

Supporting Information

Nano-drug System Based on Hierarchical Drug Release for Deep Localized/Systematic Cascade Tumor Therapy Stimulating Antitumor Immune Responses

Yuchu He^{1,2}, Cong Cong¹, Xiaoling Li¹, Ruiyan Zhu^{1,3}, Anshuo Li⁴, Shuxian Zhao¹,
Xiaowei Li¹, Xin Cheng¹, Mengxue Yang¹, Dawei Gao^{1,2*}

¹Applying Chemistry Key Lab of Hebei Province, Department of Bioengineer, Yanshan
University, No.438 Hebei Street, Qinhuangdao, 066004, China.

²State Key Laboratory of Metastable Materials Science and Technology, Yanshan University,
Qinhuangdao 066004, P. R. China.

³Hebei Province Asparagus Industry Technology Research Institute, Qinhuangdao, 066004, China.

⁴Department of Prosthodontics Ninth People's Hospital Shanghai Jiao Tong University School of
Medicine, 639 Zhizaoju Road, Shanghai 200011, China.

*Corresponding author: Prof. Dawei Gao, Tel: (+86)13930338376.

E-mail: dwgao@ysu.edu.cn

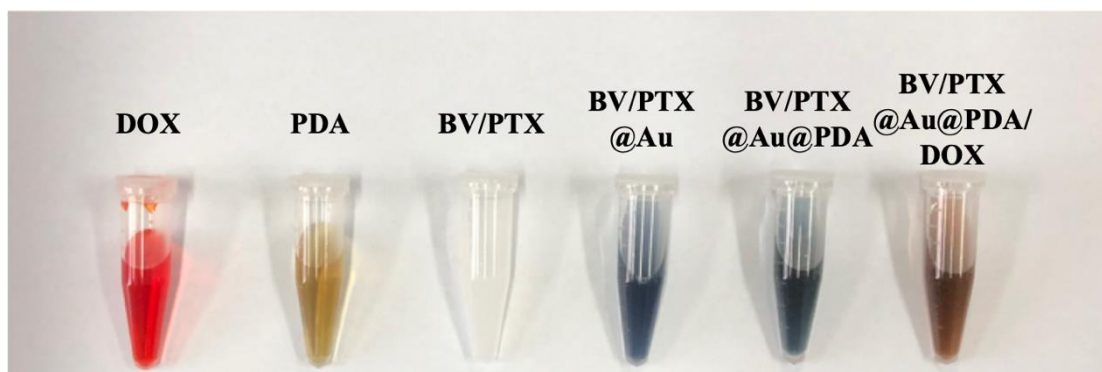


Figure S1. Photographs of free DOX, PDA, BV/PTX, BV/PTX@Au, BV/PTX@Au@PDA and BV/PTX@Au@PDA/DOX.

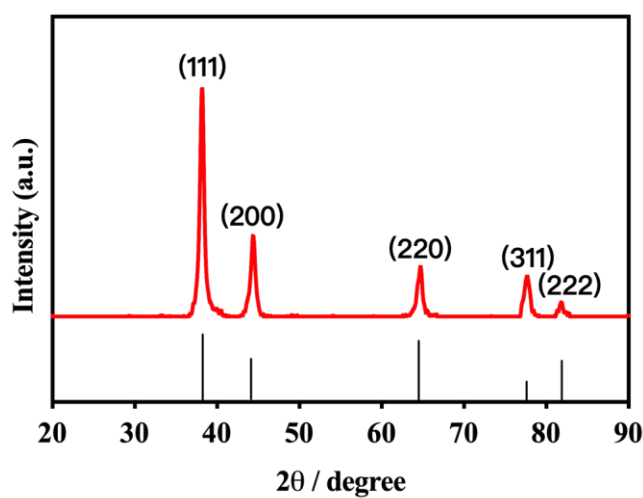


Figure S2. XRD pattern of BV/PTX@Au.

