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Supporting Information

Smart Wound Dressing for Infection Monitoring and NIR-triggered Antibacterial Treatment

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Examination of Amino Groups of SNP-NH2 and SNP-Cy3 by Acid Orange[1]

10 mg SNP-NH_2 and SNP-Cy3 respectively into 10 mL acid orange solution (5×10^{-4} M, pH 3). And then the mixture was stirred at 37 ºC for 5 h. The amino groups can react with sulfonic acid group of acid orange in the same molar ratio. And then nanoparticles were washed with HCl (1×10^{-3} M) for several times to remove the unreacted dye. Finally, the nanoparticles were immersed to 10mL NaOH (1×10^{-3} M) solution at 37 ºC for 12 h to realize the desorption of acid orange, the UV absorption of which is at 485 nm. The amino density on the surface of the nanoparticles was determined according to the standard curve of acid orange.

Synthesis and Characterizations of 1-(5-Methoxy-2-nitro-4-prop-2-ynyloxyphenyl) ethyl N-succinimidyl Carbonate (UV-cleavable linker)[2]

Linker-1: The UV-cleavable Linker was prepared according to literature with some modifications (Figure S2a). 500 mg 4-hydroxy-5-methoxy-2-nitroacetophenone and 476 mg of K_2CO_3 were dissolved in 25 mL dried acetonitrile solution, and then 280 μL propargyl bromide was subsequently added. The solution was refluxed at 100 ºC for 3 h under nitrogen atmosphere and concentrated using a rotary evaporator. After that, the solid was dissolved with 5 mL HCl solution (2 M) and 50 mL water, then extracted with 50 mL chloroform for three times. The lower organic layer was dried over $MgSO_4$, and the solution was removed under a reduced pressure to obtain the yellow solid product (Linker-1). The structure of the product was characterized by ^{1}H NMR (500 MHz, $CDCl_3$, Avance III HD, Bruker, CH) (Figure S2 b) and FTIR ((Figure S2 e).

Linker-2: Then, 570mg of Linker-1 and 690mg of sodium tetrahydroborate were subsequently added into tetrahydrofuran (10mL) and methanol (20mL) on an ice bath and stirred for 3 h. After concentrating

the solution on a rotary evaporator, the solid was re-dissolved with 5mL of HCl solution (2 M) and 50mL of water, then extracted with 50mL of chloroform for three times. The organic layer was collected and dried over $MgSO_4$, and the solid product (Linker-2) was obtained under reduced pressure.

UV-cleavable Linker: Finally, 550 mg Linker-2, 1.68 g N, N'-Disuccinimidyl carbonate and 1mL triethylamine was dissolved in 25 mL dried cetonitrile solution. The solution was stirred at room temperature for 5 h under nitrogen atmosphere then concentrated using a rotary evaporator. After concentrating the solution on a rotary evaporator, the solid was re-dissolved with 5 mL HCl solution (2 M) and 50mL water, then extracted with 50mL of chloroform for three times. The organic layer was washed with saturated $NaHCO_3$ for three times and dried over $MgSO_4$. The final product (UV-cleavable Linker) was obtained under reduced pressure and dried in vacuum. The structures of Linker-1, Linker-2 and UV-cleavable linker were characterized by ^1H NMR ($CDCl_3$, Avance III HD500 MHz, Switzerland) and FTIR (Nicolet 6700, Themo Fisher scientific LLC, USA) (Figure S2).

Synthesis and Characterizations of UV-responsive Polyprodrug (GS-Linker-MPEG)

The synthesis of the UV-responsive polyprodrug was provided in Figure S3a. In brief, 127 mg gentamiacin sulfate (GS) and 85 mg UV-cleavable Linker were dissolved in 8 mL tetrahydrofuran, 4 mL water and 1 mL triethylamine. The solution was stirred under nitrogen atmosphere for 12 h at room temperature. Then the solution was directly added into azide-PEG5000-methoxyl (N_3-MPEG, Mn = 5000 Da) solution (2% w/w in tetrahydrofuran) in the presence of copper (II) sulfate (0.1 M, 5% mol of alkynyl group) and L-ascorbic acid (0.1 M, 10% mol of alkynyl group). After stirring under nitrogen atmosphere for another 12 h at 60 ºC the reaction solution was cooled and dialyzed against distilled water for 3 days to remove the

unreacted molecular (MWCO: 3500). Finally, the dialysis solution was lyophilized to obtain the UV-responsive polyprodrug (GS-Linker-MPEG), the structure of which was characterized via ^{1}H NMR (500 MHz, D_2O).

