Supporting information

Platelet-camouflaged nanococktail: Simultaneous inhibition of drug-resistant tumor growth and metastasis via a cancer cells and tumor vasculature dual-targeting strategy

Lijia Jing[1], Haijing Qu[1], Dongqi Wu[1], Chaojian Zhu[1], Yongbo Yang[2], Xing Jin[1], Jian Zheng[1], Xiangsheng Shi[1], Xiufeng Yan[1] and Yang Wang[1]*

1. Center for Bioactive Products, Northeast Forestry University/Key Laboratory of Saline-Alkali Vegetation Ecology Restoration, Ministry of Education, Harbin 150040, China.
2. State Key Laboratory of Veterinary Biotechnology, Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin 150069, China.

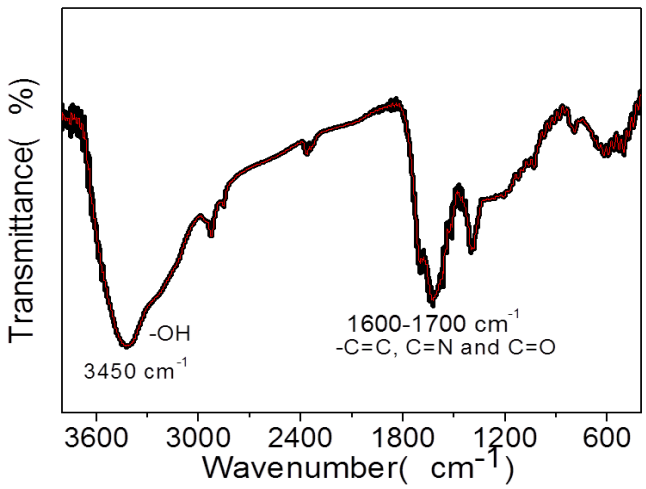

Figure S1. FTIR spectra of MNPs.

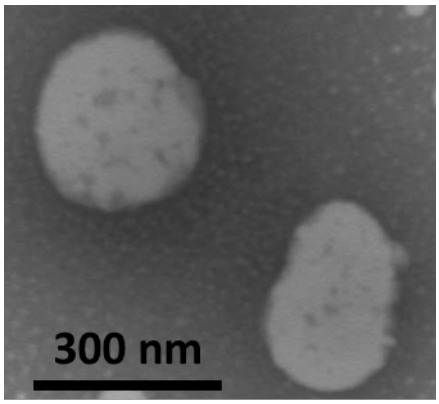

Figure S2. TEM image of platelet membrane (PM).

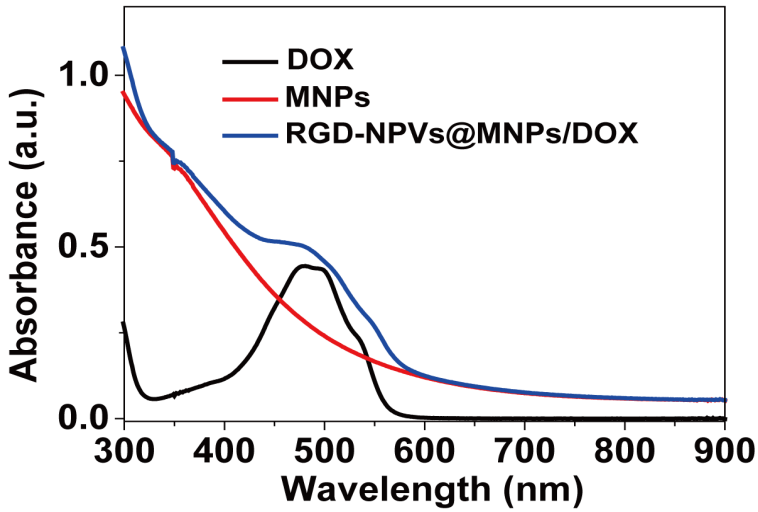

Figure S3. UV/vis absorption spectra of DOX, MNPs and RGD-NPVs@MNPs/DOX in aqueous solution.

