

Supporting Information

A Stimuli-Responsive Drug Release Nanoplatform for Kidney-Specific Anti-Fibrosis Treatment

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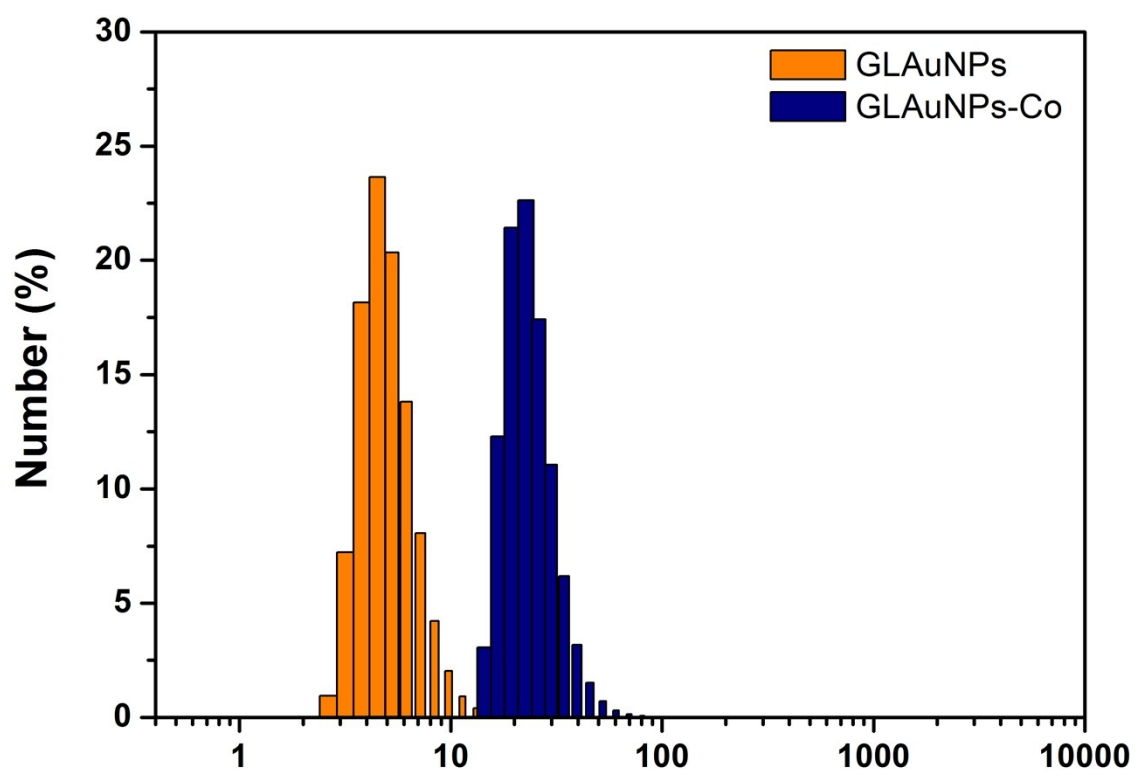


Fig. S1. Hydrodynamic size distributions of GLAuNPs and GLAuNPs-Co.