The UV-responsive Properties of GS-Linker-MPEG

The UV-cleavage reactions of GS-linker-MPEG with different UV irradiation time were traced by UV-vis absorption spectrum (Figure S4b). GS-Linker-MPEG solution was irradiated by a UV spot light source (365 nm, 1 W/cm2, UVEC-4II, LAMPLIC) for different time, and UV-vis absorption spectrum was traced.

GS release under NIR irradiation

20 mg GS-Linker-MPEG was dissolved in 2 mL UCNP solution (2.5 mg/mL in water) by vortex. Then 200 μL mixture was injected into 96-wells-plate. After irradiating with NIR light (4W) for scheduled time (0, 5, 10 and 15 min), the mixture was transferred to amicon centrifuge filters (MWCO: 3500) and then centrifuged at 12000 rpm for 35 min. The filter liquid was collected to examinate the amount of released GS. The solution without UCNP was conducted by the same procedure as control.

The amount of released GS was determined by a derivative method and the principle was based on o-phthaldialdehyde reacting with the primary amino group of gentamicin sulfate to form chromophoric products, whose UV absorbance was at 332 nm.[3] Generally, derivative agent was prepared by dissolving 125 mg o-phthalaldehyde into 28 mL boric acid (0.04 M). After dissolution, 3.125 mL methanol and 150 μL 2-mercaptoacetic acid were added in sequence. Before using, the mixture was preserved in 4 ºC for 24 h. Then 100 μL released GS was added into the mixture of 100μL prepared derivative agent and 100 μL 2-propylalcohol, and then incubated at 37 °C for 45 min. The cleavage amount of GS was tested by UV-vis

measurement.

The grafted GS on GS-Linker-MPEG was determined by a standard addition method.[4] At first, 500 μL GS-Linker-MPEG (1 mg/mL) with different volumes (0, 10, 20, 30 and 40 μL) of GS solution (1 mg/mL) was prepared, and then replenished the total volume to 550 μL with PBS, to which 550 μL prepared derivative agent and 550 μL 2-propylalcohol, and then incubated at 37 °C for 45 min. The UV absorption was measured at 332 nm. The curve in which UV absorption as the Y-axis and GS concentration as the X-axis was plotted and the density of grafted GS was obtained by extrapolating the curve to Y=0. The percentage of released GS was calculated as following: The percentage of released GS (%) = Amount of released GS/ (density of grafted GS × mass of GS-Linker-MPEG).

Swelling Ratio of Hydrogels

The hydrogels were dried at 50 ºC in oven for 6 h and weighed to obtain the initial weight (W_0). Then the samples were immersed into 1mL PBS (pH 7.4) at 37 ºC with shaking. At selected intervals, the hydrogels were weighed again to obtain the current weight (W). The swelling ratio was calculated as following: Swelling ratio (%) = $(W-W_0) / W_0 \times 100\%$.

Cytotoxicity Assay of NIH 3T3 Cells after Irradiated by NIR

For the NIR irradiation experiment groups, the 96-wells-plate was exposed under 6W 980 nm laser from the top of the plate, the laser was turned on for 10 s and off for 50 s alternatively to prevent the cells from overheating, until the accumulate irradiation time up to 20 min. Then incubated for 1, 3, 5 days. At scheduled time, the culture medium was removed, to which 20 μL CCK8/DMEM solution (10 %, v/v) was added and incubated for 1.5 h at 37 °C. Cell viability was measured by testing the absorbance at 450 nm using a microplate reader (Model 200 PRO, TECAN, USA).

