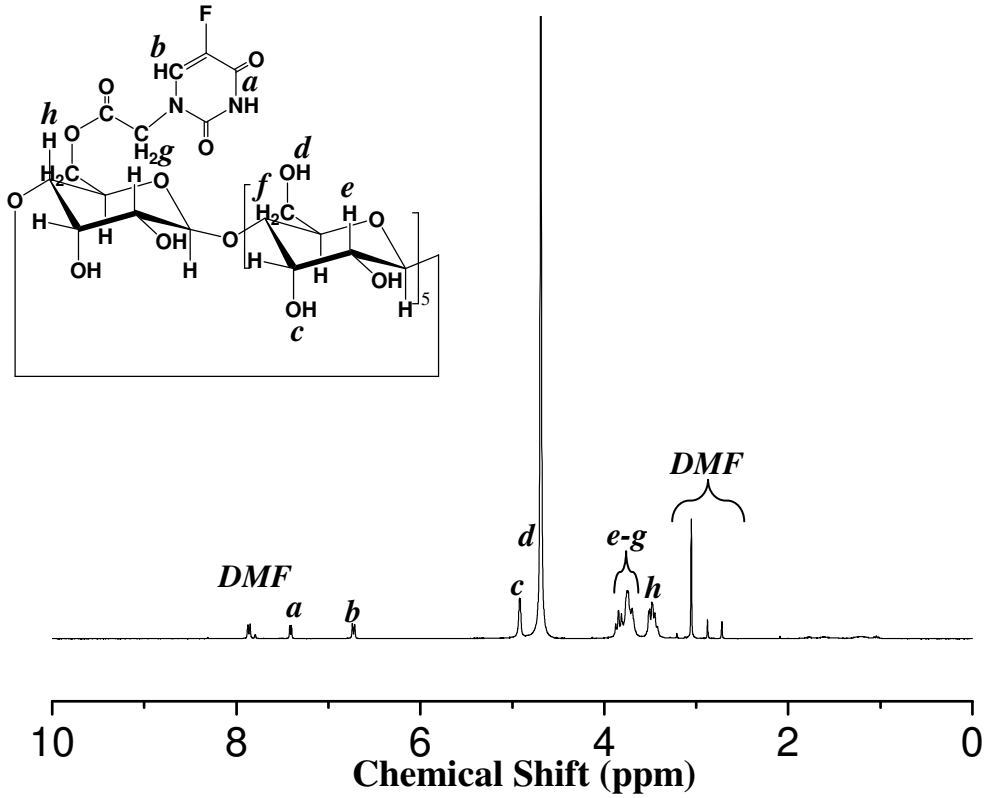

Figure S1. 300 MHz ^{1}H NMR spectra of the α-cyclodextrin-5-fluorouracil (*α*-CD-5FU) conjugate