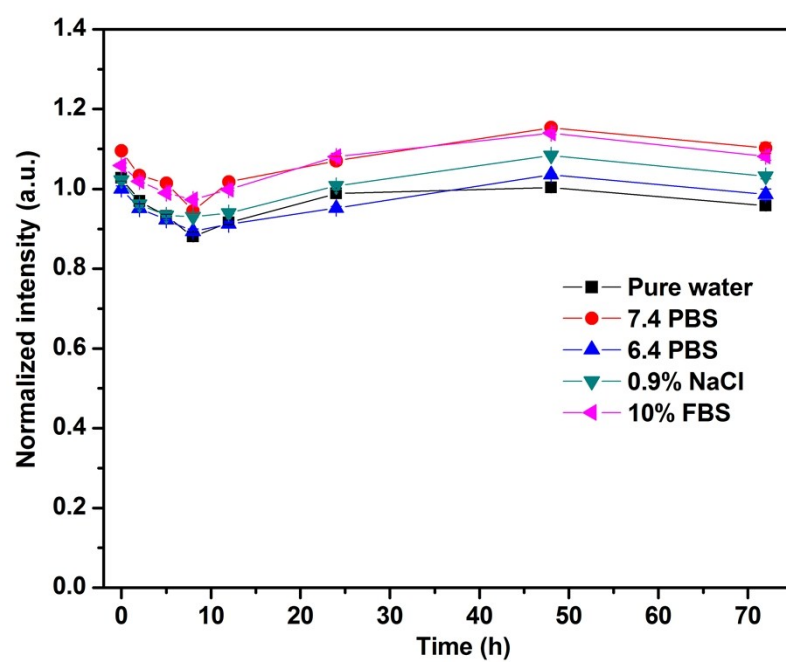


Fig. S2. Normalized fluorescence spectrum intensities of the GLAuNPs-Co at different time in different mediums.

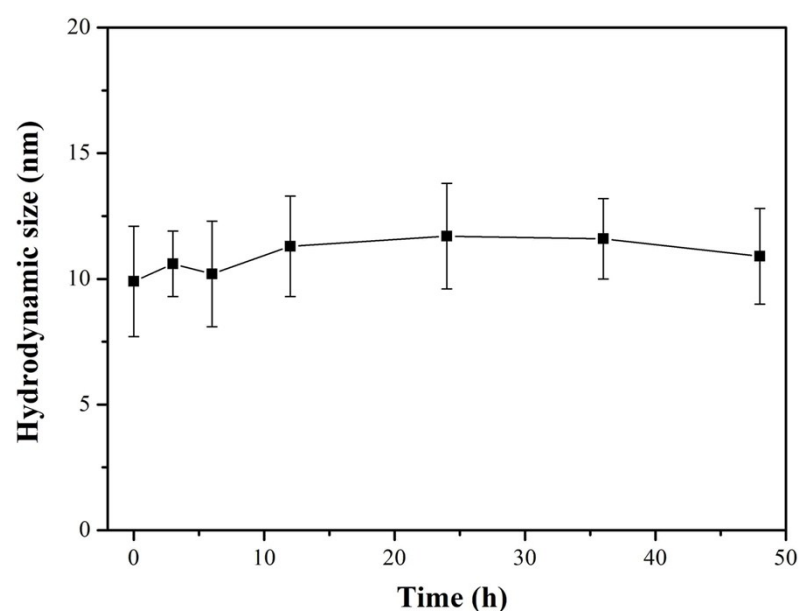


Fig S3. Hydrodynamic size of GLAuNPs-Co at predetermined time points.