Supplementary Figures S1-S8

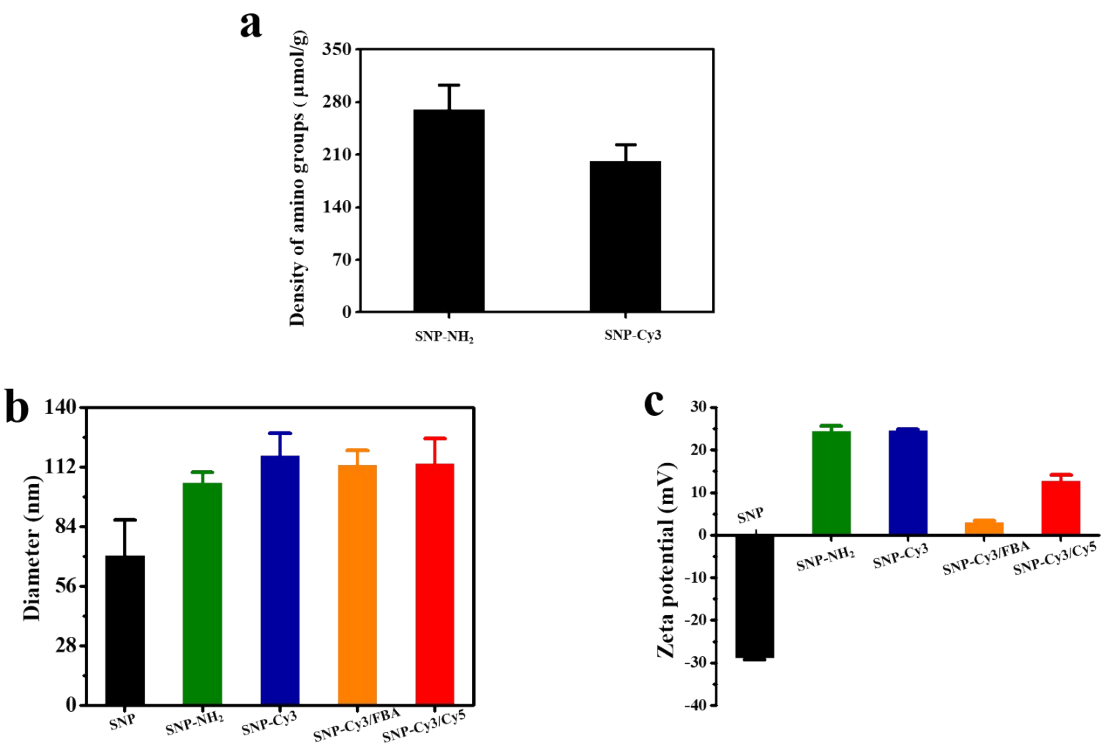

Figure S1. (a) The amounts of amino groups before and after Cy3 modification. (b) Diameters and (c) zeta potentials of nanoparticles from each synthetic step.

