Supporting Information

Sequential administration of virus-like particle-based nanomedicine to elicit enhanced tumor chemotherapy

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Supplementary Table 1. Characterization of multiple VLPs

VLPs	DOX-loading(%)	Particle size(nm)	PDI
HBc	-	30.43±1.90	0.228±0.008
RGD-HBc	-	28.79±2.44	0.218±0.008
RGD-WHc	-	32.83±2.06	0.225±0.004
RGD-DHBc	-	24.17±3.22	0.232±0.015
DOX@RGD-HBc	9.46±1.11	30.00±2.12	0.347±0.006
DOX@RGD-WHc	15.21±2.24	27.72±2.45	0.339±0.012
DOX@RGD-DHBc	17.91±1.14	19.83±2.52	0.362±0.009

Table S1. Characterization of multiple VLPs.

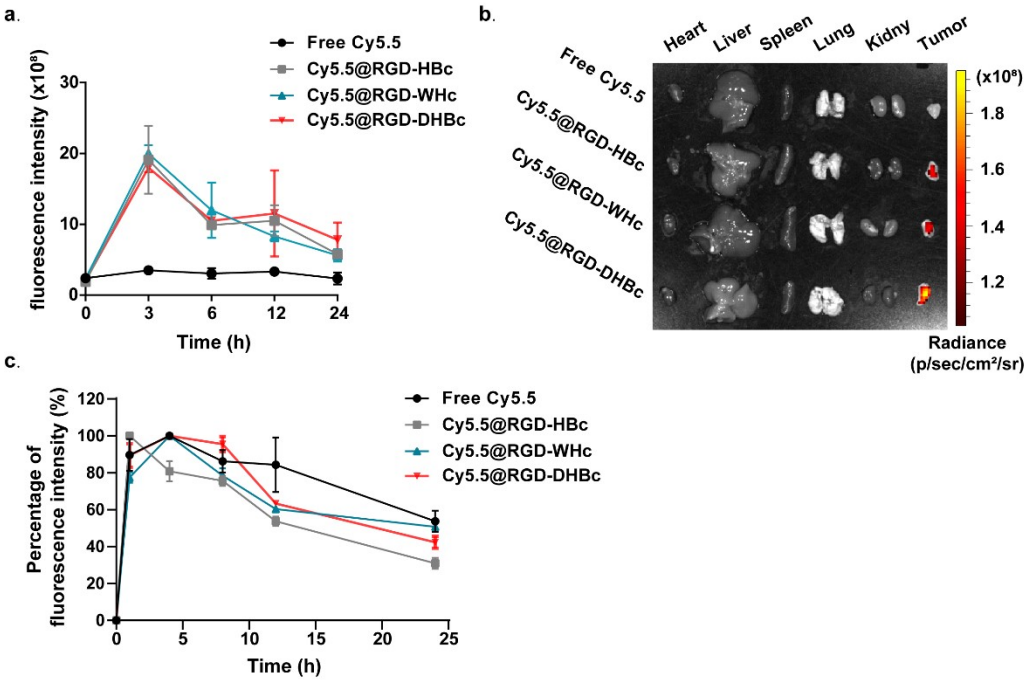

Figure S1. *In vivo* clearance and tumor accumulation of Cy5.5 labelled RGD-VLPs. (a) Time-course fluorescence intensity from the tumor in live mice. (b) The biodistribution in the major organs (heart, liver, spleen, lung, kidney) and tumor. Major organs (heart, liver, spleen, lung, and kidney) and tumor were collected at 24 h post *i.v.* injection for *ex vivo* imaging. (c) Whole-blood concentrations of Cy5.5 labelled RGD-VLPs in tumor bearing mice.

