Supplementary Information

Convection-enhanced delivery of a virus-like nanotherapeutic agent with dual-modal imaging for besiegement and eradication of brain tumors

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Tables. S1 and S2

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Table S1. Primers used for pCDFDuet-1-QβCP- GFP construction

Primer name	Primer sequence
QβCP-Fwd	5'-GTGGCCATGGATGGCAAAATTAGAGACTGTTA-3'
QβCP-Rev	5'-CACCAAGCTTTCAATACGCTGGG-3'
GFP-Fwd	5'-GTGGAGATCTCATGGCTAGCAAAGGAGAAGAACTC-3'
GFP-Rev	5'-CACCCCTAGGTCAGTTGTACAGTTCATCCATGCC-3'

Restriction sites: QβCP-Fwd (NcoI), QβCP-Rev (HindIII), GFP-Fwd (BglII), GFP-Rev (AvrII)

Table S2. Characterization of gVLPs, EPI@gVLPs, and EPI@CPP-gVLPs by dynamic light scattering (n = 3)

	Size average (nm)	PDI	Zeta potential (mV)
gVLPs	32.1±0.6	0.11±0.05	-0.71±0.36
EPI@gVLPs	33.2±0.2	0.18±0.02	-0.87±0.41
EPI@CPP-gVLPs	40.3±0.5	0.27±0.04	0.03±0.05

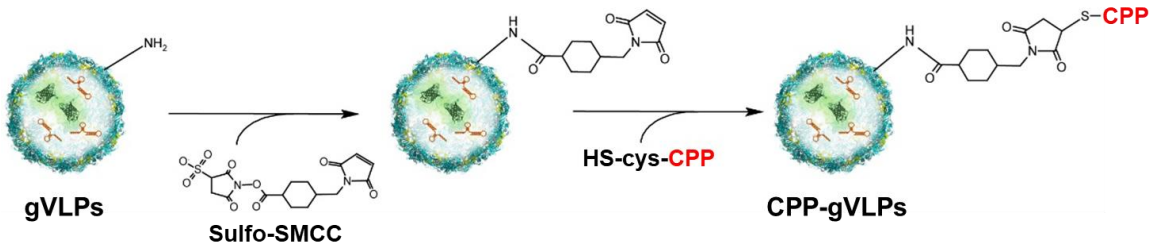


Figure S1. Chemical structural formula of each component and preparation of the CPP-modified gVLPs (CPP-gVLPs) using sulfo-SMCC as a linker