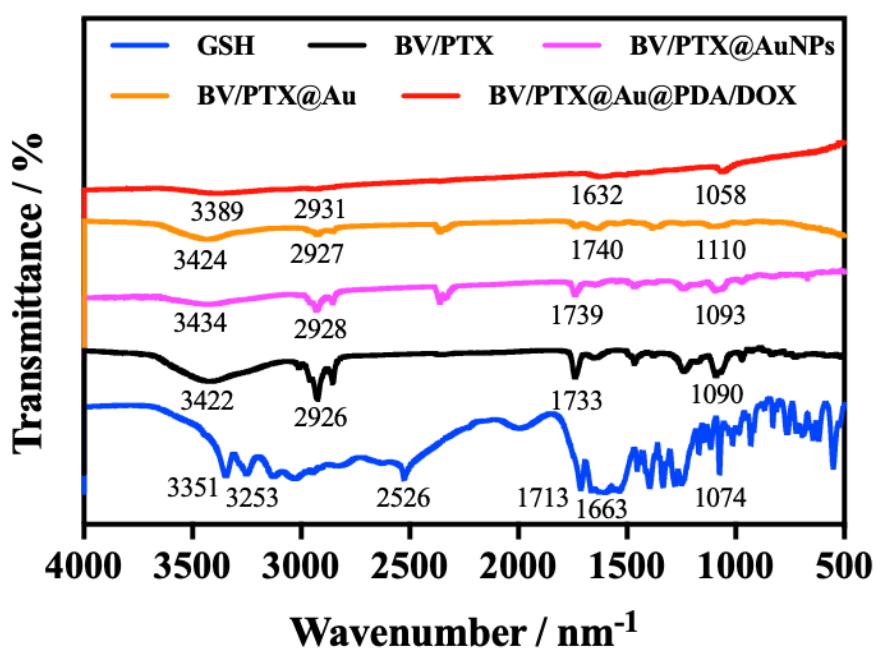


Figure S3. FTIR of free GSH, BV/PTX, BV/PTX@AuNPs, BV/PTX@Au and BV/PTX@Au@PDA/DOX.

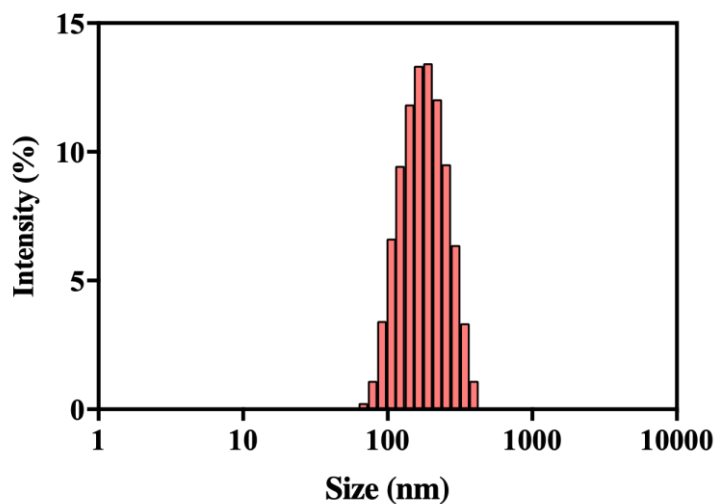


Figure S4. Size distribution of BV/PTX.

