Supporting Information

ROS-Responsive Curcumin-Encapsulated Nanoparticles for AKI Therapy via Promoting Lipid Degradation in the Renal Tubule

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S1. Materials

D-glucosamine hydrochloride, 4-hydroxymethylphenyl boronic acid pinacol ester (HMPBE), 4-cyanopentanoic acid dithiobenzoate (CPADB), azobisisobutyronitrile (AIBN), acryloyl chloride, tetra-n-butylammonium iodide (TBAI), Nile red, hydrogen peroxide (H_2O_2, 3 wt.%), were purchased from Beijing Innochem Technology Co., Ltd. Palmitate, Oil Red O dye was purchased from Sigma-Aldrich. Cy5.5, curcumin (Cur), cis-diaminedichloroplatinum(II) (cisplatin) were purchased from Tianjin Heowns Biotechnology Co., Ltd.. Reactive oxygen species detection fluorescent probe (dihydroethidium, DHE) was purchased from Jiangsu KeyGen Biological Technology Co., Ltd. Lysosome red fluorescence probe (Lyso-tracker Red) was purchased from Shanghai Beyotime Biotechnology Co., Ltd. p62, LC3, ADFP, LAMP2 antibodies were purchased from Abcam, UK. Cleaved-caspase 3 antibody was purchased from Cell Signaling Technology, USA. Donkey Anti-Rabbit (Alexa Fluor® 647) and Goat Anti-Mouse (Alexa Fluor® 647) were purchased from Abcam, UK. Donkey Anti-Rabbit (Alexa Fluor™ 488) and Mito-tracker were purchased from Thermo Fisher, USA. Other reagents were of analytical grade and used as obtained.

S2. Synthesis of 2-(acrylamido) glucopyranose (AGA)

AGA was prepared using the reported method with slight modification. Briefly, *D*-glucosamine hydrochloride (5.0 g, 23.2 mmol), potassium carbonate (3.205 g, 23.2 mmol), and methanol (125 mL) were added into a 250 mL single neck round-bottomed flask. The flask was cooled to 0 °C using an ice bath. Acryloyl chloride (2.1 g, 23.2 mmol) was slowly added into the flask during 30 min under vigorous stirring. The

mixture was vigorous stirred in ice bath for another 30 min and then reacted for 3 h at 25 °C. The crude product was concentrated under reduced pressure to obtain off-white slurry, and purified using silica gel column chromatography. The eluent was ethyl acetate/methanol (v/v, 4:1).