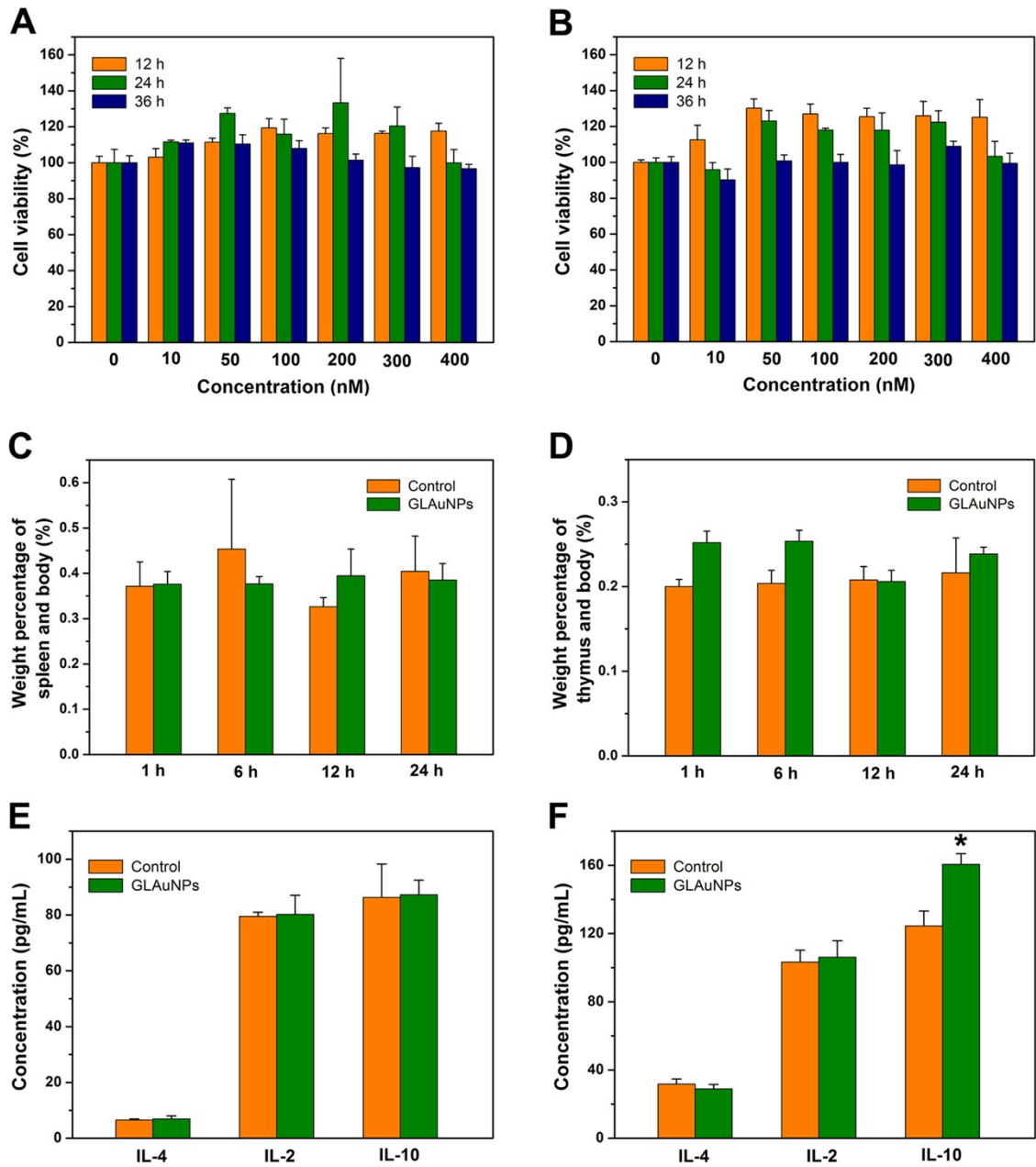


Fig. S4. (A,B) *In-vitro* cytotoxicity of NRK-52E and NRK-49F cells treated with GLAuNPs in a range of concentrations (0-400 nM) for 12, 24 and 36 h, respectively. (C,D) Weight percentages of spleen and thymus in whole body post injected with normal saline or GLAuNPs in 1, 6, 12 and 24 h, respectively. (E,F) IL-2, IL-4 and IL-10 levels in supernatants of primary splenocytes after incubation with normal saline or GLAuNPs for 12 and 24 h.

