SUPPORTING INFORMATION

Photo-Responsive Block Copolymer Prodrug Nanoparticles as Delivery Vehicle for Single and Dual Anticancer Drugs

Gargi Biswas[†], Bikash Chandra Jena[‡], Saikat Maiti[†], Pousali Samanta[†], Mahitosh Mandal[‡], Dibakar Dhara[†,*]

[†]*Department of Chemistry,*
[‡]*School of Medical Science and Technology,*
Indian Institute of Technology, Kharagpur,
West Bengal 721302, India

Methods:

Synthesis of 3-bromopropyl acrylate: 3-Bromopropyl acrylate was synthesized following a reported procedure.[S1] Briefly, to a solution of 3-bromopropyl alcohol (1 g, 7.2 mmol) and Et_3N (0.754 g, 7.45 mmol) in dry DCM (10 ml), acryloyl chloride (0.651 g, 7.2 mmol) was added slowly at 0 °C under nitrogen atmosphere in a 50 ml two necked round bottomed flask and then stirred overnight at room temperature. After that, excess acryloyl chloride was quenched by MeOH. After 30 min, the reaction mixture was extracted with DCM and organic layer was washed with saturated aq. $NaHCO_3$ solution for three times and dried over anhydrous $MgSO_4$. 3-Bromopropyl acrylate (0.944 g, 68% yield) was obtained as colourless liquid by silica column chromatography eluted with 5% ethyl acetate-hexane mixture. ^{1}H NMR ($CDCl_3$, 400MHz) (Fig.S1): δ (ppm) 2.12-2.15 (t, 1H), 2.21-2.24 (t, 1H), 3.46-3.50 (t, 1H), 3.62-3.65 (t, 1H), 4.30-4.31 (t, 2H), 5.84 (d, 1H), 6.08-6.15 (m, 1H), 6.41 (d, 1H).

Synthesis of poly(NIPA) macro CTA, **P0**: PNIPA macroCTA, **P0**, was prepared by RAFT polymerization process. 3-(Benzylthiocarbonothioylthio)propanoic acid (BCTPA) was used as chain transfer agent and AIBN was taken as initiator. BCTPA was synthesized following reported procedure.[S2] BCTPA (0.0688 g, 0.2528 mmol), AIBN (0.01245 g, 0.076 mmol) and recrystallized NIPA (1 g, 8.849 mmol) were taken in a 25 ml round bottomed flask and dissolved in 5 ml of 1,4-dioxane. The solution was degassed by nitrogen and allowed to stir overnight at 65 °C. The reaction was quenched by keeping it in the refrigerator for one hour, the product was isolated by precipitation in cold ether for two times followed by drying in vacuum ^{1}H NMR (DMSO-d_6, 400MHz) (Fig. S5): δ (ppm) 1.024 (s, Me), 1.417-1.438 (br, $CHCH_2$ polymer backbone), 2.481-2.489 (br, $CHCH_2$ polymer backbone), 3.823 (br, CH of PNIPA), 7.115-7.230 (br, NH of PNIPA).