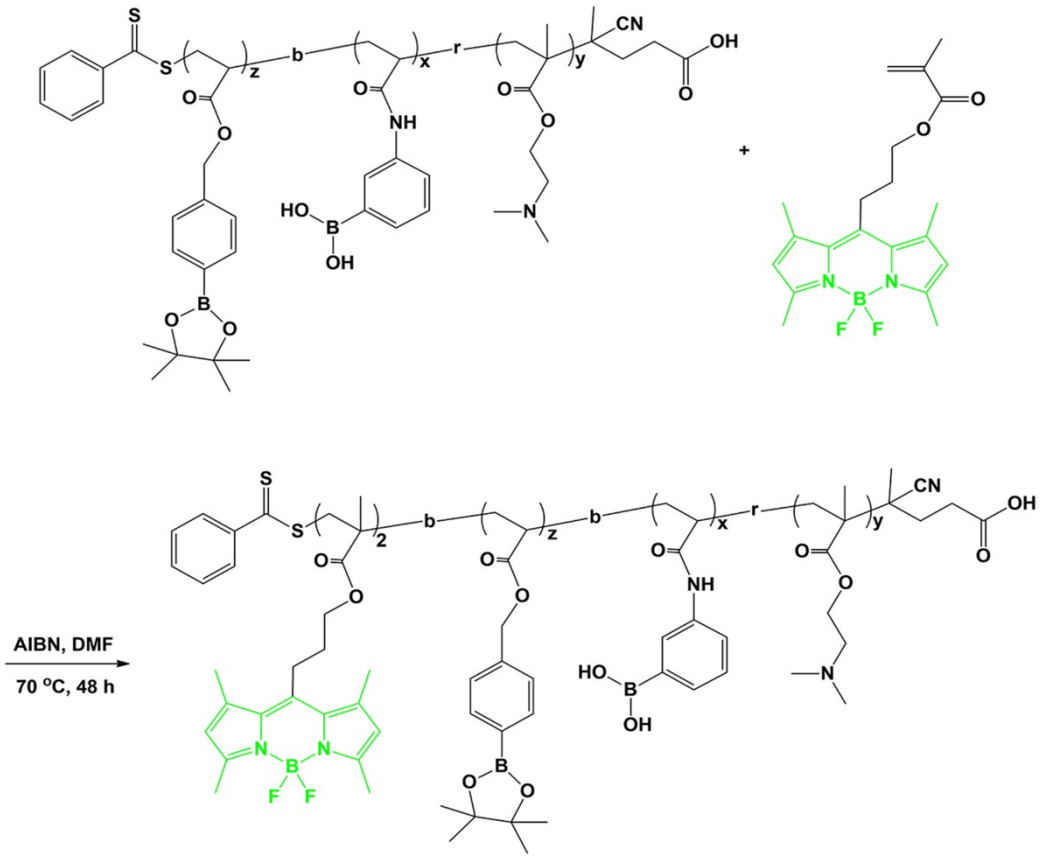
S3. Synthesis of PBAE

4-Hydroxyphenylboronic acid pinacol ester (5.85 g，25 mmol), dry DCM (30 mL), and triethylamine (TEA, 3.05g, 30 mmol) were added into a dry flask in an ice bath. Acryloyl chloride (2.7 g, 30 mmol) was dissolved in anhydrous DCM (2.5 mL), and added dropwise into the flask. The system was reacted for 10 h at 25 °C. After that, the mixture was filtrated, concentrated via rotary evaporation, extracted with diethyl acetate, washed with salt water, and dried with anhydrous magnesium sulfate. The crude product was purified with silica gel column chromatography, and the eluent was petroleum ether/diethyl acetate (v/v, 30:1).

S4. Synthesis of PAGA-*b*-PPBAE-*b*-BODIPY

PAGA-*b*-PPBAE-*b*-BODIPY was prepared by RAFT polymerization using AIBN as the initiator, PAGA-b-PPBAE as the macromolecular RAFT agent, and BODIPY as the monomer. AIBN (1.6 mg, 0.01 mmol), PAGA-b-PPBAE-RAFT (167.5 mg, 0.02 mmol), and BODIPY (14.8 mg, 0.04 mmol) were added to a polymerization reaction vial and dissolved in DMF (1.5 mL). The reaction mixture was purged with argon gas for 30 minutes, and after removing the air from the vial, the reaction vial was placed in a 70 °C water bath for 48 hours. After the reaction, the reaction solution was precipitated and dried in petroleum ether three times to obtain the BODIPY-labeled

polymer PAGA-b-PPBAE-b-BODIPY.



Scheme S1. Synthetic route of (PDMAEMA-*r*-PAAPBA)-*b*-PPBAE-*b*-BODIPY

S5. Preparation of NPS_{BG}-BODIPY@Cy5.5

Cy5.5-loaded nanoparticles were prepared for localization and distribution imaging in mouse kidneys. PAGA-*b*-PPBAE-*b*-BODIPY was dissolved in a mixed solvent of DMSO/H_2O (v/v, 25:1) to obtain a 50 mg/mL polymer solution. Cy5.5 was dissolved in DMSO to obtain a drug solution of 5 mg/mL. PAGA-*b*-PPBAE-*b*-BODIPY (0.16 mL, 50 mg/mL) and Cy5.5 (0.16 mL) solutions were thoroughly mixed. Under ultrasound, 2 mL of PBS buffer (pH 7.4) was added dropwise to the mixed solution. Then, the solution was placed in a dialysis bag (MWCO = 3500) and dialyzed for 24 hours, resulting in a solution of Cy5.5-loaded nanoparticles named NPS_{BG}-BODIPY@Cy5.5.