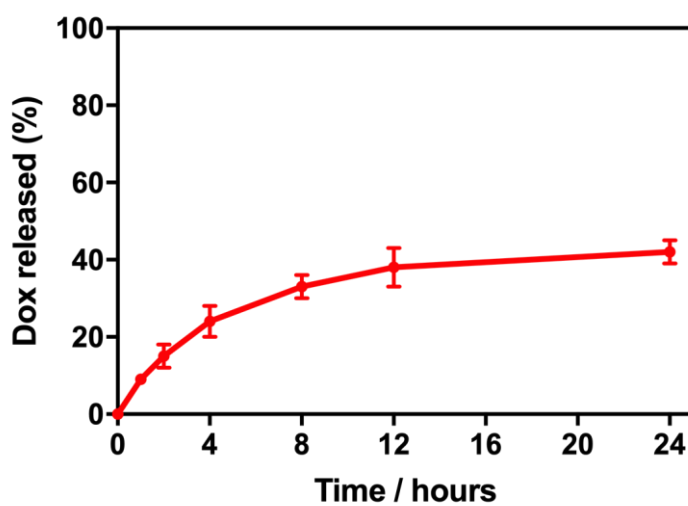


Figure S5. DOX release profile from BV/PTX@Au@PDA/DOX at pH 7.4 +10% FBS

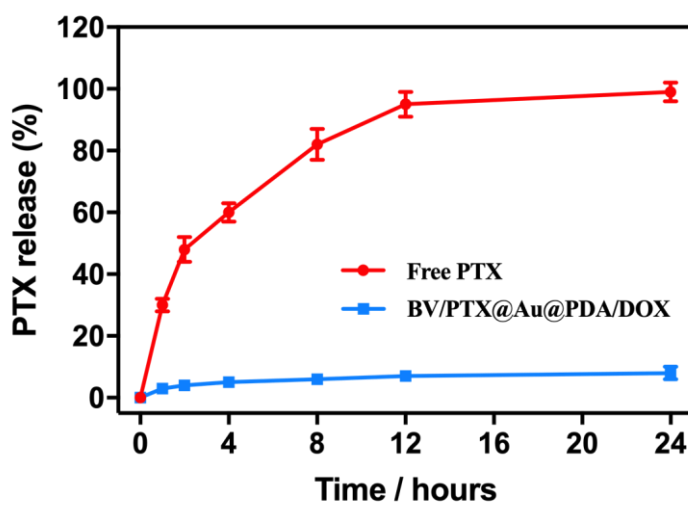


Figure S6. PTX release profile of free PTX and BV/PTX@Au@PDA/DOX.

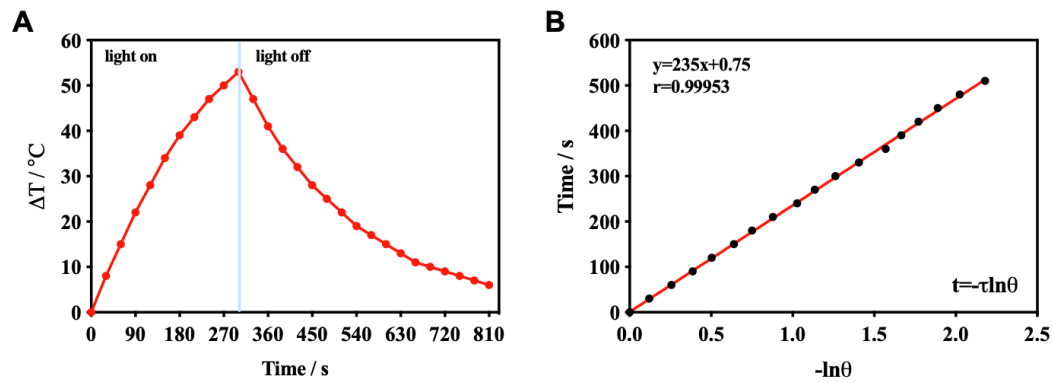


Figure S7. (A) The photothermal response of the BV/PTX@Au@PDA/DOX for 300 s with laser irradiation, and then the laser was shut off. (B) Linear time data versus $-\ln\theta$ ($R=0.99953$).