SUPPORTING FIGURES

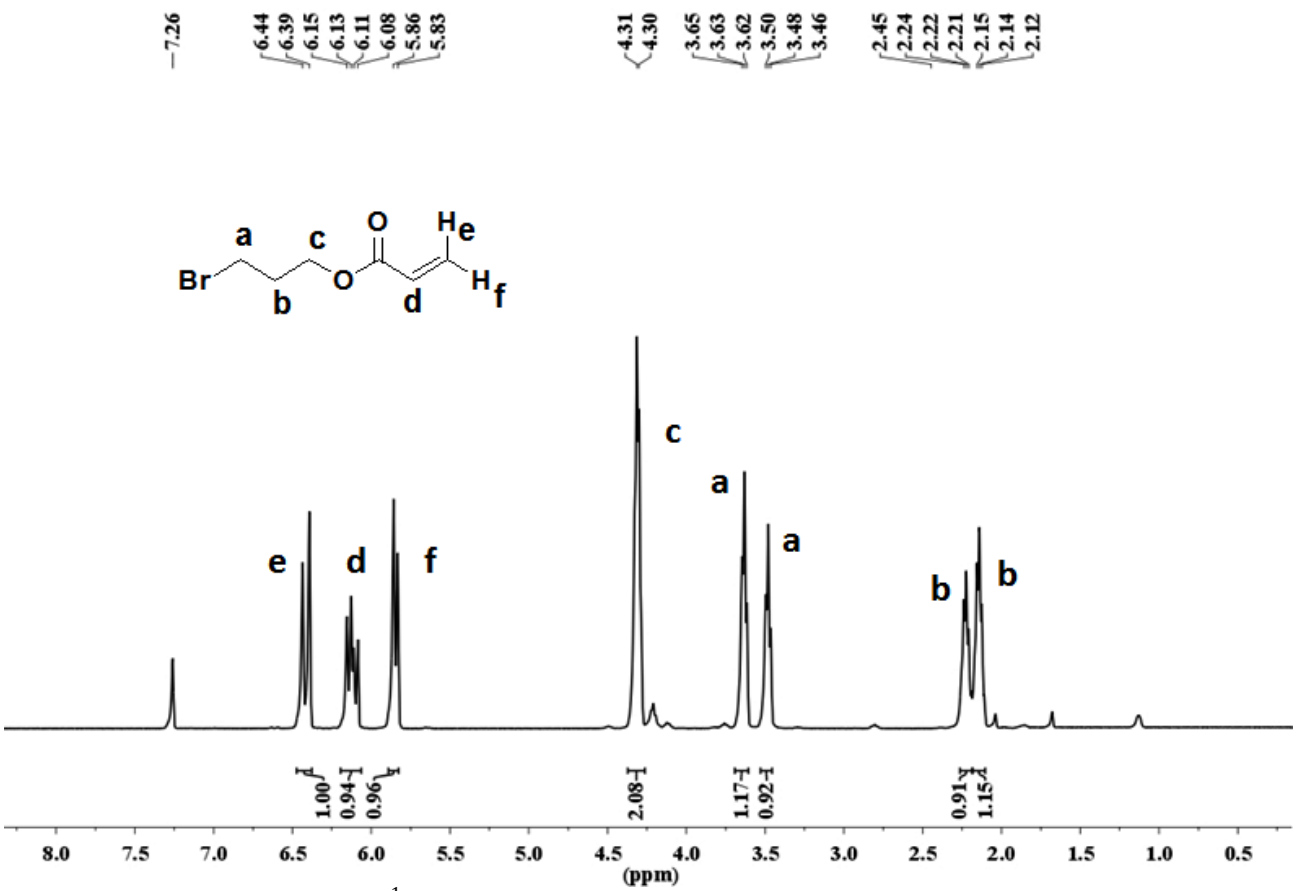

Figure S1: ^{1}H NMR (in $CDCl_3$) of 3-bromo propyl acrylate.