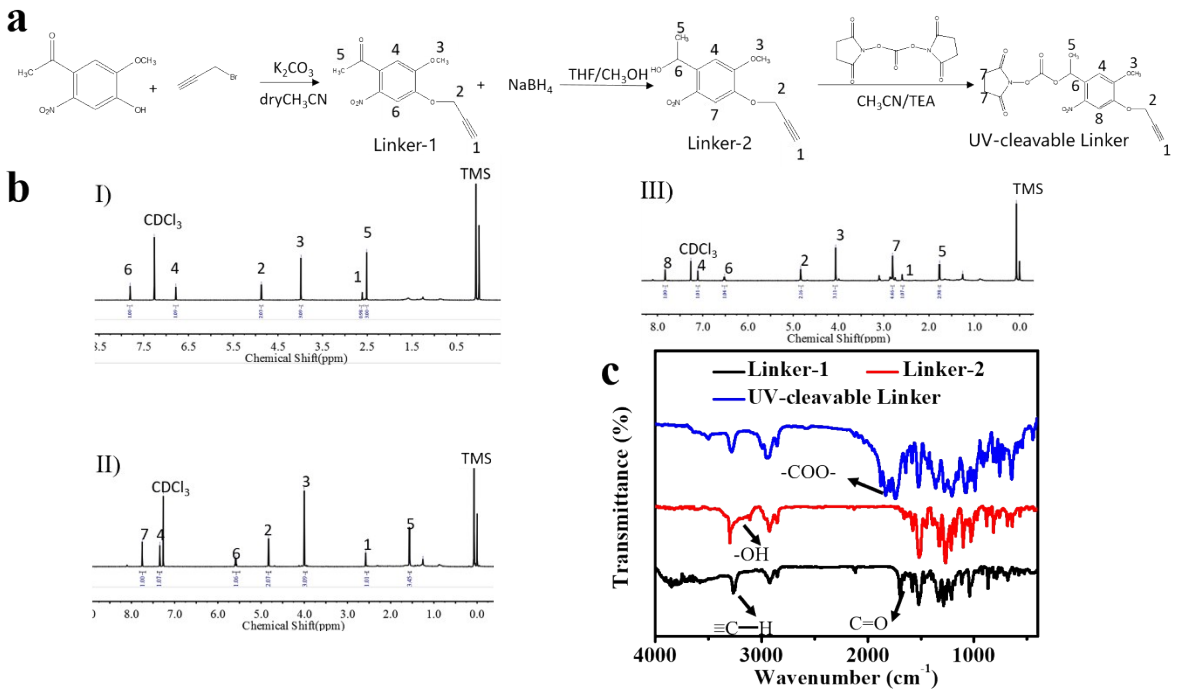

Figure S2. (a) Synthetic route of UV-cleavable Linker. (b) ^{1}H NMR spectra recorded in $CDCl_3$ for Linker-1 (I), Linker-2 (II) and UV-cleavable Linker (III). (c) FTIR spectra of Linker-1, Linker-2 and UV-cleavable Linker.

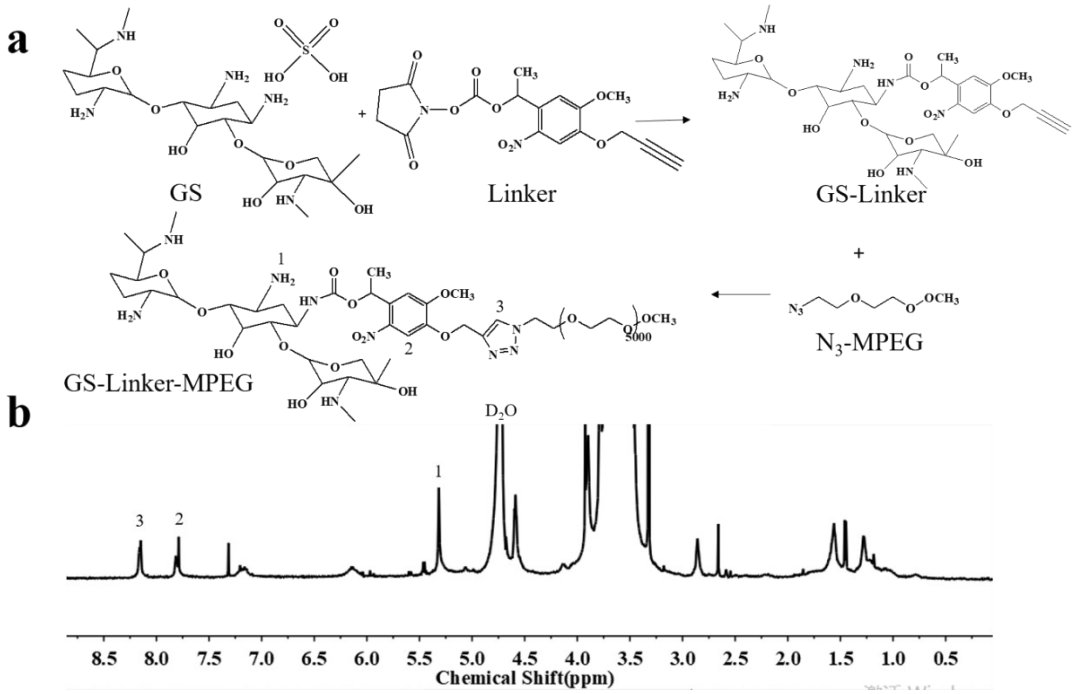

Figure S3. (a) Synthesis route UV-responsive polyprodrug (GS-Linker-MPEG). (b) ^{1}H NMR spectra of GS-Linker-MPEG.

