Electronic Supplementary Information
for

Light-Responsive Nanogated Ensemble Based on Polymer Grafted Mesoporous Silica Hybrid Nanoparticles

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Materials. Tetraethylorthosilicate, 3-(triethoxysiliyl)propyl isocyanate, *N*-cetyltrimethylammonium bromide (CTAB), *N*-isopropylacrylamide (NIPAM), 2,2′-azobisisobutyronitrile (AIBN), 2-aminoethanethiol hydrochloride, acrylic acid, 2-nitrobenzyl bromide and Cesium carbonate were all purchased from Aldrich or JKchemical and used as received.

Characterization.

UV-vis absorption spectra were recorded on a Hitachi U3900-H absorption spectrophotometer. FT-TR spectra were collected on an Avatar Nicolet FT-IR330 spectrometer. ^{1}H NMR and ^{13}C NMR were acquired in $CDCl_3$ on Bruker AV400 NMR spectrometer in $CDCl_3$ using TMS as an internal standard. Polymer molecular weights were determined in THF with a gel permeation chromatography (GPC, Water, Styragel HR3), using polystyrene as standards. Transmission electron microscopy (TEM) was performed on a JEOL 2100 electron microscope at 200 kV. Sample preparation was carried out by placing a drop of the freshly prepared colloidal solution on a carbon-coated copper grid and allowing the solution to evaporate. Small-angle powder X-ray diffraction (XRD) was performed on a Panalytical X’Pert PRO (Philips， Holland) to study the crystallinity of the products using a diffractometer equipped with a rotating copper anode source. The data were collected over a range of $1.5° \leqslant 2\theta \leqslant 10°$. Thermal gravimetric analyses (TGA) were collected on a TG 209 F1 Thermogravimetric Analyzer, under a nitrogen atmosphere, at a heating rate of 10 °C/min. A LINOS für lamp (50 W, UV-A) with a UV 310 nm filter was used as light source for photochemical reaction.

Determination of Phase Transition Temperatures (LCST).

Determination of the phase transition temperature of random amine-terminated poly(NIPAMNBAE) was performed using a Fluoromax®-4 Spectrofluorometer with a Peltier Sample Cooler F-3004. To determine the transition temperature, the temperature dependence of the scattering intensity from 1 mL of solution in a quartzose cuvette was measured (λ = 500 nm). The temperature was increased by discrete temperature increments in the range 0-60 °C, and the readings were taken after 2 min equilibration at each temperature.

Determination of the phase transition temperature of polymer@MS nanoparticles was performed on a ZetaPALS instrument (Brookhaven, USA) equipped with 35 mW solid-state laser (658 nm). To determine the transition temperature, the temperature dependence of the scattering intensity at 90° from 1 mL of solution in a glass cuvette was measured. The temperature was increased by discrete temperature increments in the range 0-60 °C, and the readings were taken after 3 min equilibration at each temperature.

Synthesis of light-responsive monomer, 2-nitrobenzyl acrylate ester.

Acrylic acid (0.35 g, 5.0 mmol), 2-nitrobenzyl bromide (0.216 g, 1.0 mmol) and Cs_2CO_3 (0.65 g, 2.0 mmol) were dissolved in anhydrous *N,N*-dimethylformamide (DMF) (30 mL). The mixture was stirred at room temperature for 12 h in dark condition. After removal of the solvent, the resulting mixture was extracted with ethyl acetate and washed with brine (3×50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by flash chromatography on a silica gel column using DCM as eluent (0.18 g, 0.87 mmol).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96(d, *J* = 8.4 Hz, 1H), 7.55(t, *J* = 7.6 Hz, 1H), 7.49(d, *J* = 7.6 Hz, 1H), 7.37(t, *J* = 7.6 Hz, 1H), 6.37(dd, *J*1 =17.2, *J*2 = 1.2 Hz, 1H), 6.10(dd, *J*1 = 17.2, *J*2 = 10.4 Hz, 1H), 5.80(dd, *J*1 = 17.2, *J*2 = 1.2, Hz 1H), 5.47(s, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 147.1, 133.6, 131.8, 131.6, 128.5, 127.5, 124.7, 62.6 ppm.