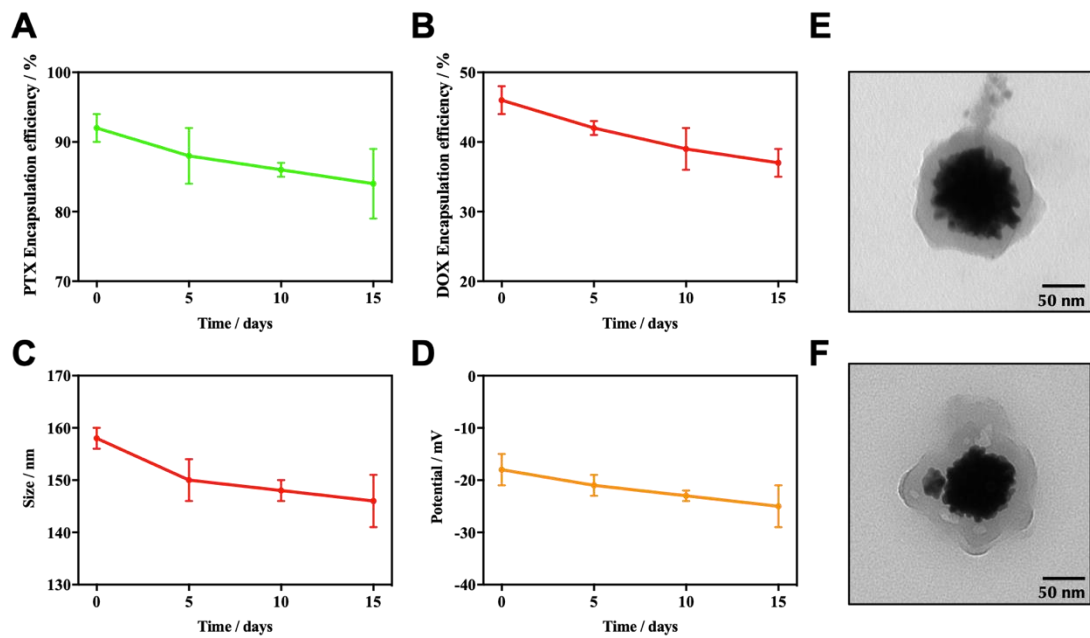


Figure S8. (A) PTX and (B) DOX leakage at 4°C for 15 days. The change of (C) size distribution and (D) zeta potential for 15 days. (E) and (F) TEM images before and after storage at 4°C for 15 days. Data were expressed as mean \pm S.E. ($n = 3$).

