

Supplementary Information (SI) for Nanoscale.

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Kidney Functional Stages Influence the Role of PEG End-group on the Renal Accumulation and Distribution of PEGylated Nanoparticles

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Table S1 AKI stage is defined by different creatinine increase ratios.

AKI stage	Increase rate of creatinine concentration
AKI stage 1/2	1.5 - 3
AKI stage 3	3 - 6
AKI stage 4	> 6

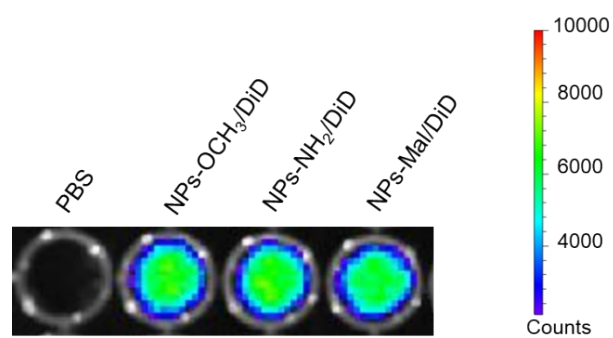


Fig. S1 Fluorescence images of PBS, NPs-OCH₃/DiD, NPs-NH₂/DiD, and NPs-Mal/DiD.

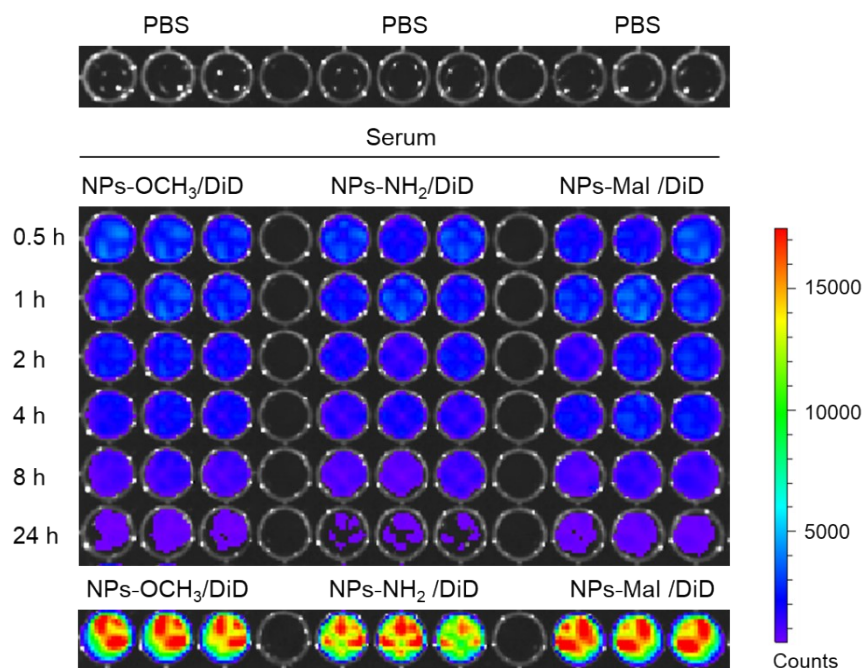


Fig. S2 Fluorescence images of NPs-OCH₃/DiD, NPs-NH₂/DiD, and NPs-Mal/DiD in serum. The blood was harvested from mice at 0.5h, 1 h, 2 h, 4 h, 8 h, and 24 h after *i.v.* injection of NPs-OCH₃/DiD, NPs-NH₂/DiD, and NPs-Mal/DiD, and serum was obtained by centrifugation. The DiD fluorescent images of serum and NPs/DiD were obtained on an IVIS imaging system (n = 3 per group).