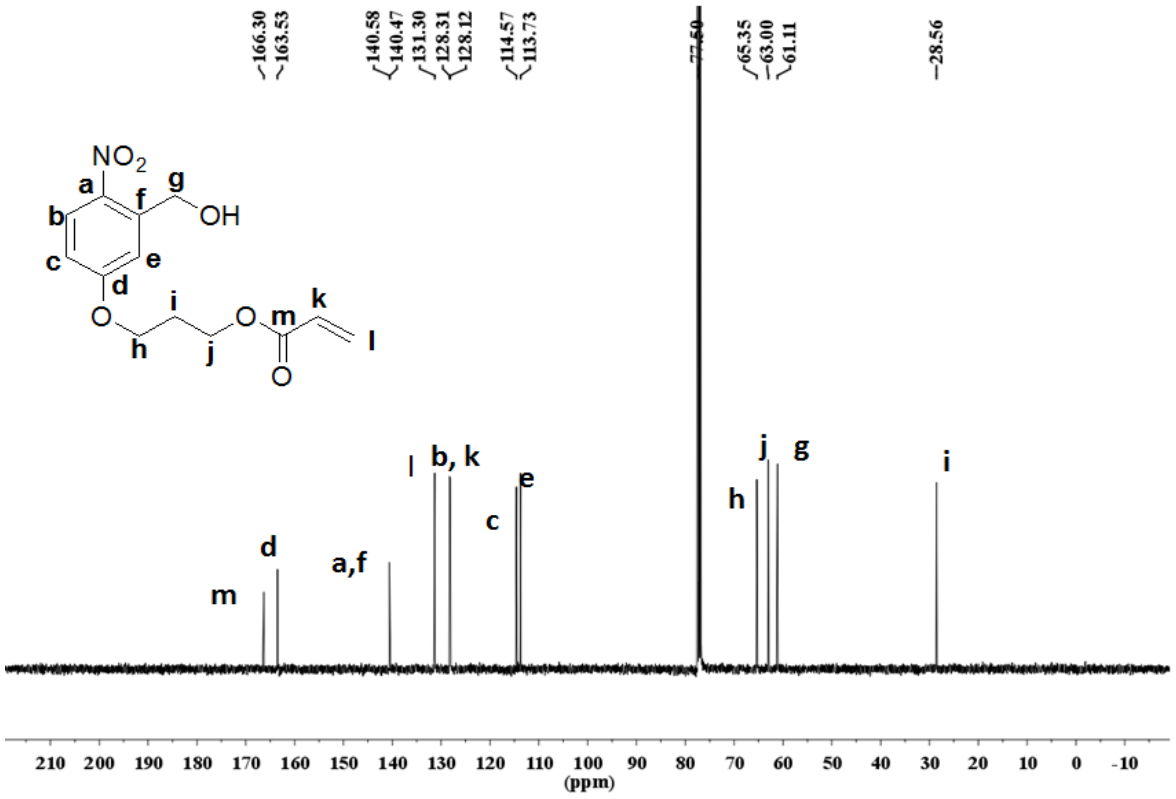

Figure S2: ^{13}C NMR (in $CDCl_3$) of 3-(3-(hydroxymethyl)-4-nitrophenoxy)propyl acrylate (HMNPPA).