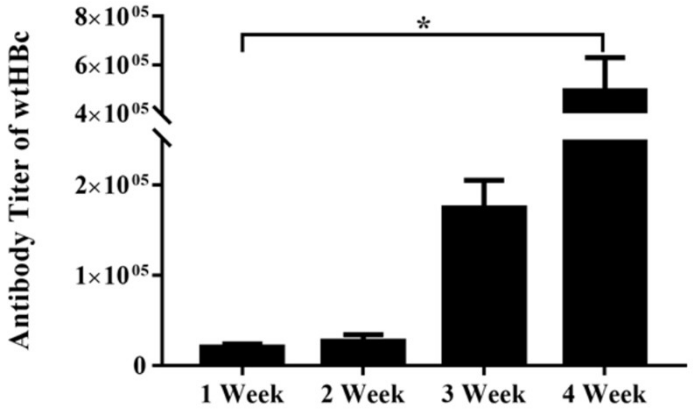

Figure S2. Humoral immune response to the HBcAg. Balb/C mice (n = 5) were immunized (s.c.) with HBc core proteins (4mg/g). Sera was collected on day 7, 14, 21 and 28 after the first injection on day 0, and the IgG anti-core end point titers that against the HBcAg were determined by ELISA.

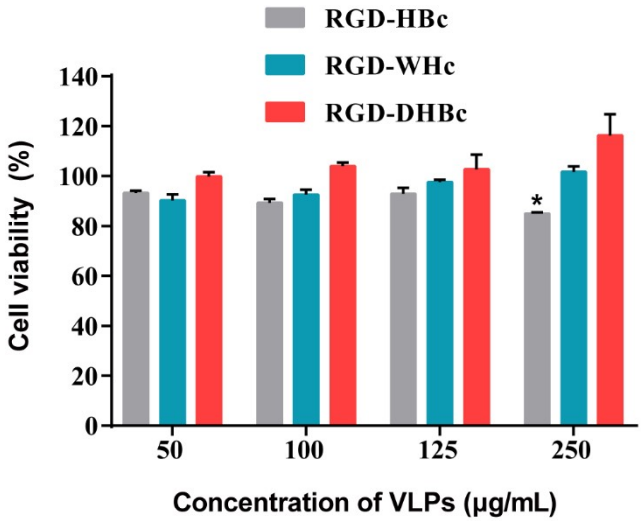

Figure S3. Cell viability after 24 h of incubation with various VLPs at increasing concentrations in CT26 cells.

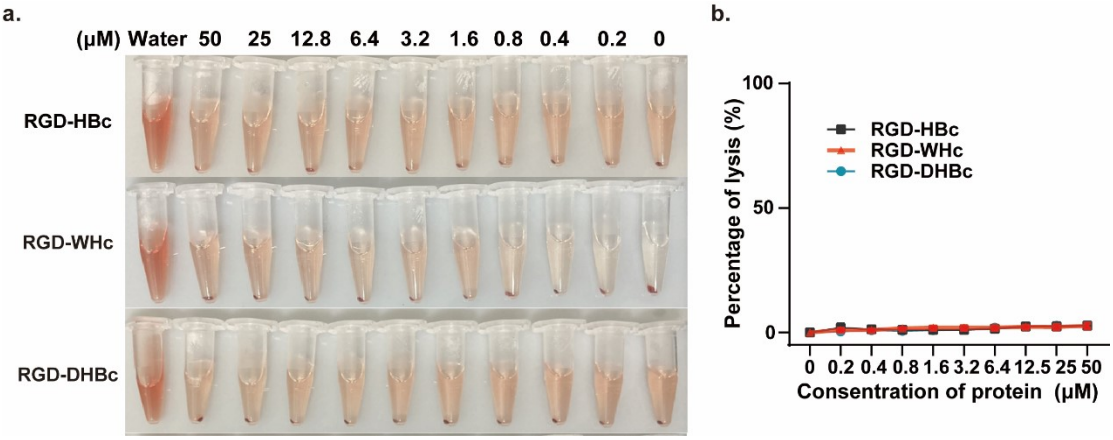

Figure S4. The hemocompatibility of various VLPs *in vitro*. (a, b) Hemolysis assays for RGD-HBc, RGD-WHc, RGD-DHBc VLPs in RBC.