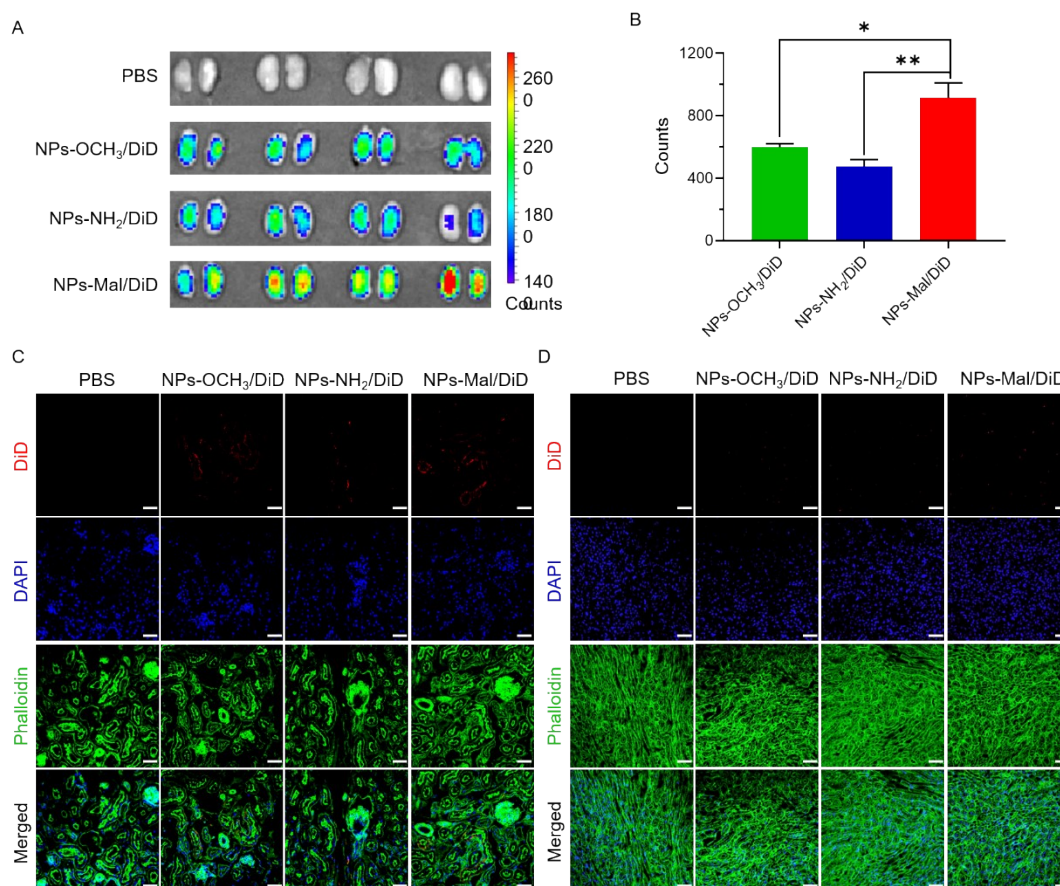


Fig. S3 The PEG end-group significantly affects the accumulation and distribution of PEGylated NPs in kidney. (A, B) Fluorescence images (A) and fluorescence intensity (B) of the blood-perfused kidneys harvested from C57BL/6 mice at 24 h after intravenous injection of PBS, NPs-OCH₃/DiD, NPs-NH₂/DiD, or NPs-Mal/DiD (n = 4 per group). (C, D) Representative confocal laser scanning microscopy (CLSM) images showing the distribution of NPs-OCH₃/DiD, NPs-NH₂/DiD, and NPs-Mal/DiD in the renal cortex (C) and renal medulla (D) in the kidneys after blood perfusion. The cell nuclei were stained with DAPI (blue), and the cytoskeleton was stained with AF555-phalloidin (green). Scale bar, 50 μ m. The proximal tubular cells were stained with fluorescein labeled phaseolus vulgaris erythroagglutinin (green). Scale bar, 10 μ m. Data are presented as mean \pm SEM. *, $p < 0.05$; **, $p < 0.01$.