Synthesis of amine-terminated poly(*N*-isopropylacrylamide-co-*2*-nitrobenzyl acrylate ester) (poly(NIPAMNBAE)).[S1]

NIPAM (1.13 g, 10 mmol), 2-aminoethanethiol hydrochloride (17 mg, 0.15 mmol), 2-nitrobenzyl acrylate ester (124 mg, 0.6 mmol) and AIBN (4 mg, 0.024 mmol) were dissolved in 5ml DMF. Polymerization was carried out at 75 °C in a nitrogen atmosphere for 12 h. The solution was concentrated to 2 mL and 15 mL ether was added to obtain floccules. The crude product was filtrated, dissolved in 1 mL THF and precipitated by 20 mL ether for three cycles to obtain amine-terminated poly(NIPAMNBAE). The polymer molecular weight was determined to be 6,300 and the content of light-responsive monomer in the polymer chain was determined to be 5.3% (Fig. S1).

Synthesis of MCM-41 type mesoporous silica (MS) nanoparticles.[S2]

In a typical synthesis procedure, 28 mg of NaOH and 100 mg of cetyltrimethylammonium bromide (CTAB) in sequence were completely dissolved into 50 mL of deionized water under vigorous stirring at 80 °C. After the solution became clear, 0.5 mL of tetraethoxysilane (TEOS) was added dropwise with the whole dropping time of about 10 min. The vigorous stirring was continued for 20 h, and then milk-white as-synthesized materials were collected by centrifugation. In order to remove the surfactant, the as-synthesized materials were refluxed in a mixed solution of 50 mL ethanol and 0.5 mL hydrochloric acid (36-38%) at 78 °C for 12 h, then centrifugalized and washed for several times with ethanol. The final products were dried for 12 h at 120 °C in vacuum.

Preparation of polymer grafted MS nanoparticles.[S2]

To a 0.5 mL THF was added 0.2 g of amine-terminated poly(NIPAMNBAE) and 20 μL 3-(triethoxysiliyl)propyl isocyanate. The solution was stirred in dark for 12 hours then added in dropwise to 60 mL of pH 4 hydrochloric acid solution of ethanol and water (at the volume ratio of 1:2) that contains 50 mg of MS nanoparticles under vigorous stirring. After vigorous stirring for 24 h, the mixed solution was dried for 12 h at 100 °C in vacuum. The obtained particles were dispersed in DMF and collected by centrifugation for three times to remove the random polymer. The light-responsive polymer grafted MS nanoparticles were obtained as a slight yellow powder.

Measurement of Cytotoxicity.[S3]

The viabilities of Hep-G2 cells that incubated with or without MS@polymer hybrid nanoparticles (5 μg/mL) were measured by quantifying the cellular ability to reduce the water-soluble tetrazolium dye 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) to its insoluble formazan salt. Data points were collected in triplicate and expressed as normalized values for control cells (100%). And the results revealled that the cells incubated with 5 μg/mL hybrid nanoparticles for 24 h show 92±4% viability of that of controlled panel.

Evaluating dispersion of MS@polymer hybrid nanoparticles in 10 mM pH7.4 PBS at 37 °C.

Fluorescein load hybrid nanoparticles (1 μg) were dispersed in 1 mL 10 mM pH7.4 PBS at 37 °C with ultrasonic treatment for 30 min, and fluorescence emissiones of the solution at 525 nm was measured as F_0 (λ_{ex} = 365 nm). Then the solution was filtrated by a filter membrane with pore diameter of 0.45 μm (a commercial filtrates membrane for HPLC) and the fluorescence emissiones of the filtrates was measured to be F_1. Thus, the dispersions of the hybrid nanoparticles was caculated by F_1/F_0. The dispersions of hybrid nanopartilces at other concentrations (5, 10, 20, 50 and 100μg/mL) have also been determined. The resluts of these experiments are shown in Fig. S8.