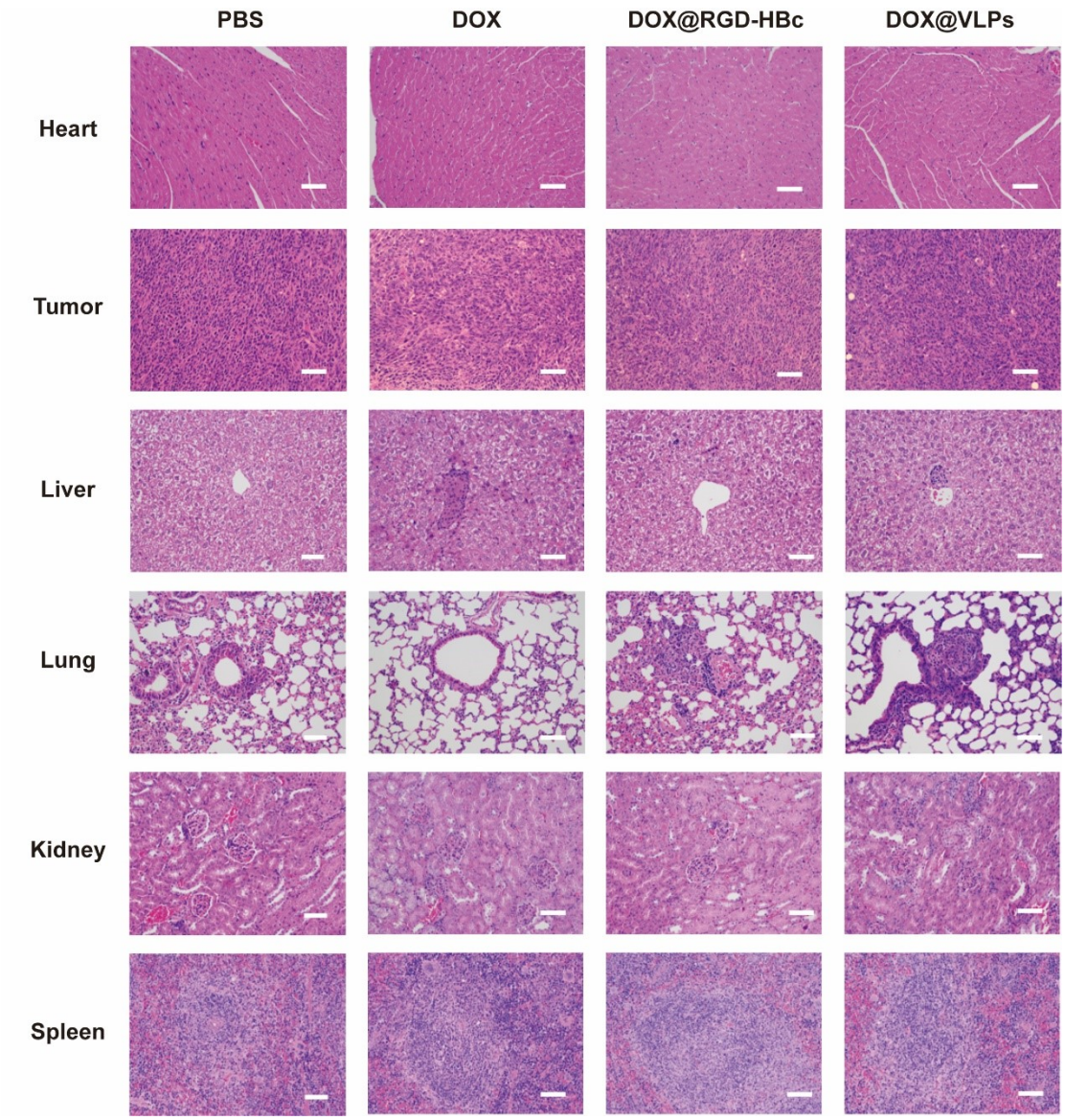

Figure S5. Histological analysis through H&E staining of organ sections of CT26 tumor-bearing mice subjected to various DOX@VLPs sequential treatment. Representative sections (200 X magnification) of major organs and tumors of mice treated with DOX, DOX@RGD-HBc and DOX@VLPs combination. The tissue sections from mice administered with PBS were used as controls.