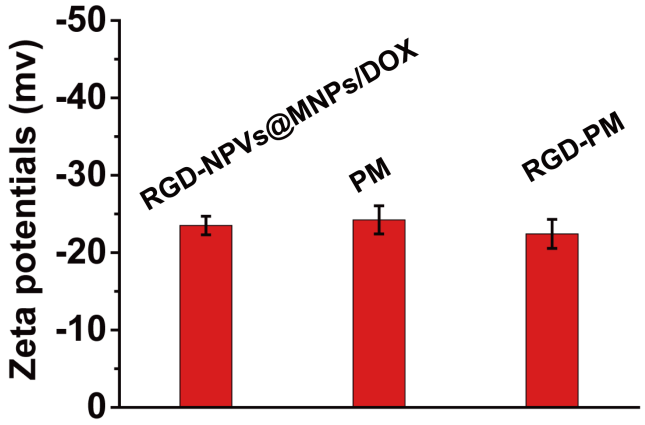

Figure S4. Zeta potentials of RGD-NPVs@MNPs/DOX, PM and RGD-PM.

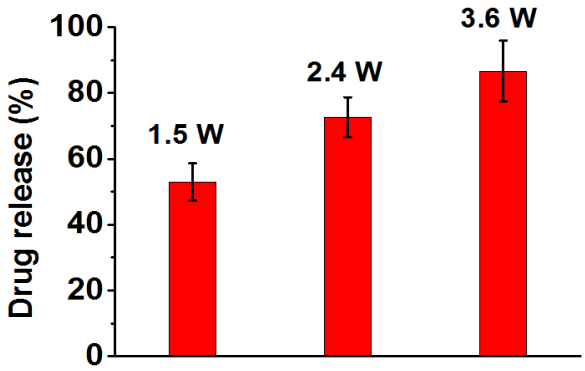

Figure S5. The DOX release rate from RGD-NPVs@MNPs/DOX at 8h after laser irradiation (808 nm, 10 min) at the power of 1.5, 2.4 and 3.6 W, respectively.

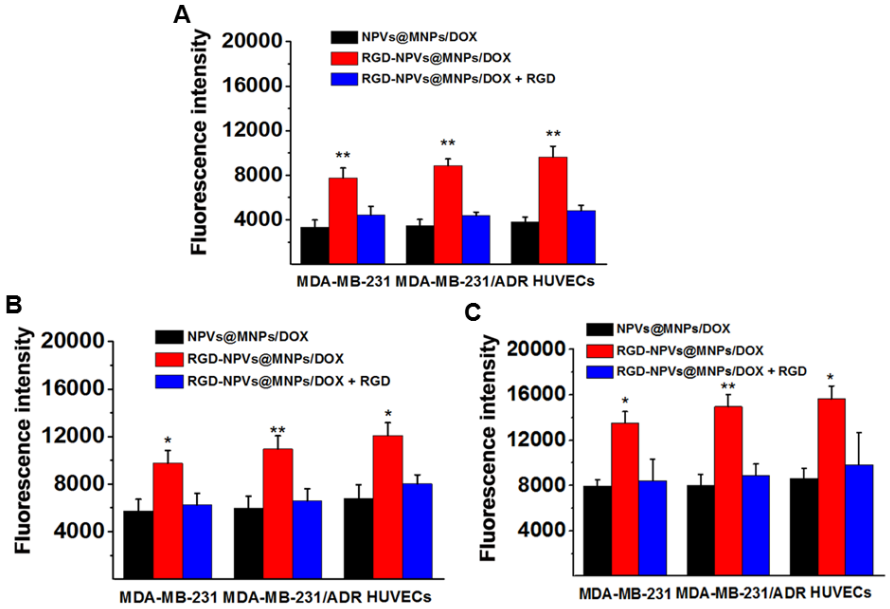

Figure S6. Fluorescence intensities of the tested cells after incubation with RhB labeled NPVs@MNPs/DOX and RGD-NPVs@MNPs/DOX with or without free RGD peptide for (A) 4 h, (B) 8 h and (C) 12 h. *, $P < 0.05$; **, $P < 0.01$.

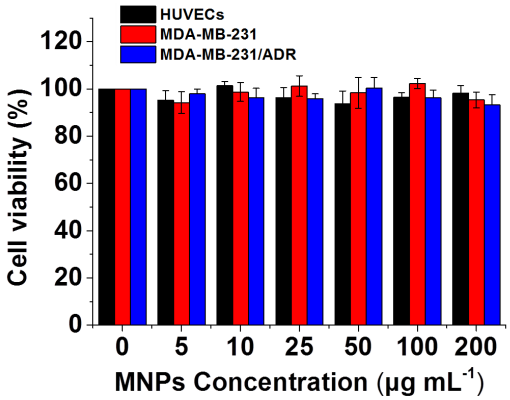

Figure S7. Viabilities of HUVECs, MDA-MB-231 and MDA-MB-231/ADR cells after incubation with different concentration of MNPs for 48 h.