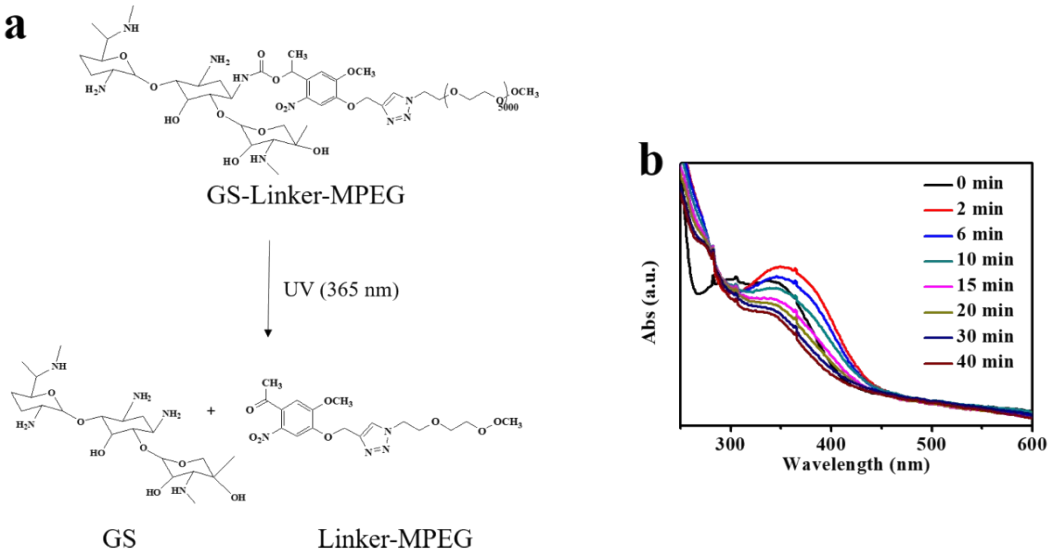

Figure S4. (a) UV-cleavable mechanism of GS-Linker-MPEG. (b) UV-vis absorption spectra of GS-linker-MPEG with the increase of UV irradiation time.