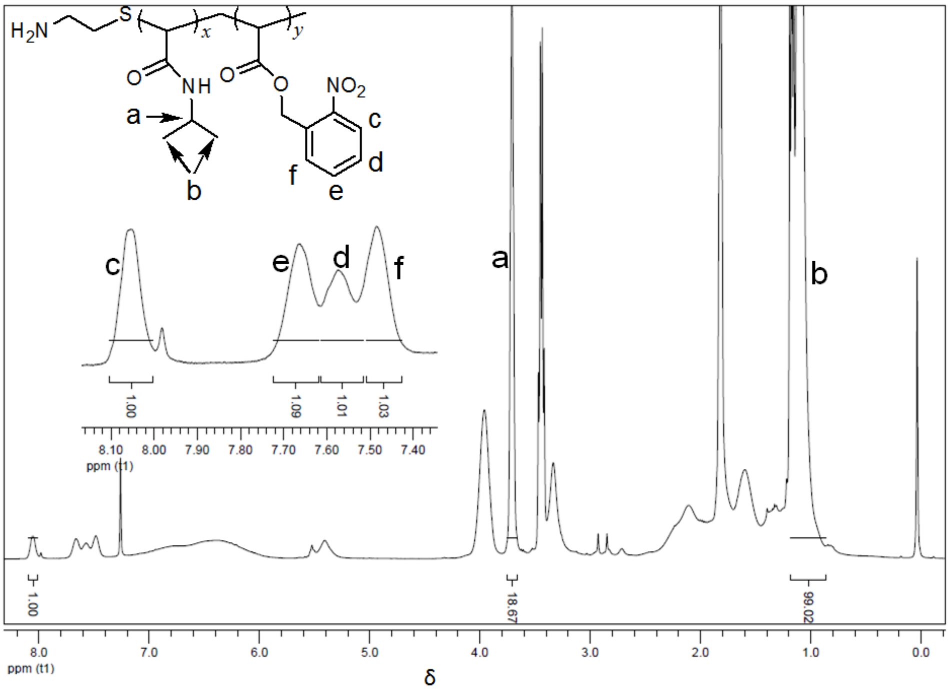

Fig. S1 H1-NMR characterization of the amine-terminated poly(NIPAMNBAE).

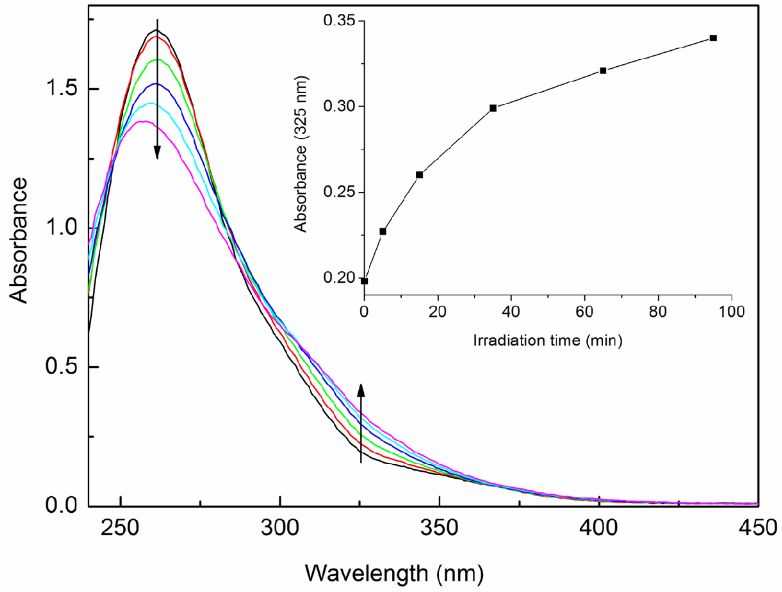

Fig. S2 UV-vis spectra of the amine-terminated poly(NIPAMNBAE) in 10 mM pH7.4 PBS after an irradiation of various periods.