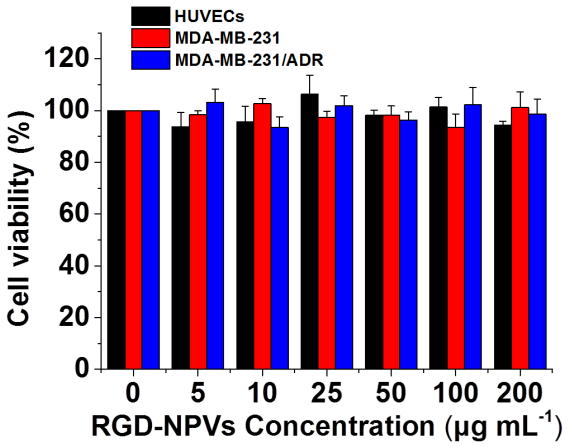

Figure S8. Viabilities of HUVECs, MDA-MB-231 and MDA-MB-231/ADR cells after incubation with different concentration of RGD-NPVs for 48 h.

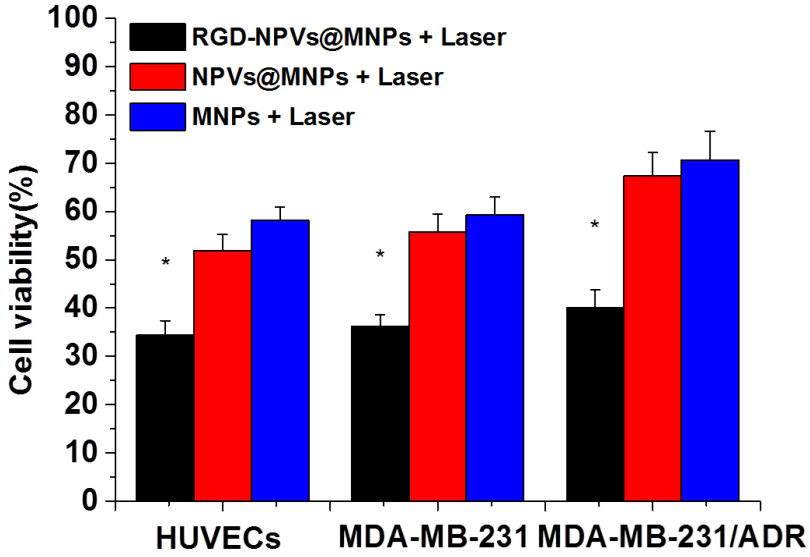

Figure S9. Viabilities of HUVECs, MDA-MB-231 and MDA-MB-231/ADR cells after treatment with RGD-NPVs@MNPs, NPVs@MNPs and MNPs at the same MNPs concentration (100 μg/mL) and the same NIR laser condition (1.5 W•cm^{-2}, 10 min) for 24h. *, $P < 0.05$.

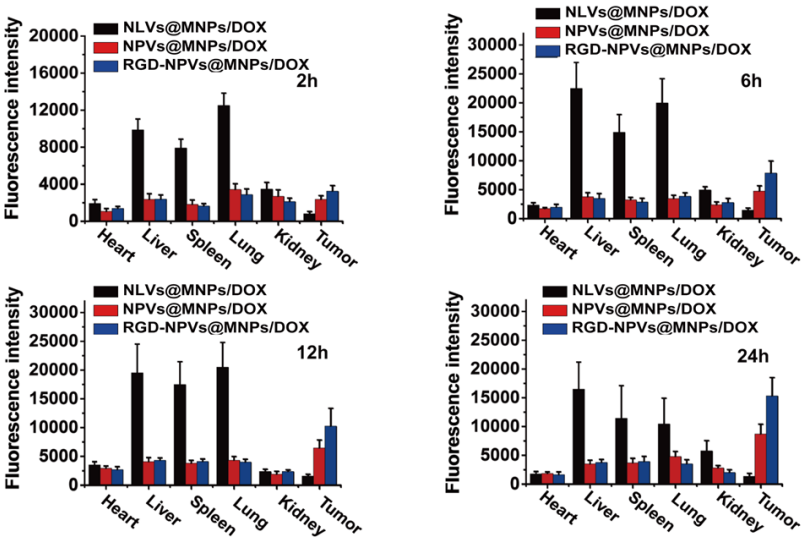

Figure S10. Fluorescence intensities of tumor and main organs in tumor bearing mice at 2, 6, 12, 24 h after the injection of RGD-NPVs@MNPs/DOX, NPVs@MNPs/DOX and NLVs@MNPs/DOX, respectively.