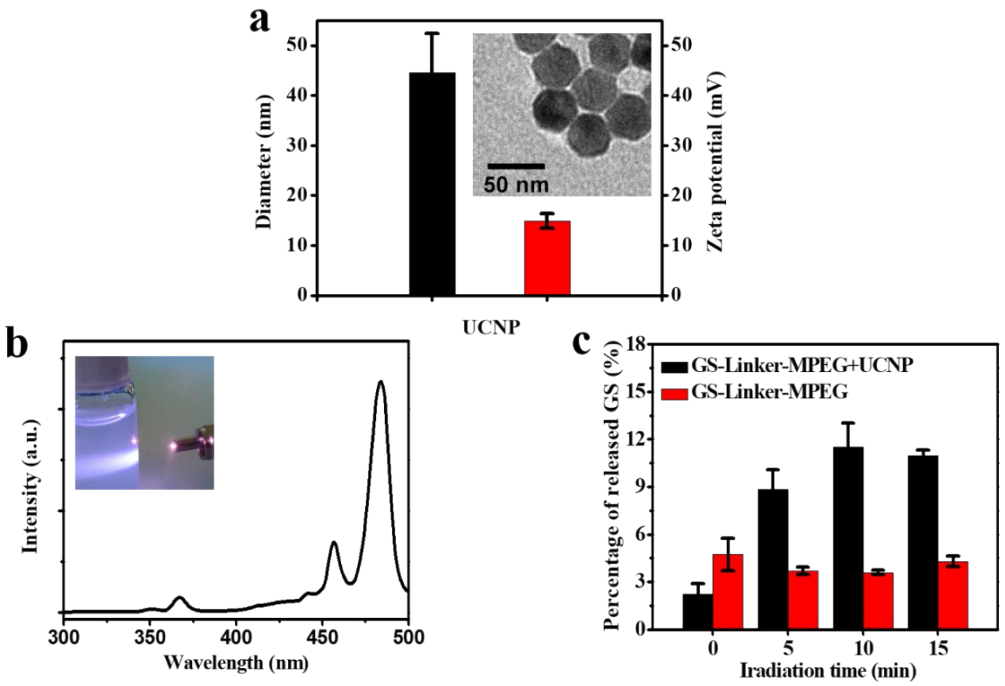

Figure S5. (a) Diameter and zeta potential of UCNP (The inserted image is SEM image of UCNP). (b) Fluorescent spectra of UCNP irradiated by NIR (The inserted image is that UCNP solution irradiated by NIR). (c) The percentage of released GS from solution of UCNP and GS-Linker-MPEG under NIR, and solution without UCNP as control.

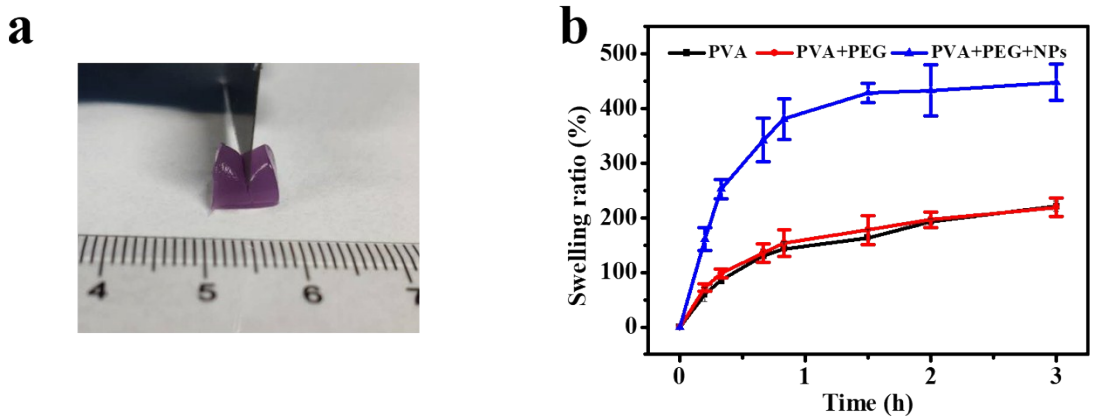

Figure S6. (a) The image that hydrogel was cut by knife. (b) The swelling ratios of hydrogels with immersing time.

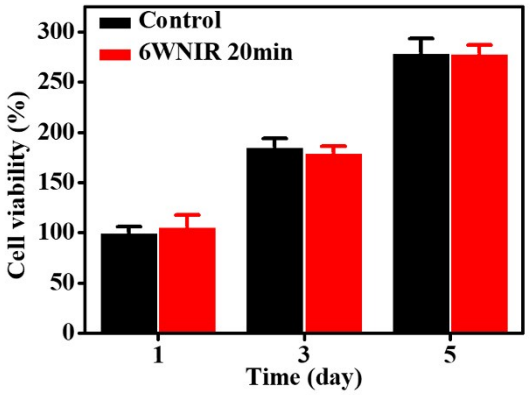

Figure S7. Cell viability of NIH3T3 after exposed to NIR irradiation for 20 min.

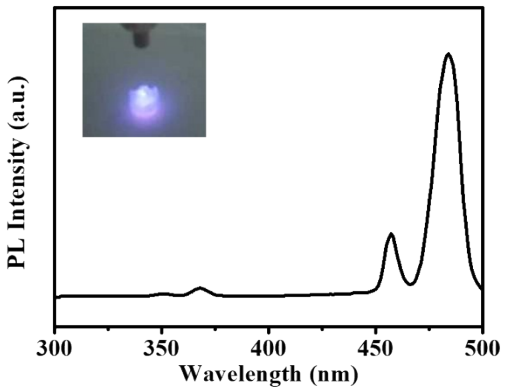

Figure S8. The fluorescent spectra of hydrogels with UCNP (The inserted image is hydrogels irradiated by NIR light).

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