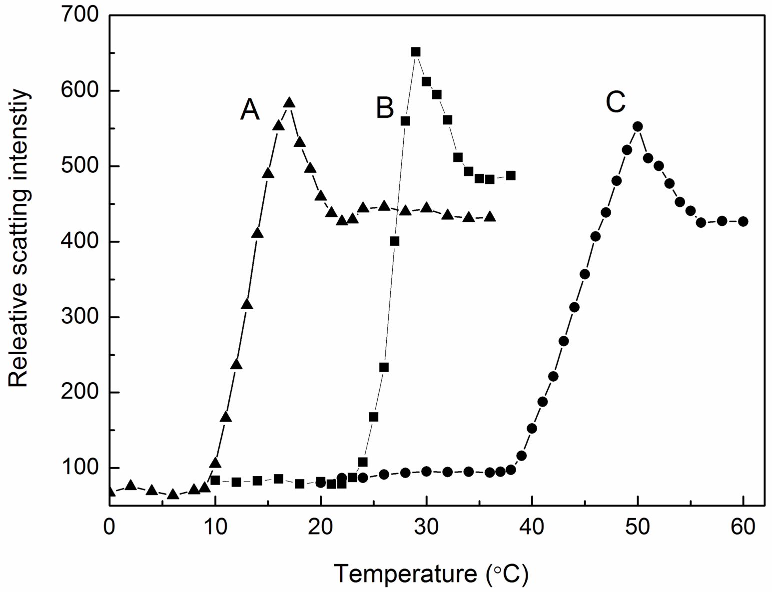

Fig. S3 LCST detections of amine-terminated poly(NIPAMNBAE) in 10 mM pH7.4 PBS after an irradiation of various periods: (A) 0 min, (B) 30 min, (C)70 min.

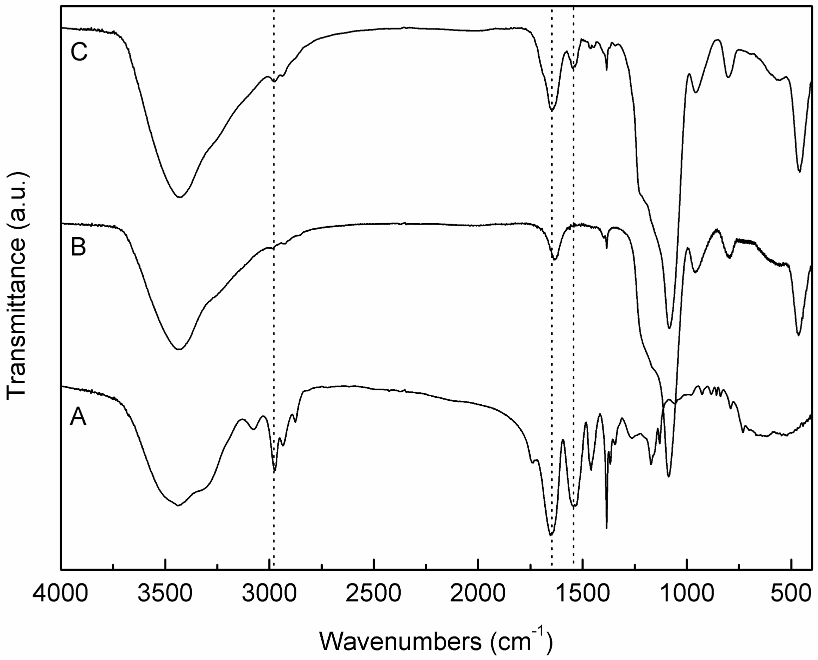

Fig. S4 FT-IR spectra of the polymer (A), MS (B) and MS@polymer nanoparticles (C).