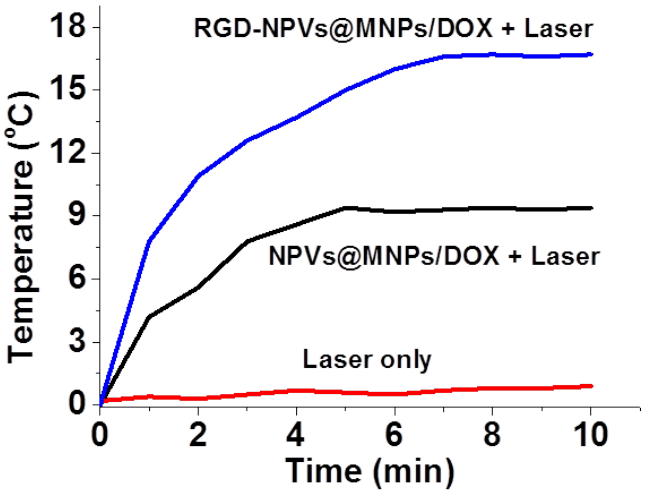

Figure S11. Temperature elevation curves of the mice tumor after treatments with NPVs@MNPs/DOX and RGD-NPVs@MNPs/DOX upon exposure to the 808 nm laser at a power density of 1.5 W·cm^{-2} for 10 min.

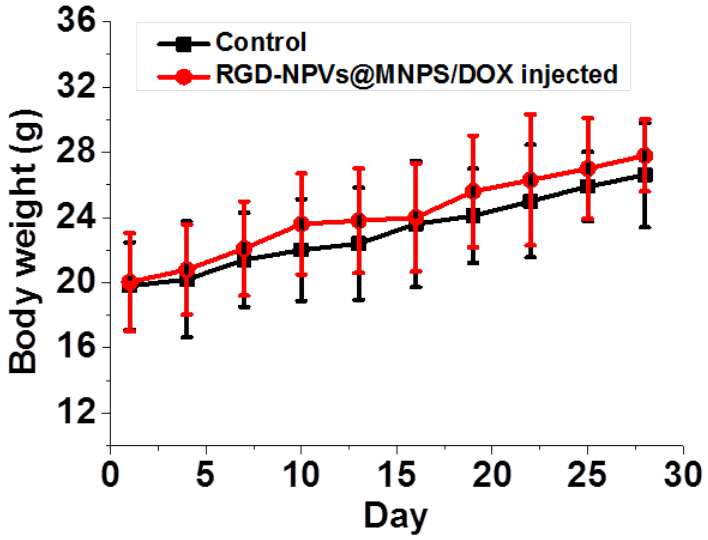

Figure S12. Body weight curves of the mice for 28 days with or without a single intravenous injection of RGD-NPVs@MNPs/DOX.