S6. Preparation of NPS_{BG} @Cy5.5

Cy5.5-loaded nanoparticles were prepared for localization and distribution imaging in mouse kidneys. PAGA-*b*-PPBAE was dissolved in a mixed solvent of DMSO/H_2O (v/v, 25:1) to obtain a 50 mg/mL polymer solution. Cy5.5 was dissolved in DMSO to obtain a drug solution of 5 mg/mL. PAGA-b-PPBAE (0.16 mL, 50 mg/mL) and Cy5.5 (0.16 mL) solutions were thoroughly mixed. Under ultrasound, 2 mL of PBS buffer (pH 7.4) was added dropwise to the mixed solution. Then, the solution was placed in a dialysis bag (MWCO = 3500) and dialyzed for 24 hours, resulting in a solution of Cy5.5-loaded nanoparticles named NPS_{BG}-BODIPY@Cy5.5.

S7. Characterization of monomer, polymer and nanoparticle

^1H NMR spectra were recorded at room temperature using a Bruker 600M NEO NMR spectrometer. The hydrodynamic diameter (D_H) was characterized by dynamic light scattering (DLS) analysis using a Brookhaven 90 Plus PALS. The morphological characteristics of the nanoparticles were observed using a transmission electron microscopy (TEM) system (Philips EM400ST).

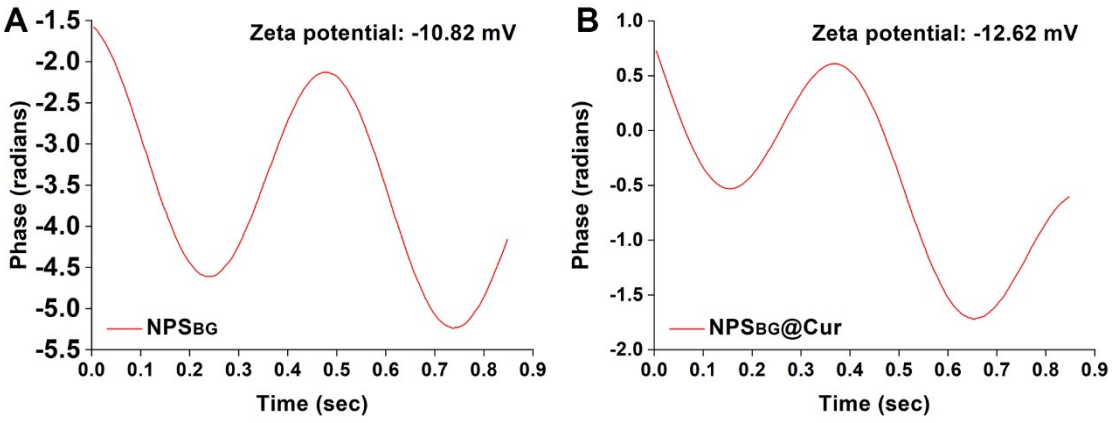


Figure S1. The zeta potential of (A) NPS_{BG} and (B) NPS_{BG}@Cur.

S8. The aggregation of Cy5.5 in the kidney

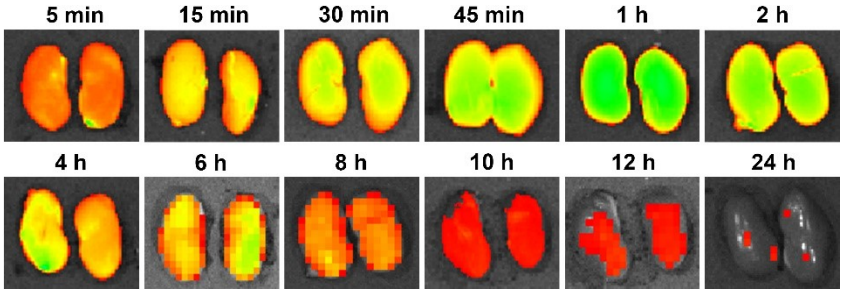


Figure S2. Ex vivo fluorescence images of kidneys collected from Cy5.5-treated AKI mice at the predetermined times.