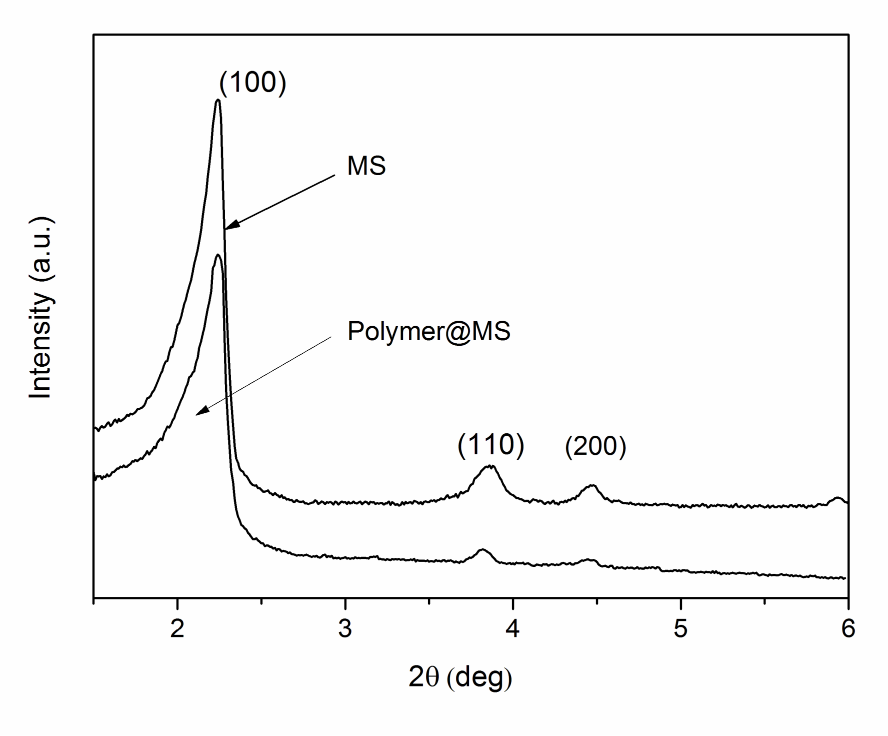

Fig. S5 low-angle XRD pattern of MS and polymer@MS nanoparticles.

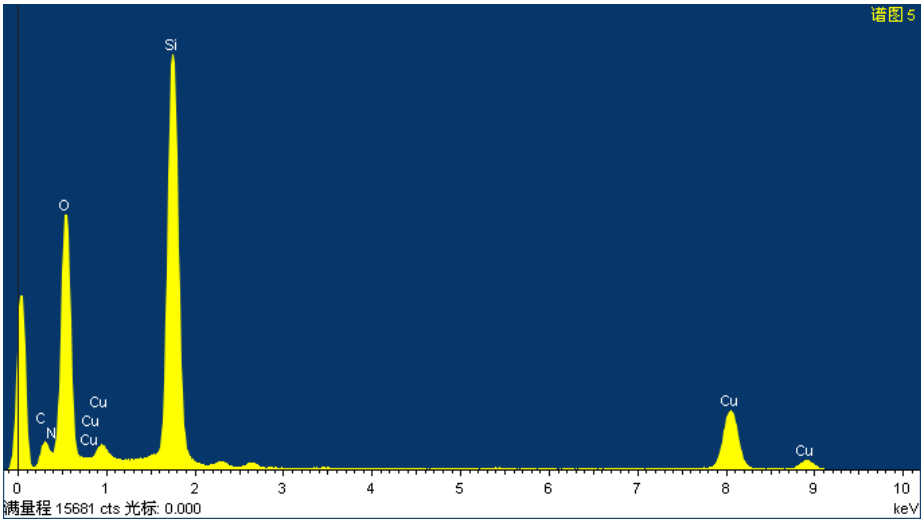

Fig. S6 EDX analysis of the polymer@MS nanoparticles.

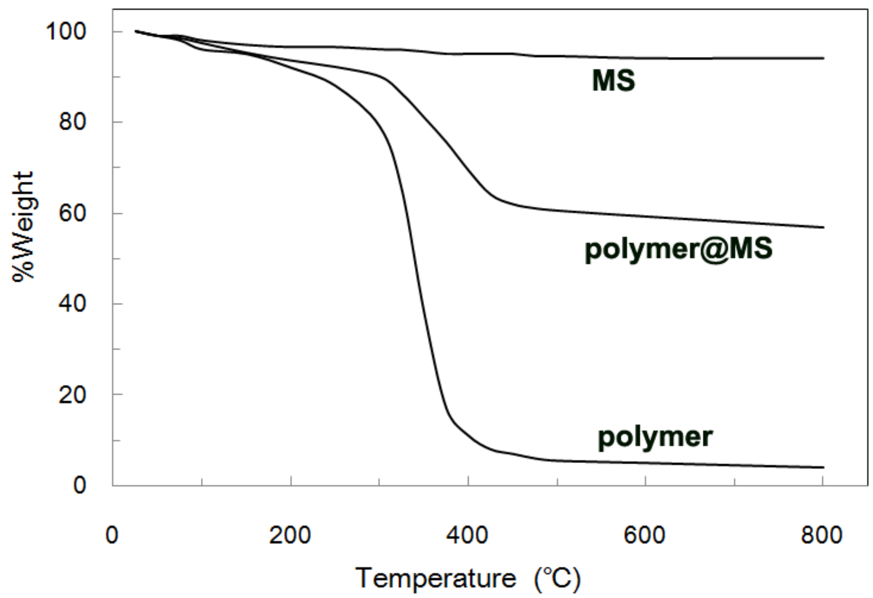

Fig.S7 TGA curves for MS, polymer@MS and polymer.