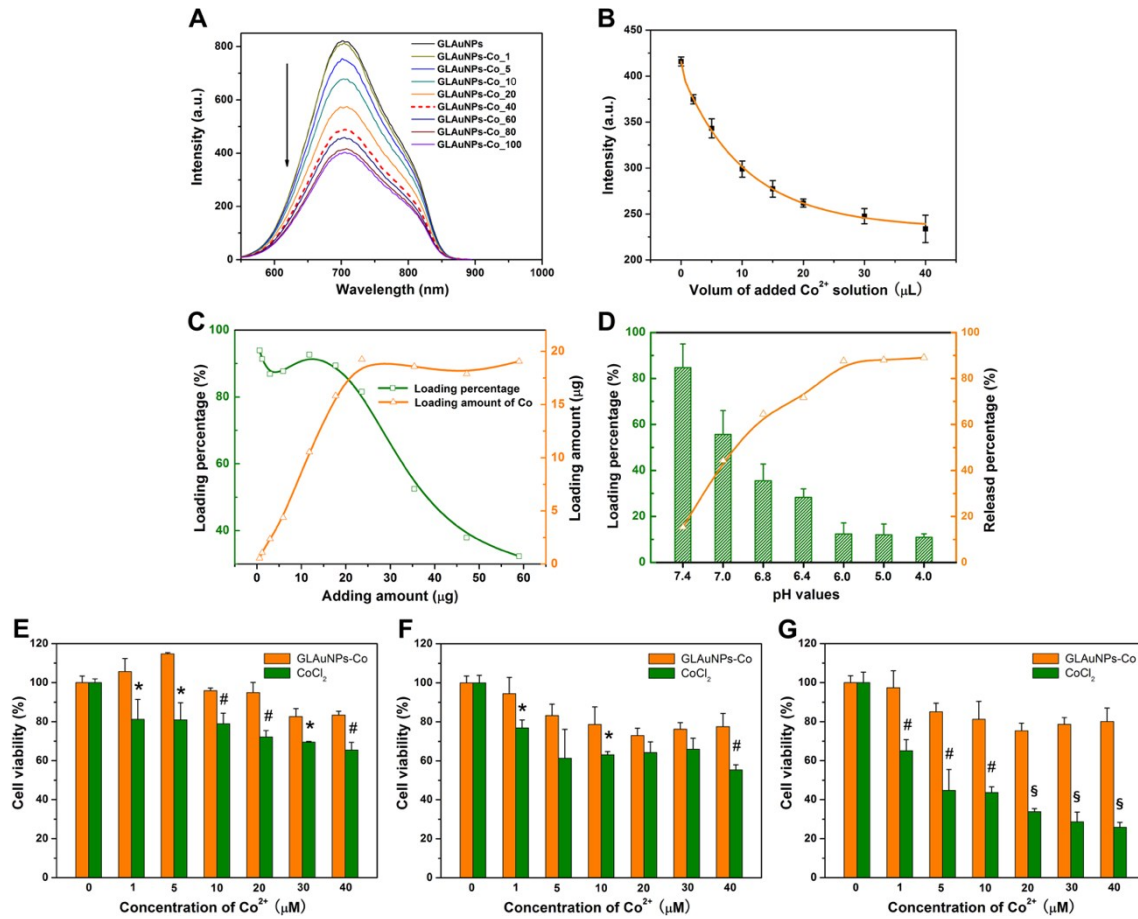


Fig. S5. (A) Fluorescence spectrum and (B) corresponding fluorescence emission intensity at 700 nm of GLAuNPs-Co_x (x represents volume (μL) of 10 mM CoCl₂). (C) Loading percentage and amount curves of Co²⁺ on GLAuNPs. (D) Loading and releasing efficiency of GLAuNPs-Co under different pHs. (E-G) Cell viability treated with GLAuNPs-Co or CoCl₂ at different Co²⁺ concentration for 12, 24 and 36 h, respectively. Data are expressed as mean ± SD, n=5. **p* < 0.05, #*p* < 0.01, §*p* < 0.001 versus same concentration and time incubation group.

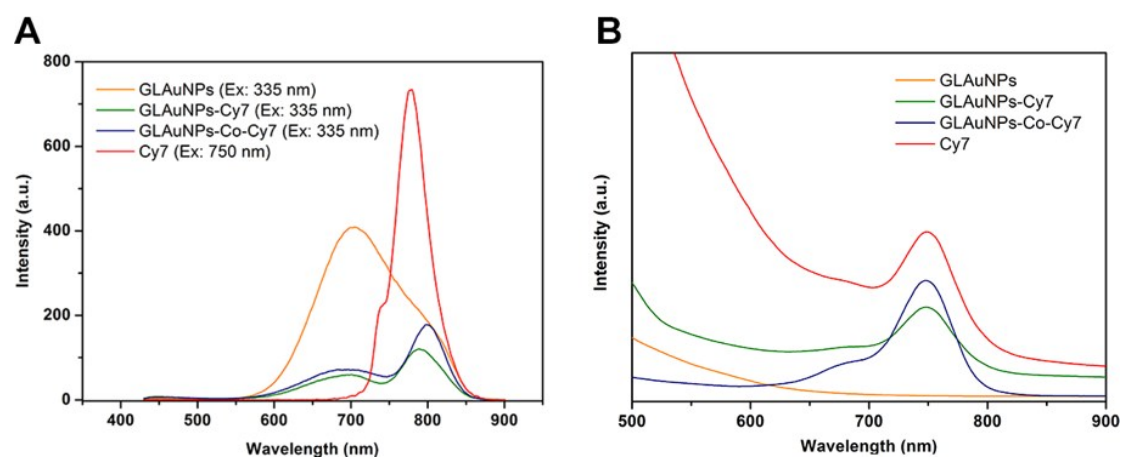


Fig. S6. (A) Fluorescence spectra and (B) UV-visible of GLAuNPs, GLAuNPs-Cy7, GLAuNPs-Co-Cy7 and Cy7, respectively.