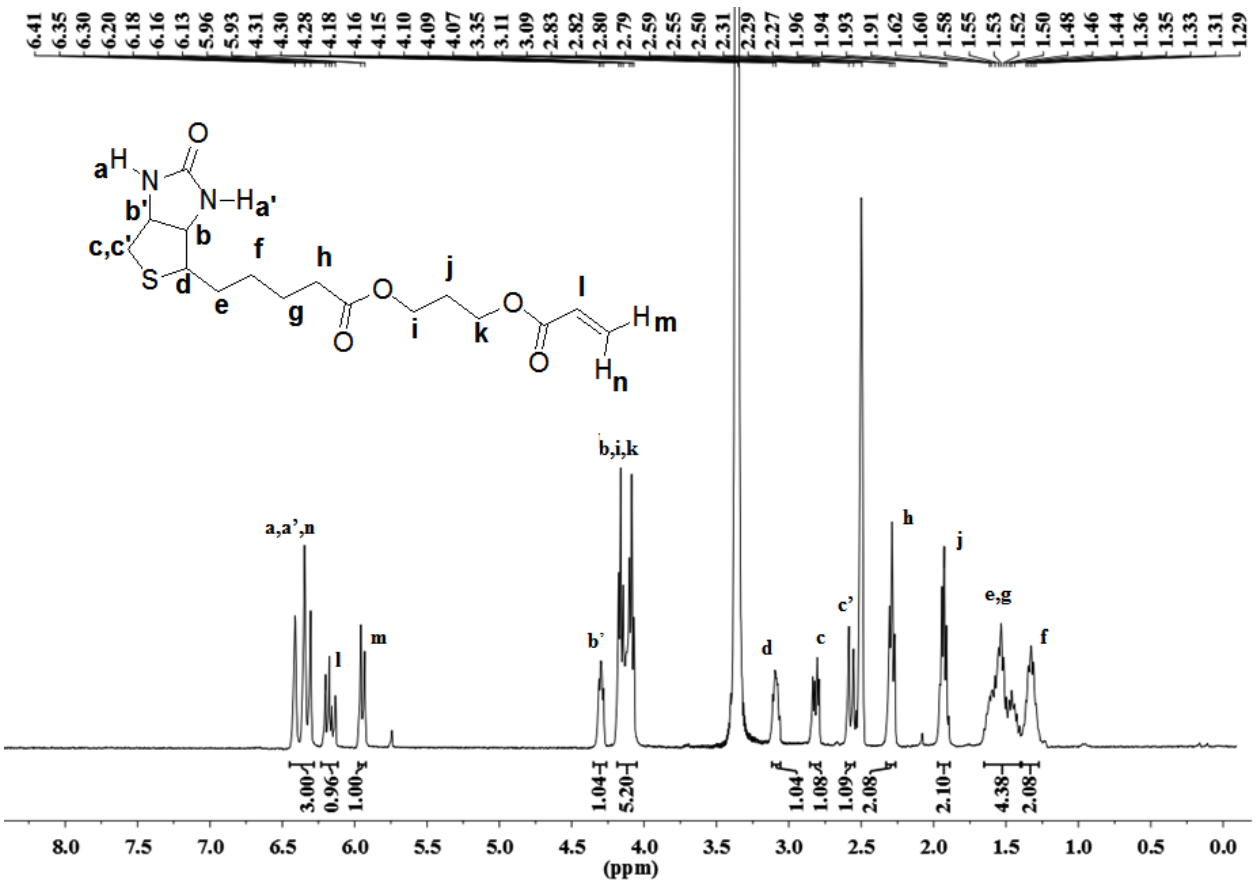

Figure S3: ^{1}H NMR (in DMSO-d_6) of biotine arylate (BA).