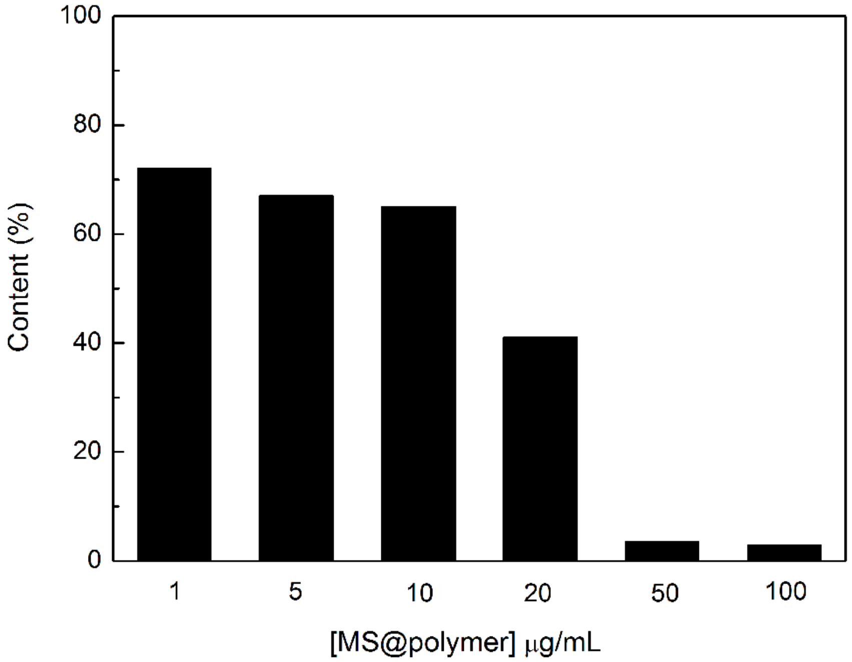

Fig. S8 Evaluating dispersion of MS@polymer nanoparticles in 10 mM pH7.4 PBS at 37 °C through membranes with pore diameters of 0.45 μm.

Note: In light of the diameter of the hybrid nanoparticles is *ca*. 120 nm, the nanoparticles contained solutions were filtrated through membranes of pores diameters of 0.45 μm (a commercial filtrates membrane for HPLC). As can be seen in Fig. S8, more than 65% of the hybrid nanoparticles can pass through the membrane when the original concentration of the nanoparticles is 1 μg/mL. More importantly, this value was found independent of the concentration of the nanoparticles over 1 to10 μg/mL, whereas at higher concentration of 20 μg/mL this value strated to drop. These observations suggest that the hybrid nanoparticles are dispersed well at concentration lower than 10 μg/mL. This assumption was further supported by the confocal fluorescence images. As shown in Fig. 4, significant fluroescence was observed in the cells incubated with 5 μg/mL dye-loaded nanoparticles, indicating that the nanoparticles are indeed well dispersived for cellular application.