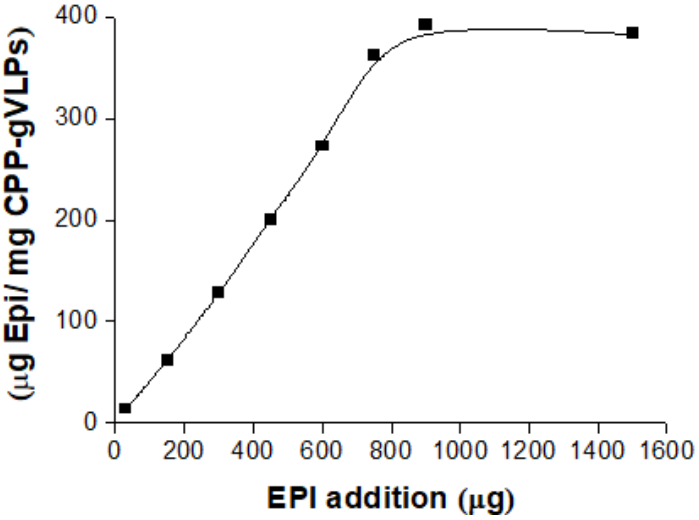


Figure S2. Quantitation of loaded EPI in 1 mg of CPP-gVLPs versus added EPI

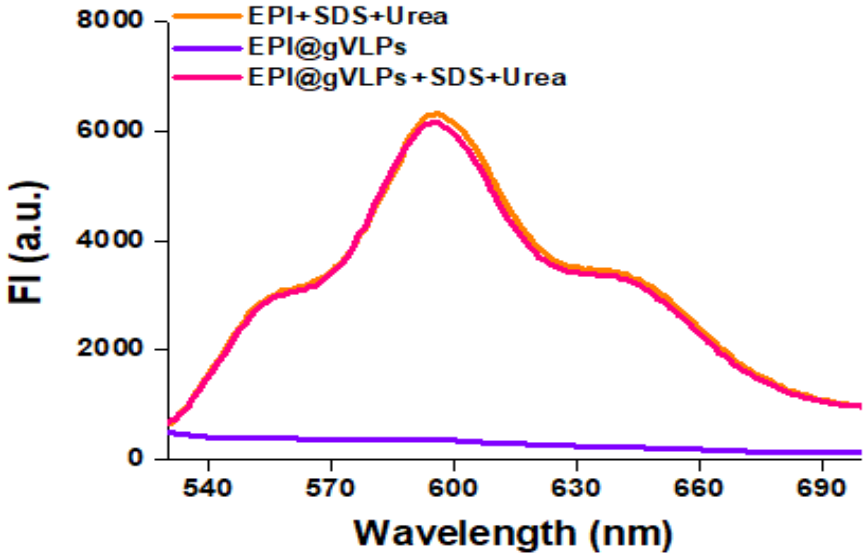


Figure S3. The fluorescence spectra of EPI+SDS+Urea, EPI@gVLPs, and EPI@gVLPs+SDS+Urea under excitation at 480 nm. SDS (10%, 10 μL) and Urea (8 M, 10 μL) were added both for protein and RNA denaturing to simulate the situation that VLPs after being up-taken by cells and destroyed followed by EPI release

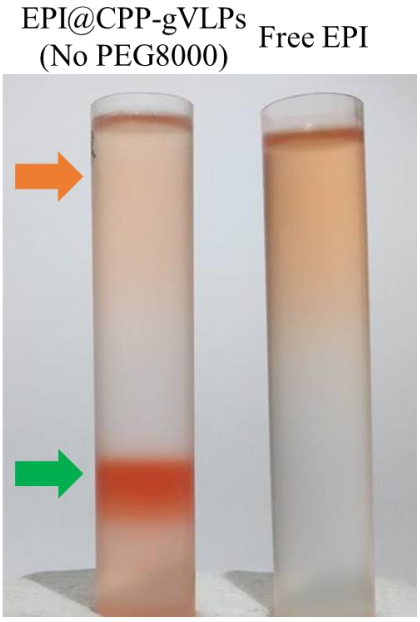


Figure S4. Ultracentrifugation of EPI@CPP-gVLPs without PEG8000/NaCl purification process; the orange arrow indicates free EPI and the green arrow indicates EPI@CPP-gVLPs

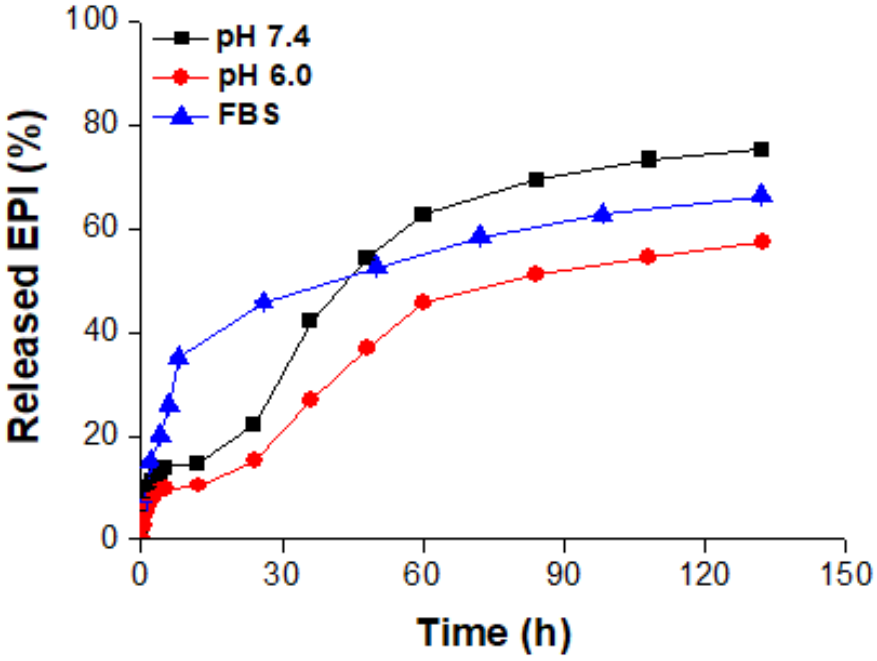


Figure S5. EPI release from EPI@CPP-gVLPs (EPI concentration, 0.23 mg/mL) in 10.4 mL of PBS (pH 6.0 or 7.4) and FBS for a period of incubation at 37℃