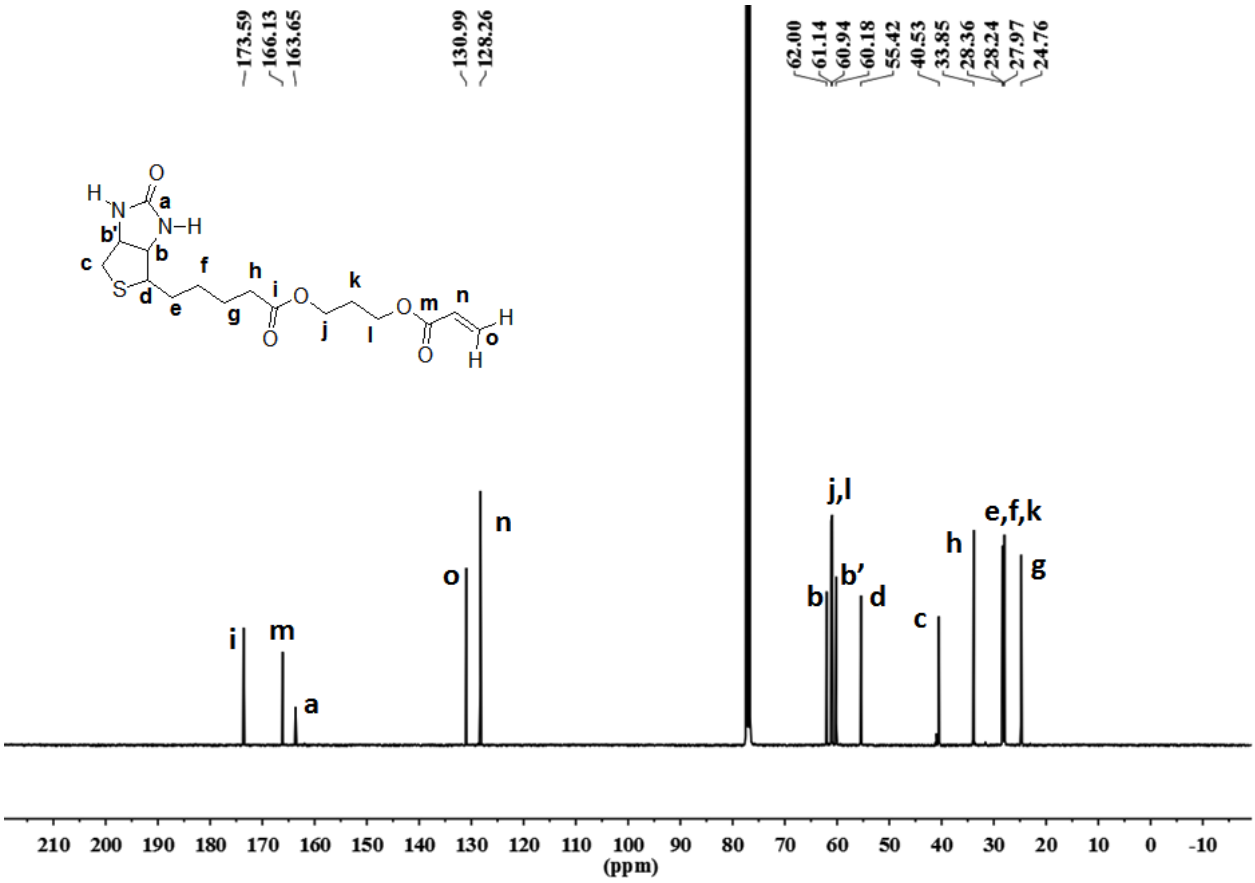

Figure S4: ^{13}C NMR (in $CDCl_3$) of biotin acrylate (BA).