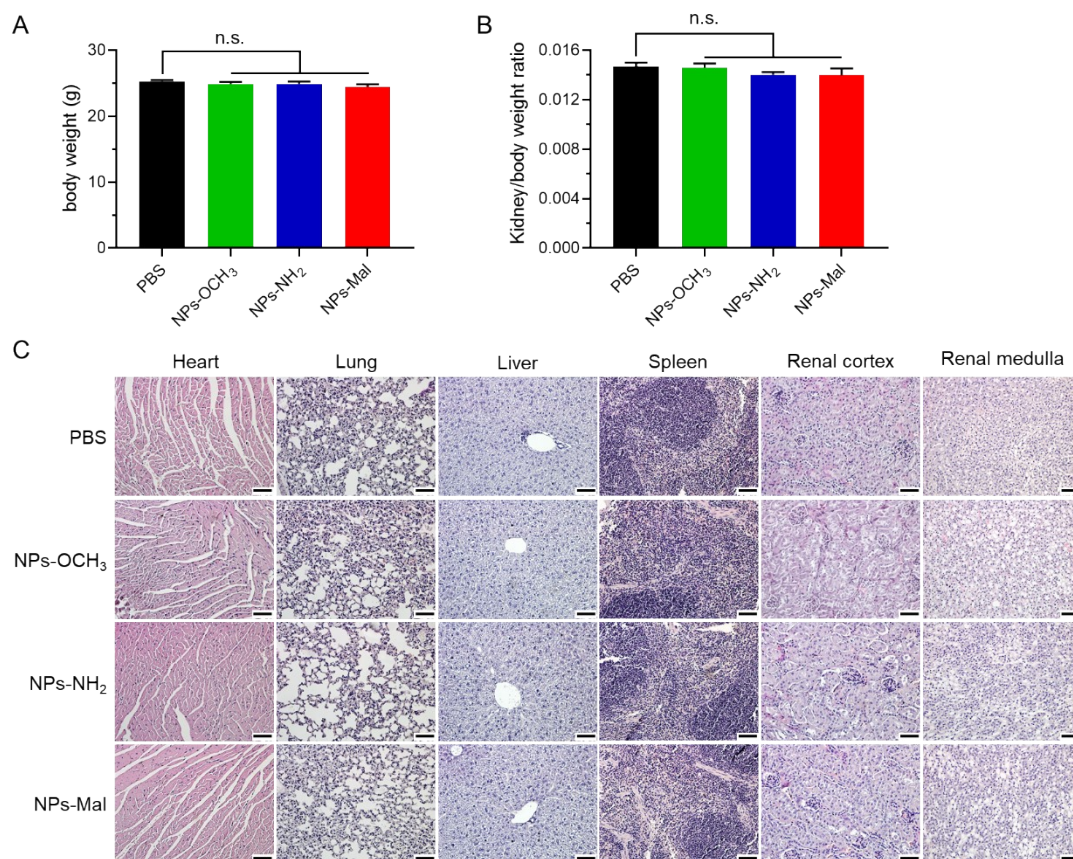


Fig. S4 The PEGylated nanoparticles with different PEG end-groups show undetectable toxicity *in vivo*. (A) The body weight and (B) kidney/body weight ratios of normal mice at 24 h after the intravenous injection of PBS, NPs-OCH₃, NPs-NH₂, or NPs-Mal (n = 7 to 11 per group). (C) Representative H&E staining images of heart, lung, liver, spleen and kidney sections harvested from the normal mice at 24 h after *i.v.* injection of PBS, NPs-OCH₃, NPs-NH₂, or NPs-Mal. Scale bar, 20 μ m. Data are presented as mean \pm SEM. n.s., not significant.