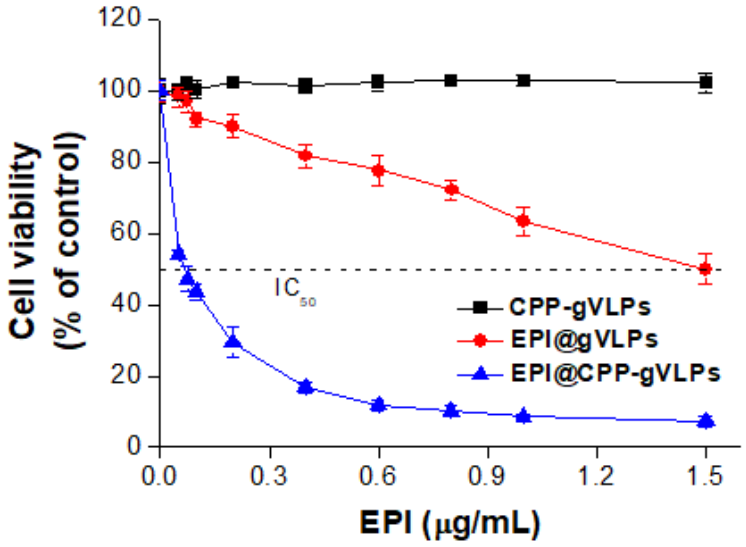
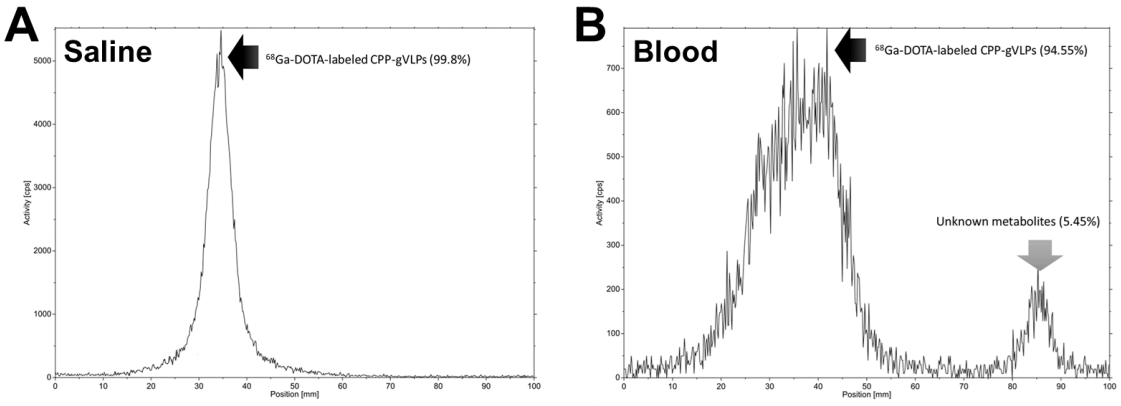


Figure S6. Cell viability of U87-MG cells treated with CPP-gVLPs, EPI@gVLPs, and EPI@CPP-gVLPs for 24 h by XTT assay



^{68}Ga-DOTA-labeled CPP-gVLPs	2 h after labeling
Saline	99.80%
Blood	94.55%*

* The 5.45% of unknown metabolites was identified in the late phase radio-TLC profile.

Figure S7. Stabilities of ^{68}Ga-DOTA-labeled CPP-gVLPs suspended in (A) saline and (B) blood for 2 h after ^{68}Ga-DOTA labeling