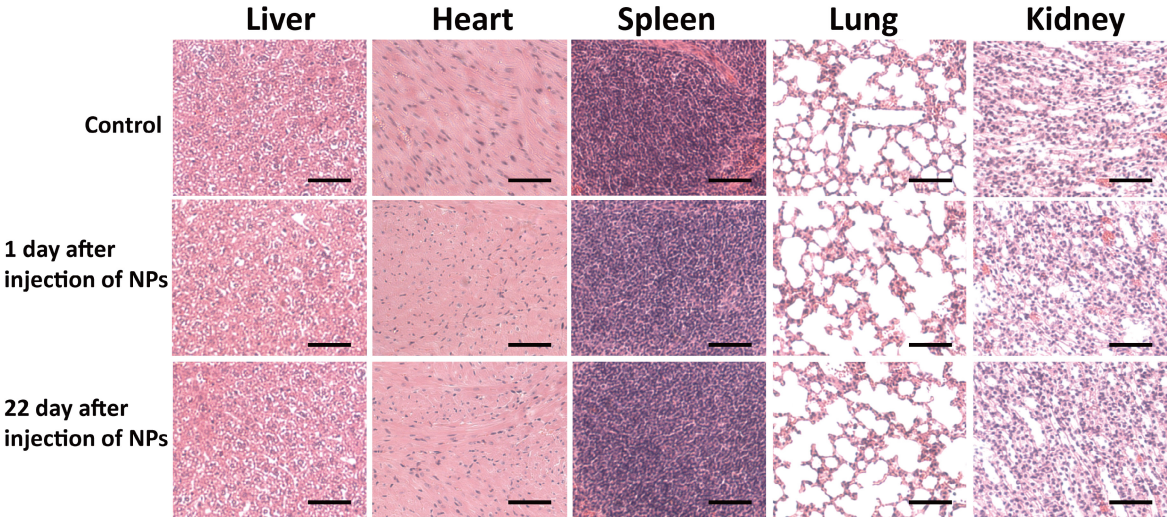

Figure S13. Histological examination for mice treated with RGD-NPVs@MNPs/DOX. Untreated healthy mice were used for comparison. Scale bar is 100 μm.

Table S1. The size distributions of the nanoparticles

Nanoparticles	Size distribution (nm)	Polymer dispersion index (PDI)

Melanin nanoparticles （MNPs）	3.8 ± 0.68	0.15
Platelet membrane (PM) vesicles	258.26 ± 77.81	0.38
NLVs@MNPs/DOX	80.52 ± 8.77	0.078
NPVs@MNPs/DOX	89.67 ± 9.66	0.089
RGD-NPVs@MNPs/DOX	85.92 ± 6.28	0.064

Table S2. Viabilities of MDA-MB-231, MDA-MB-231/ADR and HUVECs after treating with RGD-NPVs@MNPs/DOX in combine with different laser irradiations.

RGD-NPVs@MNPs/DOX (50μg/mL)	Viability of MDA-MB-231cell (%)	Viability of MDA-MB-231/ADR cell (%)	Viability of HUVECs cell (%)
(1.5 W·cm^{-2}, 5 min)	47.34 ± 4.35	75.34 ± 4.35	55.34 ± 4.35
(1.5 W·cm^{-2}, 10 min)	15.63 ± 3.35	29.4 ± 4.35	23.5 ± 4.35
(2.4 W·cm^{-2}, 5 min)	27.26 ± 7.89	31.94 ± 8.23	32.66 ± 5.32
(2.4 W·cm^{-2}, 10 min)	9.37 ± 0.94	10.82 ± 1.08	11.21 ± 0.84

Table S3. Blood circulation parameters of NLVs@MNPs/DOX, NPVs@MNPs/DOX and RGD-NPVs@MNPs/DOX.

Parameters	RGD-NPVs@MNPs/DOX	NPVs@MNPs/DOX	NLVs@MNPs/DOX
Blood half-life ($T_{1/2}$)	26.4 ± 3.2h	27.6 ± 4.1 h	5.13 ± 2.61 h
Mean residence time (MRT)	34.62 ± 5.71h	36.89 ± 7.46 h	7.79 ± 3.23 h
The plasma concentration-time curve from zero to time infinity ($AUC_{0-\infty}$)	5983.37 ± 659.46 h·μg/L	6398.42 ± 973.28 h·μg/L	726.21 ± 298.4 h·μg/L

Table S4. Blood biochemical indexes.

	Untreated mice	RGD-NPVs@MNPs/DOX injected mice	
		1 day	22 day
WBC (10^9/L)	13.35 ± 3.35	12.86 ± 4.1	14.13 ± 2.61
RBC (10^{12}/L)	9.62 ± 1.17	8.98 ± 1.46	9.04 ± 1.23
PLT (10^{12}/L)	0.87 ± 0.14	0.79 ± 0.097	0.88 ± 0.12

GRN (10^9/L)	5.83 ± 0.97	6.24 ± 0.78	5.99 ± 1.02
AST U L^{-1}	486.0 ± 99.2	523.5 ± 126.6	498.7 ±103.9
ALT U L^{-1}	86.34 ± 17.2	93.8 ± 10.8	86.7 ± 9.4
ALP U L^{-1}	187.64 ± 20.3	199. 4 ± 25.1	178.32 ± 19.61
CREA µmol L^{-1}	21.3 ± 1.2	20.9 ± 0.7	22.5± 1.3
BUN mmol L^{-1}	9.13 ± 0.8	10.2 ± 1.9	9.89 ± 0.9