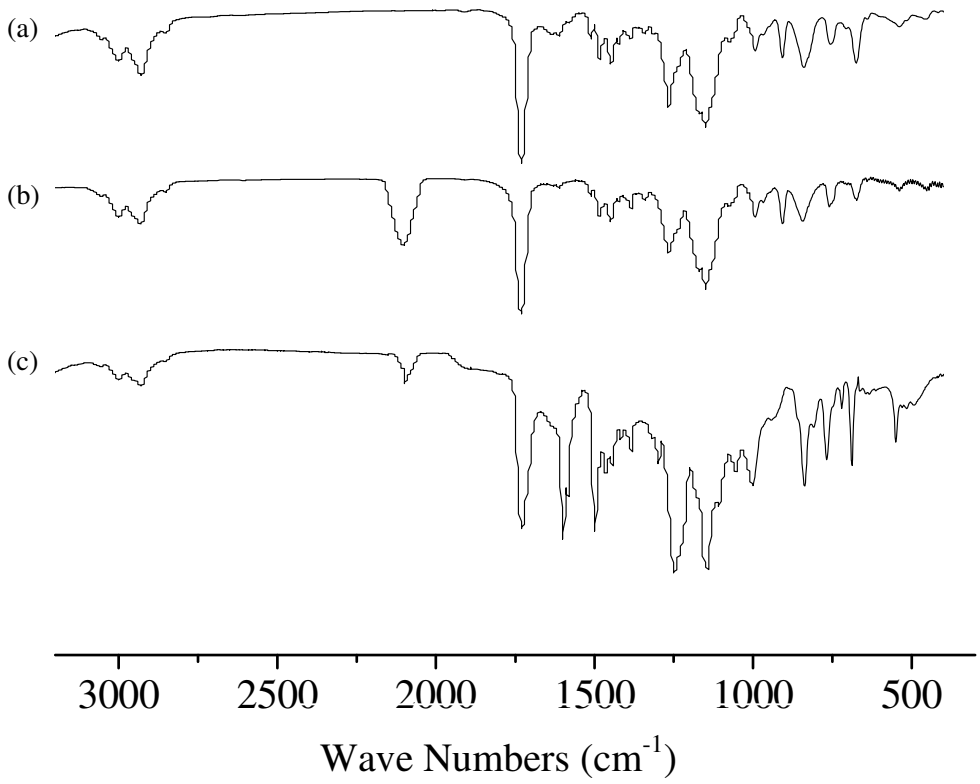

Figure S2 FTIR spectra of (a) PVBC-*b*-PGMA nanofibers, (b) $CNF_{PVBC\text{-}b\text{-}PGMA}\text{-}N_3$ nanofibers and (c) $CNF_{PVBC\text{-}b\text{-}PGMA}$-AB nanofibers.

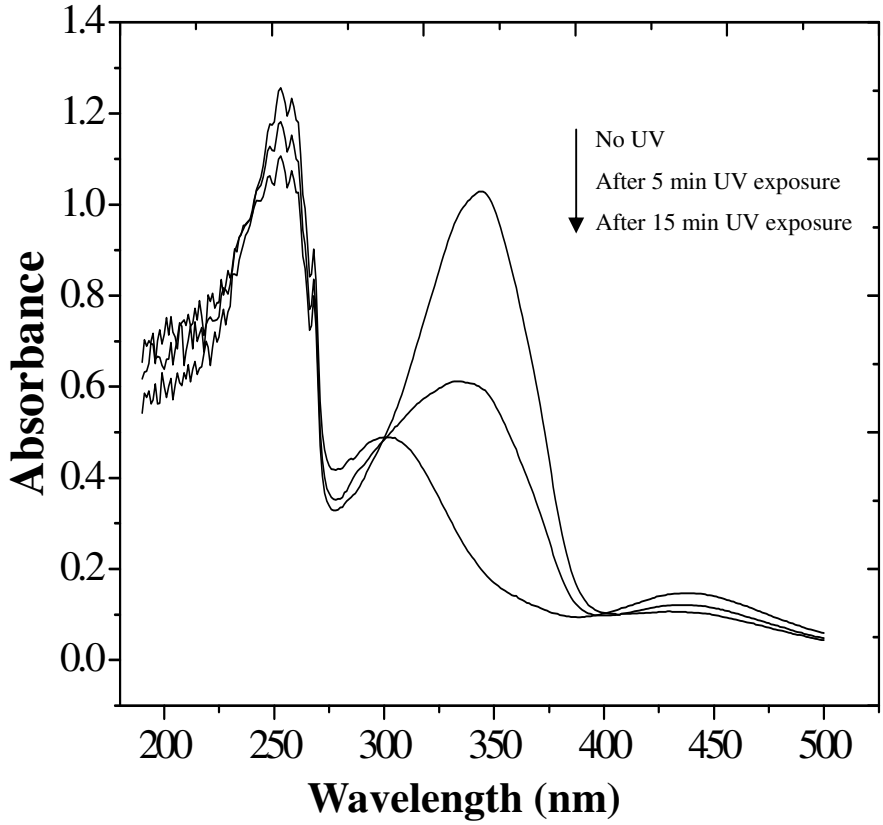

Figure S3 Photoisomerization curves of $CNF_{PVBC\text{-}b\text{-}PGMA}\text{-}N_3$ nanofibers before and after UV irradiation. The nanofibers were exposed to UV (λ=365 nm) for 0, 5, and 15 min.