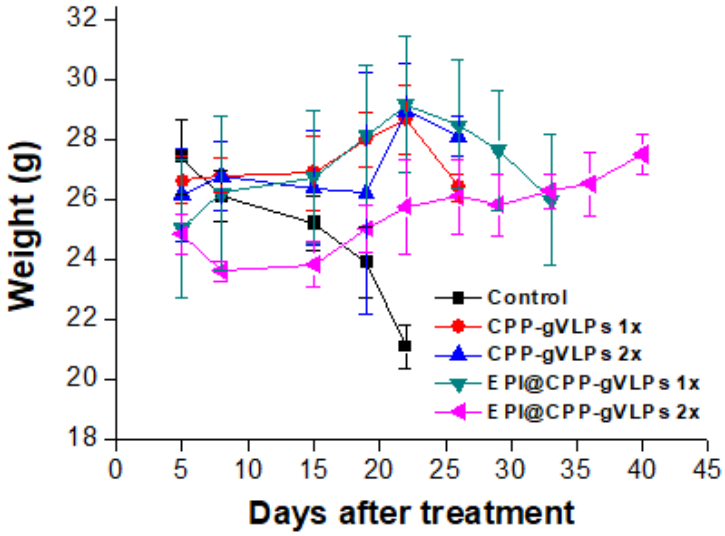


Figure S8. Body weights of mice that received CED infusions of PBS (control), 3.6 mg/kg of CPP-gVLPs, 3.6 mg/kg of CPP-gVLPs (twice; once a week), 5.0 mg/kg of EPI@CPP-gVLPs (containing 1.4 mg of EPI/kg), and 5.0 mg/kg of EPI@CPP-gVLPs (containing 1.4 mg of EPI/kg; twice; once a week)

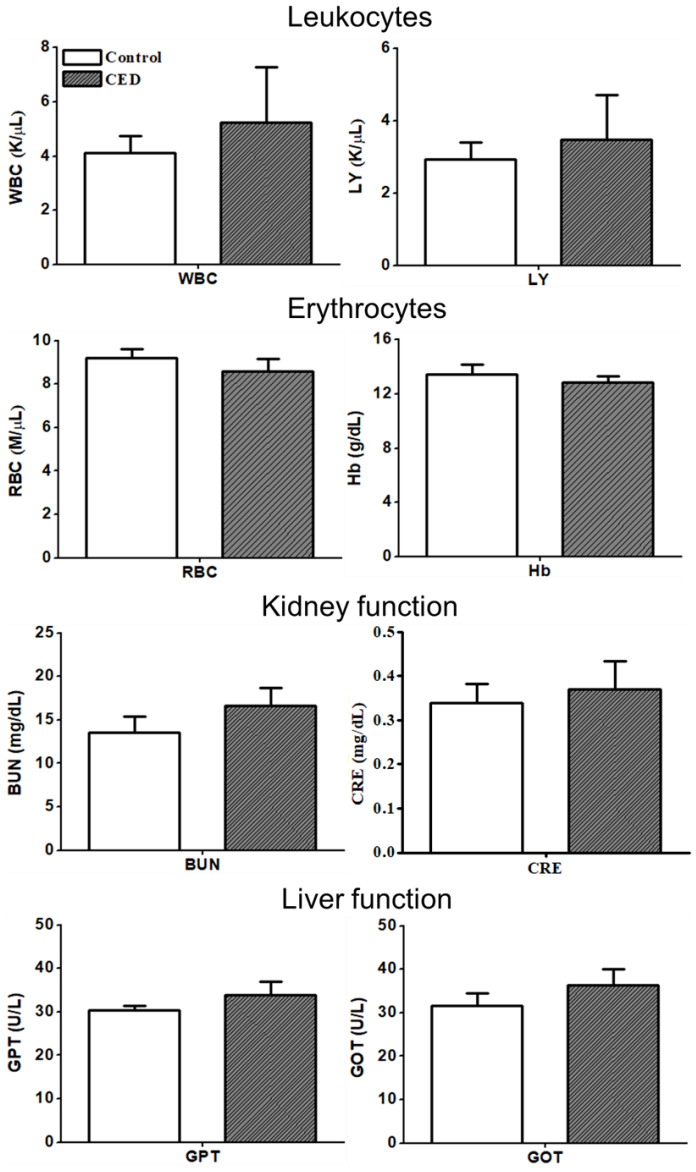


Figure S9. Blood-biochemistry analysis of the animals after 7 days of CPP-gVLPs administration through the tail vein or CED compared with the control group. Values are expressed as means ± SD (n = 3). WBC: white blood cells (normal: approximately 1.8–10.7 K/μL); LY: lymphocytes (normal: approximately 0.9–9.3 K/μL); RBC: red blood cells (normal: approximately 6.4–9.4 M/μL); Hb: hemoglobin (normal: approximately 11.0–15.1 g/dL); BUN: blood urea nitrogen (normal: approximately 6.0–21.0 mg/dL);

CRE: creatinine (normal: approximately 0.3–1.5 mg/dL); GPT: glutamic-pyruvic transaminase (normal: approximately 0–44.0 U/L); GOT: glutamic-oaa transaminase (normal: approximately 0–38.0 U/dL).