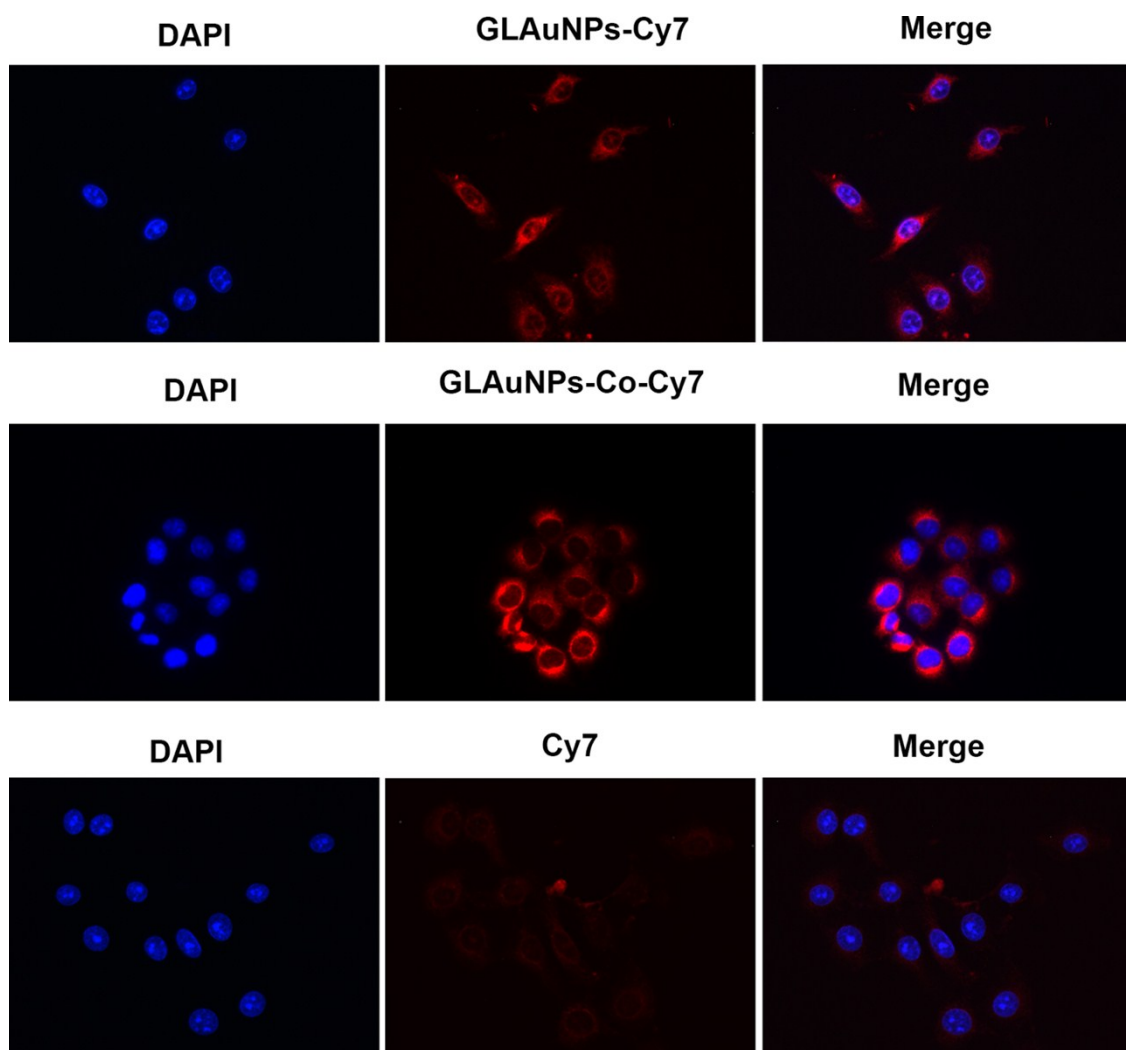


Fig. S7. Cell fluorescence images of GLAuNPs-Cy7, GLAuNPs-Co-Cy7 and Cy7 incubated with NRK-52E cells for 2 h.