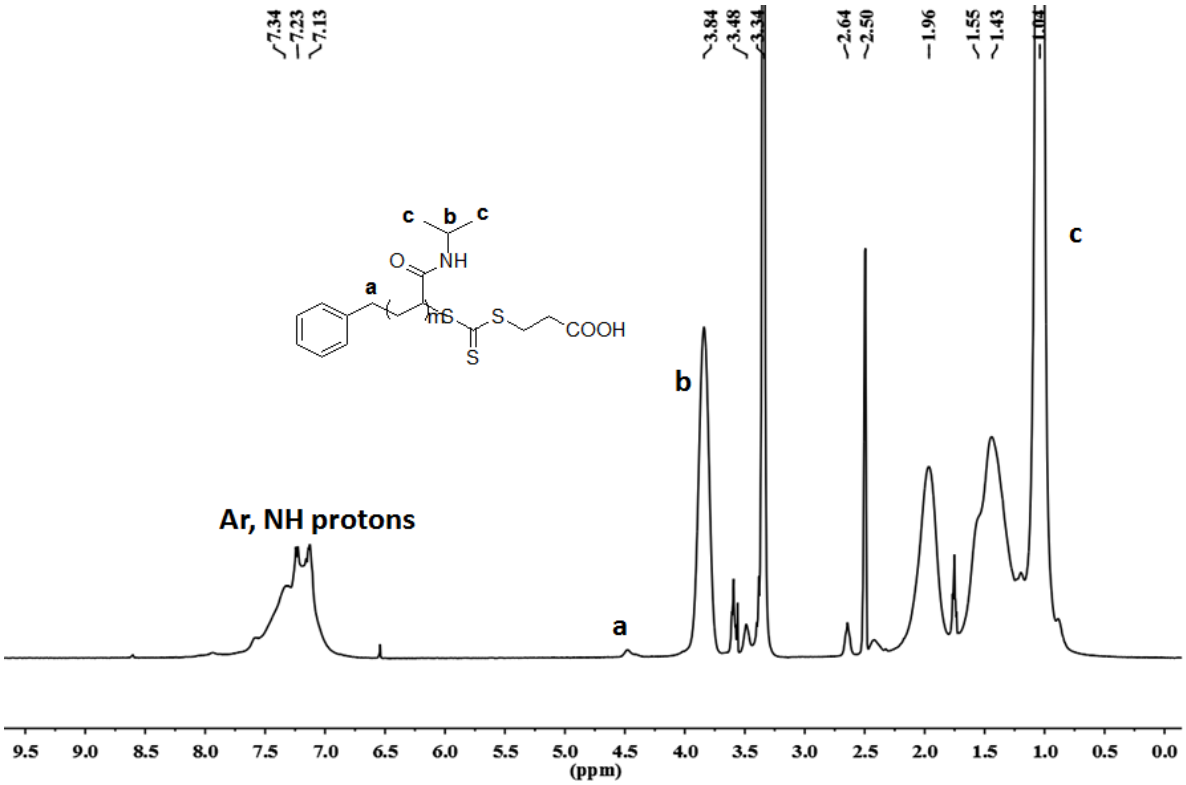

Figure S5: ^{1}H NMR (in DMSO-d_6) of PNIPA macro CTA (**P0**).

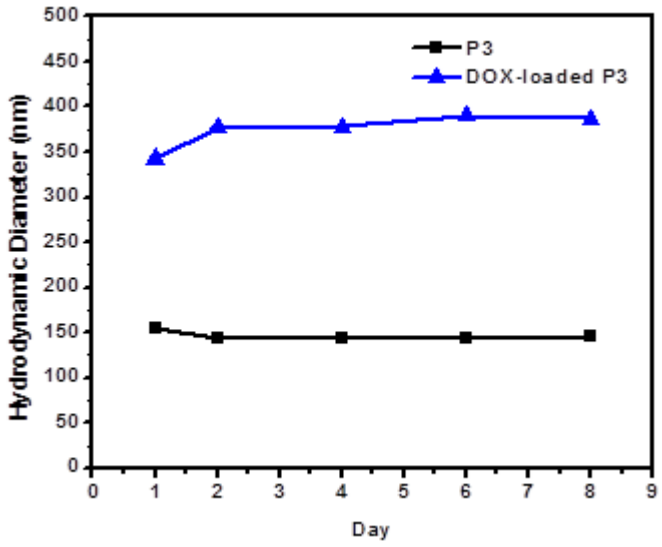

Figure S6: Time dependent hydrodynamic diameter of **P3** and **P3**-DOX.

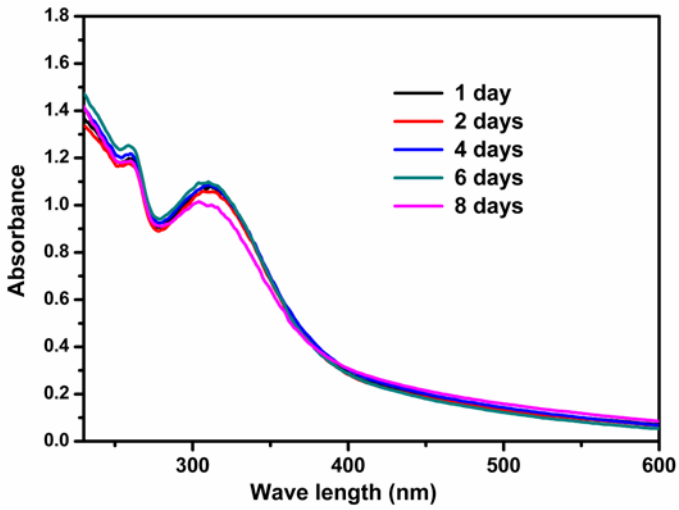

Figure S7: Time dependent UV-vis absorption spectra of **P3** prodrug.