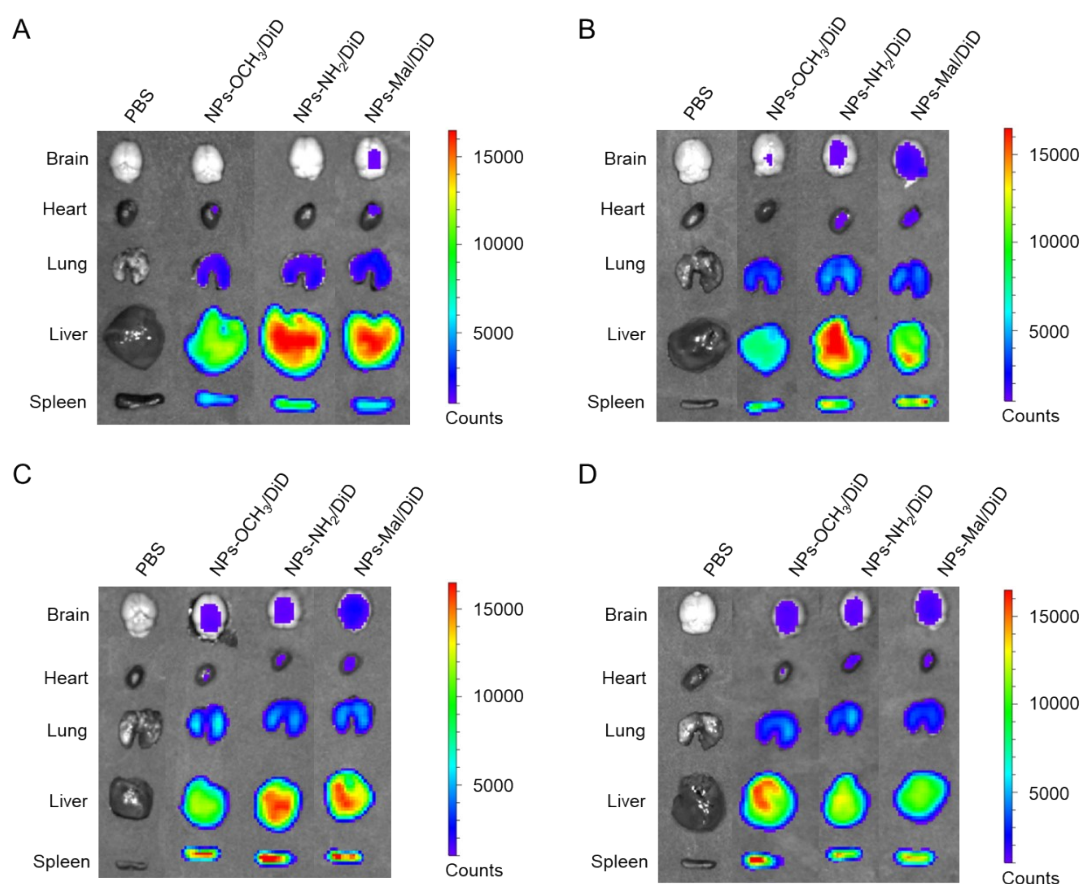


Fig. S5 The bio-distribution of PEGylated NPs with different PEG end-groups in mice with or without AKI. Representative fluorescence images of brains, hearts, lungs, livers, and spleens harvested from normal mice (A), mice with stage-1/2 AKI (B), mice with stage-3 AKI (C), and mice with stage-4 AKI (D) at 24 h after the intravenous injection of PBS, NP_s-OCH₃/DiD, NP_s-NH₂/DiD, or NP_s-Mal/DiD.

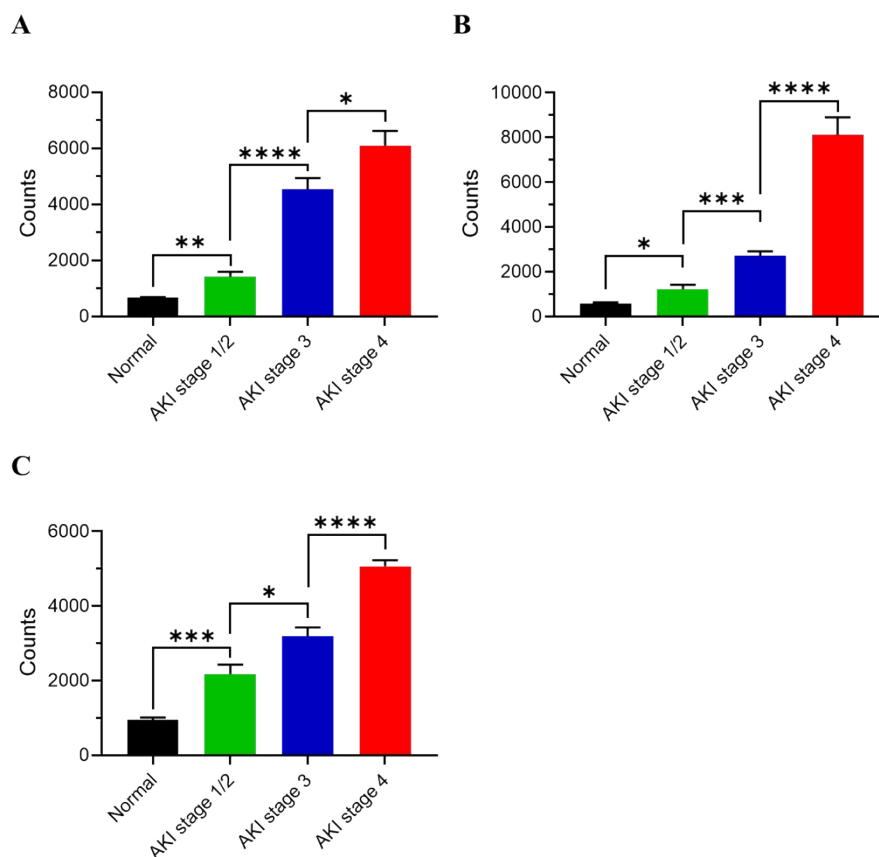


Fig. S6 Renal accumulation of PEGylated NPs increases with the aggravation of kidney damage. Fluorescence intensity of kidneys harvested from normal and AKI mice at 24 h after intravenous injection of NPs-OCH₃/DiD (A), NPs-NH₂/DiD (B), and NPs-Mal/DiD (C) in Fig. 2B, 4A, 5A, and 6A (n = 4 to 5 per group). Data are presented as mean ± SEM. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.