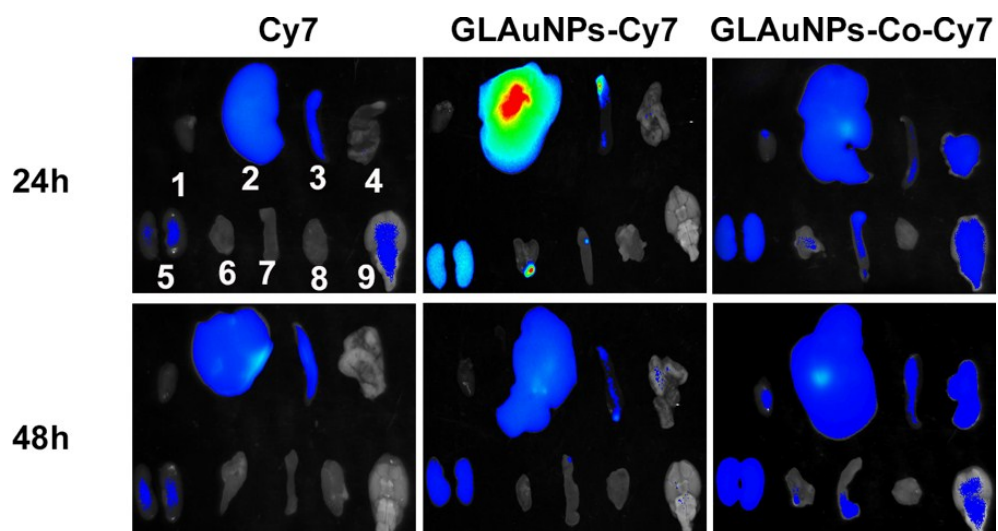


Fig. S8. *Ex-vivo* fluorescence imaging of major organs collected from mice injected with Cy7, GLAuNPs-Cy7 or GLAuNPs-Co-Cy7 at different time intervals of 24 and 48 h (1-9: heart, liver, spleen, lung, kidneys, thymus, small intestine, muscle and brain).

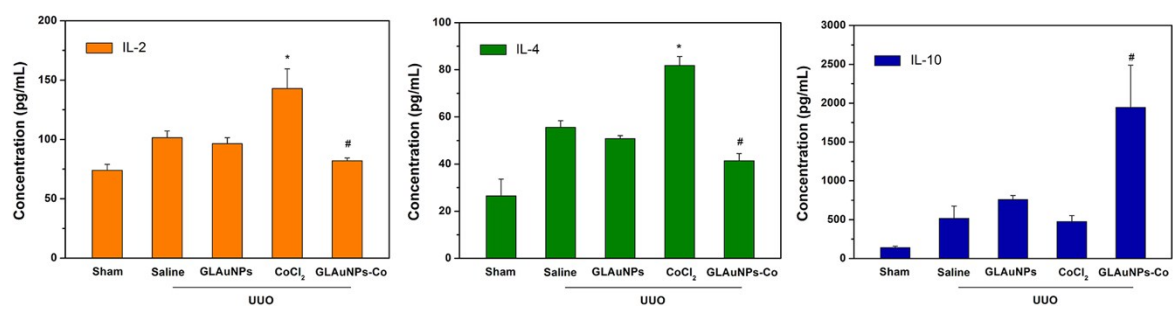


Fig. S9. (A) IL-2, (B) IL-4 and (C) IL-10 levels of mice serum after different interventions.