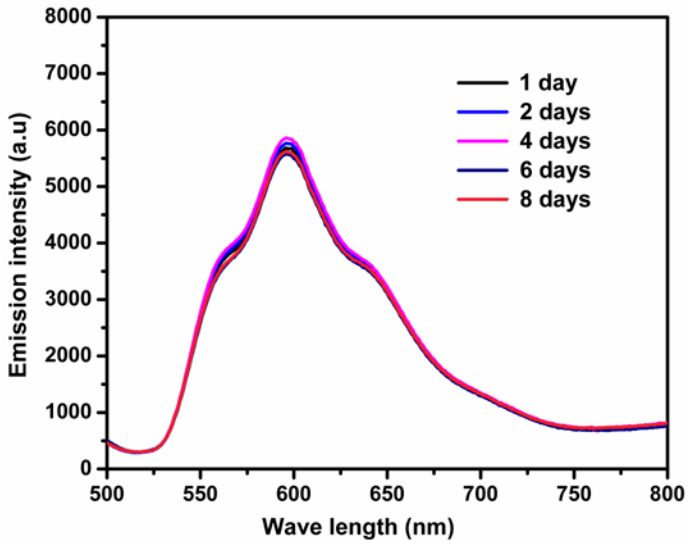

Figure S8: Time dependent emission spectra of DOX in **P3**-DOX.

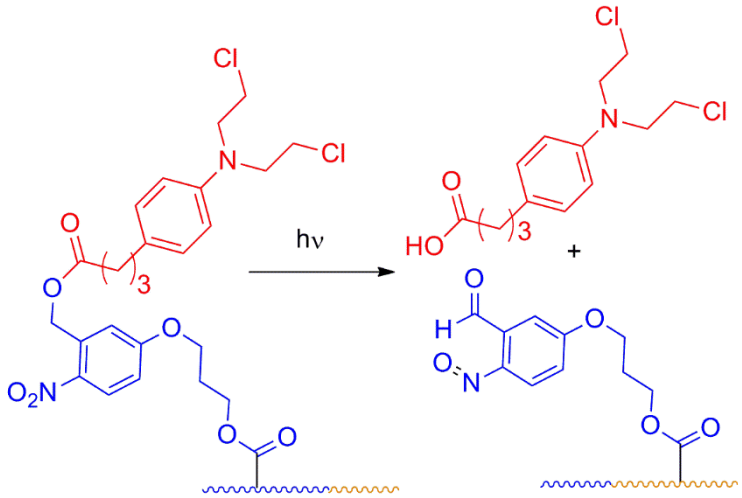

Figure S9. Schematic representation of chemical structural change of **P3** prodrug after radiation[S3].

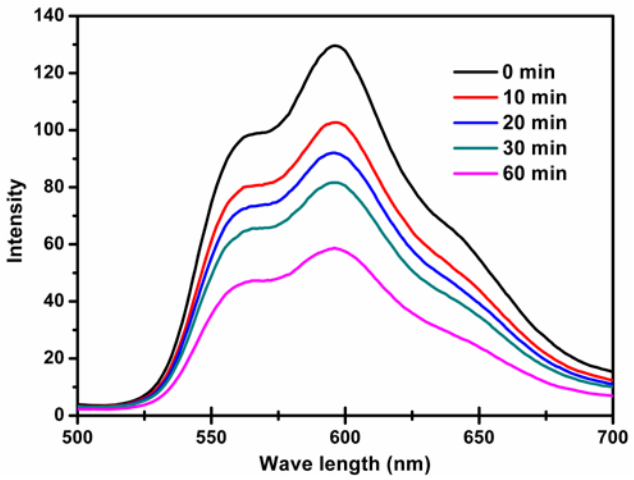

Figure S10. Fluorescence spectra of DOX loaded **P3** prodrug nanoparticles after UV irradiation of different duration.