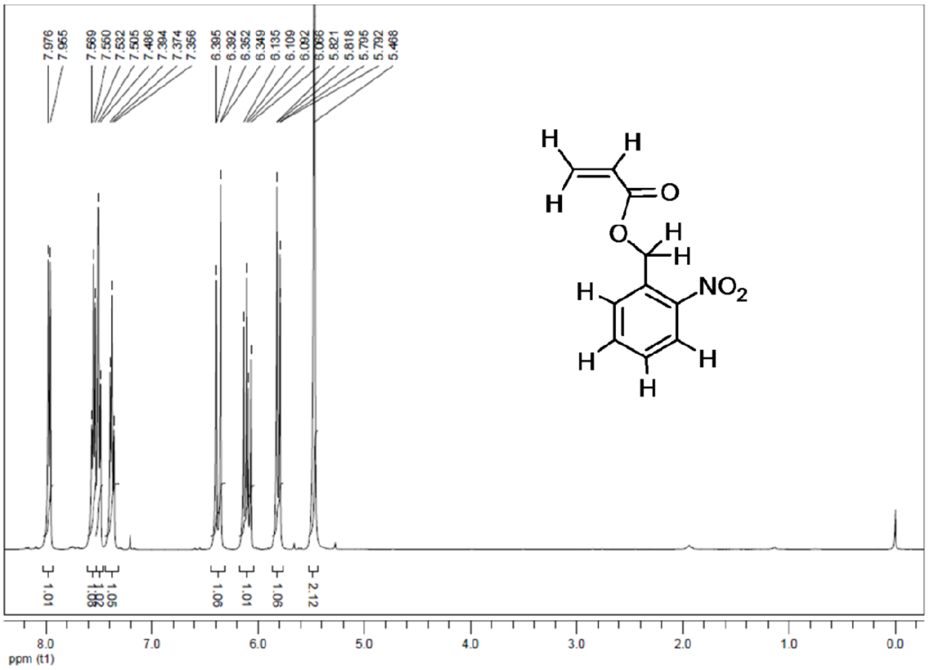

Fig. S9 ^{1}HNMR spectra of 2-nitrobenzyl acrylate ester ($CDCl_3$, 400 MHz)

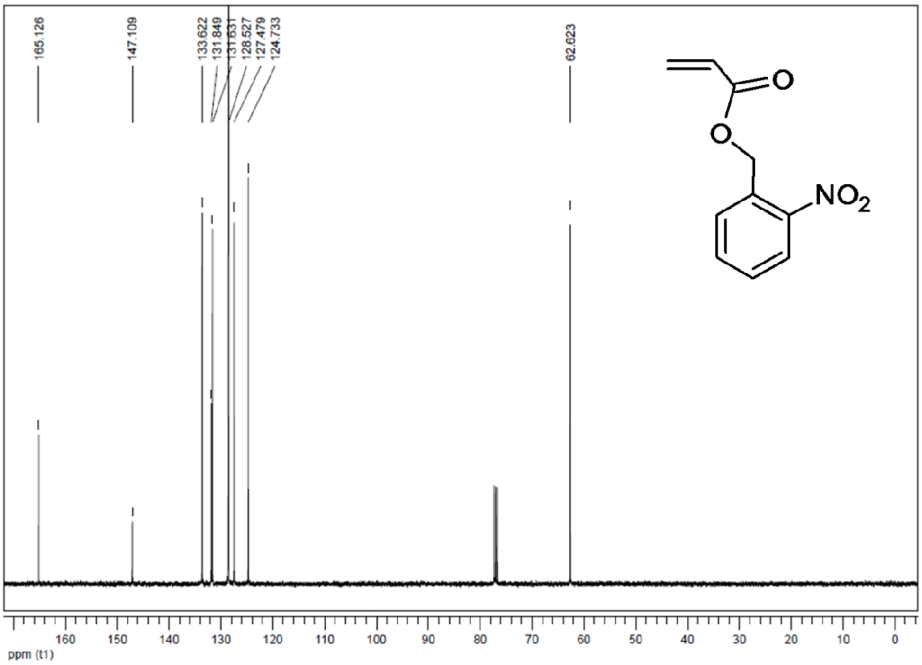

Fig. S10 ^{13}CNMR spectra of 2-nitrobenzyl acrylate ester ($CDCl_3$, 100 MHz)

[S1] T. Shimoboji, Z. L. Ding, P. S. Stayton and A. S. Hoffman, *Bioconjugate Chem.*, 2002, **13**, 915.

[S2] Q. He, J. Zhang, J. Shi, Z. Zhu, L. Zhang, W. Bu, L. Guo and Y. Chen, *Biomaterials*, 2010, **31**, 1085.

[S3] D. Sgouras, R. Duncan, *J. Mater. Sci.: Mater. Med.* **1990**, *1*, 61-68.