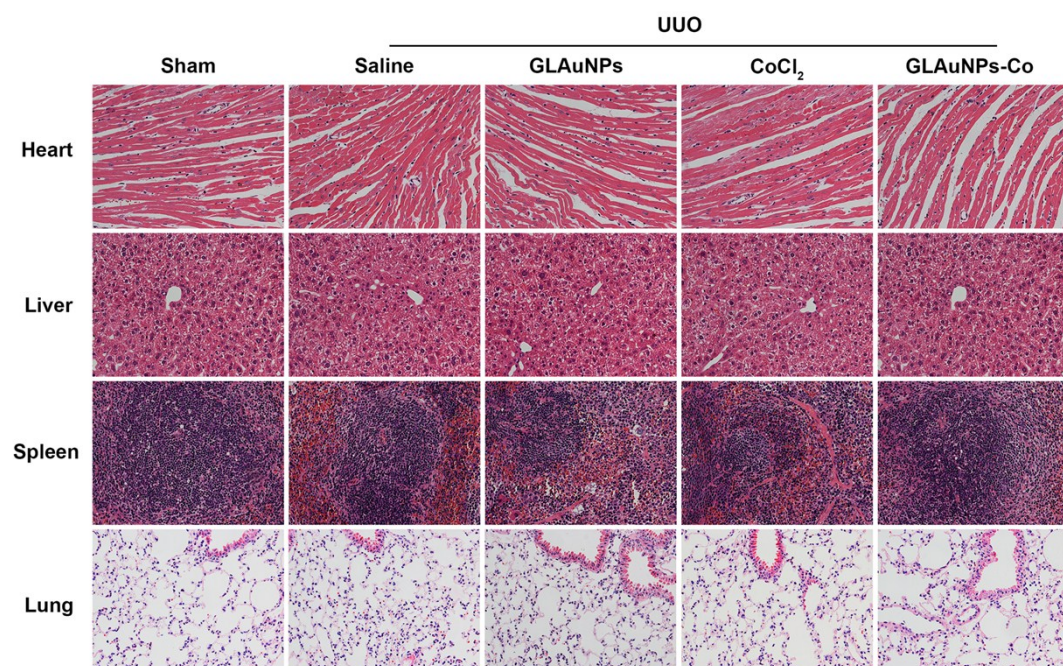


Fig. S10. Histological section images of major organs collected from mice receiving different treatments by H&E staining (200×).

Table S1. NRK-52E cell viability percentages cultured with different concentrations GLAuNPs-Co for 12h, 24h, 36h, respectively.

nM	12 h	24 h	36 h
800	115.9 $\pm$ 2.8	99.4 $\pm$ 1.5	95.0 $\pm$ 4.7
1200	112.9 $\pm$ 2.9	102.4 $\pm$ 4.4	88.1 $\pm$ 3.6
1600	115.2 $\pm$ 3.4	107.8 $\pm$ 1.6	82.1 $\pm$ 1.5
2000	115 $\pm$ 3.4	101.5 $\pm$ 10.3	82.7 $\pm$ 1.8
2400	112.9 $\pm$ 1.7	97.3 $\pm$ 4.4	75.9 $\pm$ 1.8

Table S2. Primers used for quantitative Real-time PCR

	Forward	Reverse
GAPDH	GGTGAAGGTCGGTGTGAACG	CTCGCTCCTGGAAGATGGTG
HIF-1 α	AGGATGAGTTCTGAACGTCGA AA	CTGTCTAGACCACCGGCATC
EPO	AGTCGCGTTCTGGAGAGGTA	AGGATGGCTTCTGAGAGCAG
Collagen-I	ATCTCCTGGTGCTGATGGAC	ACCTTGTTTGCCAGGTTTAC
Fibronectin	CGAGGTGACAGAGACCACAA	CTGGAGTCAAGCCAGACACA
Tie-2	GACTGTTACCGCCTGCTTCT	GGCGCCTTCTACTACTCCATA
HO-1	GGCTTTAAGCTGGTGATGGC	CCTGAGAGGTCACCCAGGTA
TPM-1	GCTGAGCTCTCAGAAGGCAA	CCGAGTTTCAGCCTCCTTCA
COL2A1	TGACTGTCCCACGTAAGCAC	GAGGGCCATAGCTGAACTGA