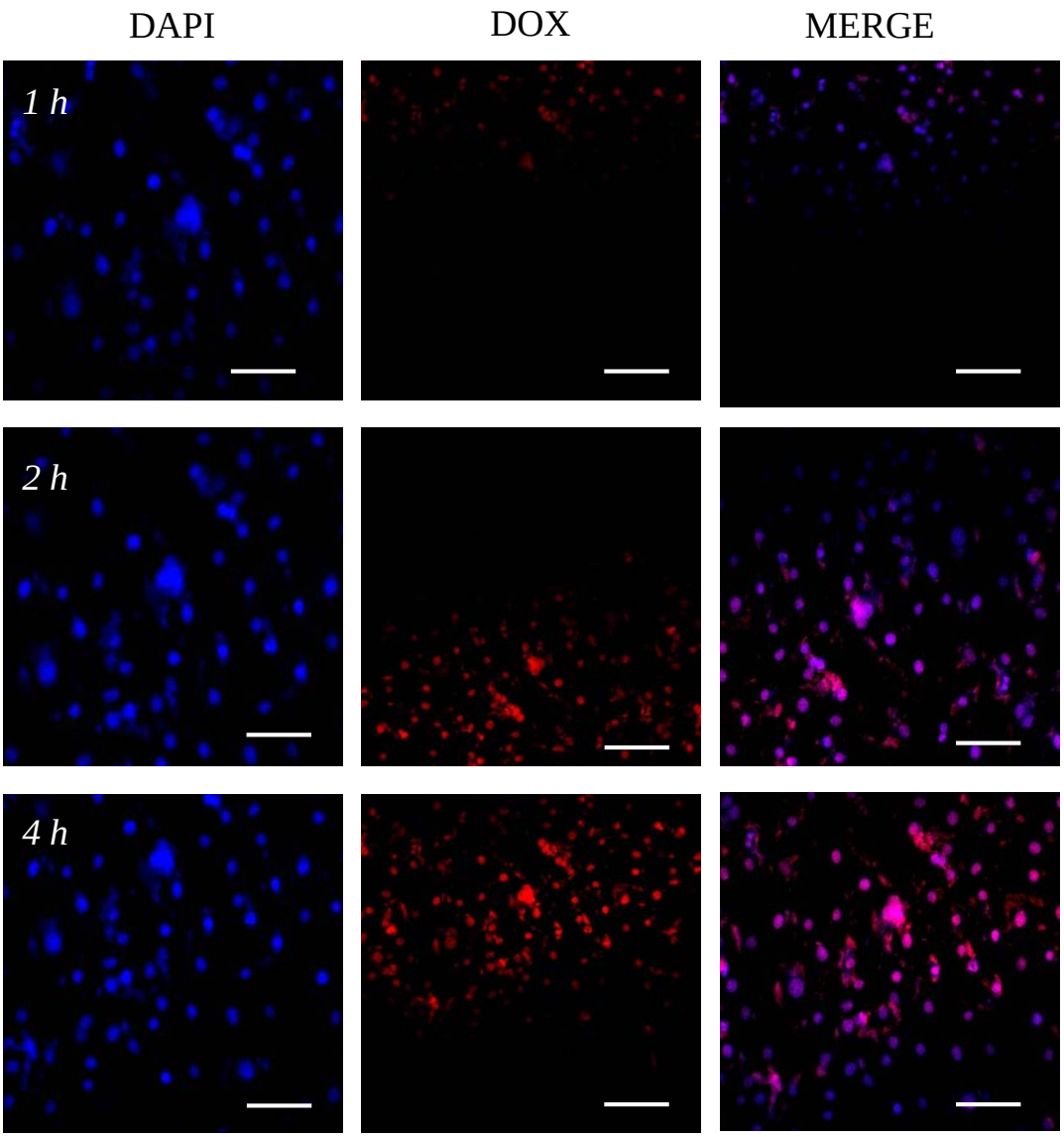

Figure S11. Confocal microscopic images of breast cancer cell lines over a time span of 1-4 h after treatment with free DOX as control. The nuclei was stained with DAPI (blue).

Supporting References

S1. Moore, B. L.; Lu, A.; Moatsou, D.; Rachel, K. The effect of polymer nanostructure on diffusion of small molecules using tryptophan as a FRET probe. *European polymer Journal* **2015**, *62*, 380−385.

S2. Stenzel, M. H.; Davis, T. P.; Fane, A. G. Honeycomb Structured Porous Films Prepared from Carbohydrate Based Polymers Synthesized via RAFT Process. *J. Mater. Chem.* **2003**, *13*, 2090−2097.

S3. Zhao, H.; Sterner, E. S.; Coughlin, E. B.; Theato, P. o-Nitrobenzyl Alcohol Derivatives: Opportunities in Polymer and Materials Science. *Macromolecules* **2012**, *45*, 1723−1736.