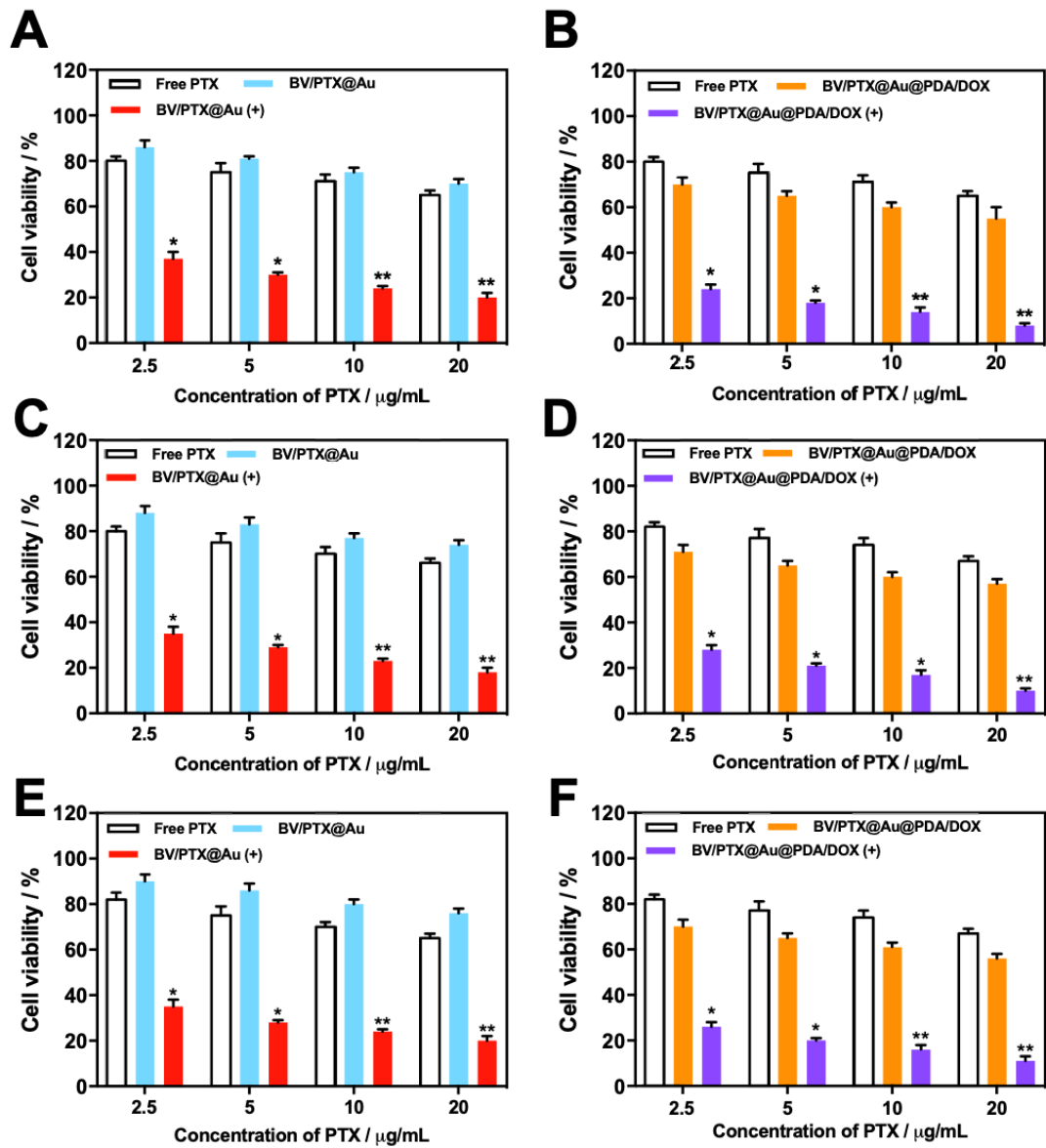


Figure S9. Cell viability of HeLa cells treated with free PTX, (A) BV/PTX@Au and (B) BV/PTX@Au@PDA/DOX with and without laser irradiation for 24 hours, (C) BV/PTX@Au and (D) BV/PTX@Au@PDA/DOX with and without laser irradiation for 48 hours and (E) BV/PTX@Au and (F) BV/PTX@Au@PDA/DOX with and without laser irradiation for 72 hours.

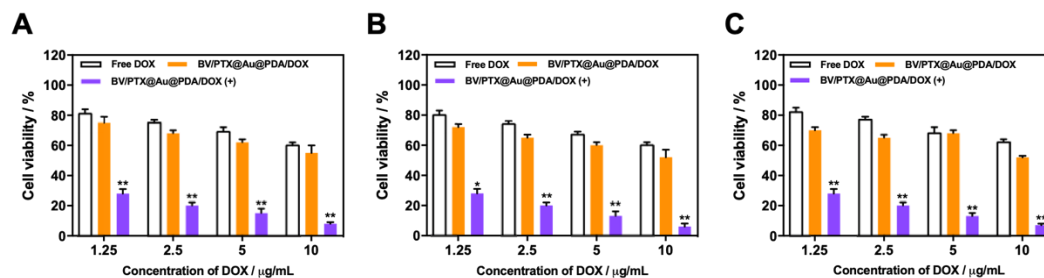


Figure S10. Cell viability of HeLa cells treated with free DOX and BV/PTX@Au@PDA/DOX with and without laser irradiation for (A) 24 hours, (B) 48 hours and (C) 72 hours.

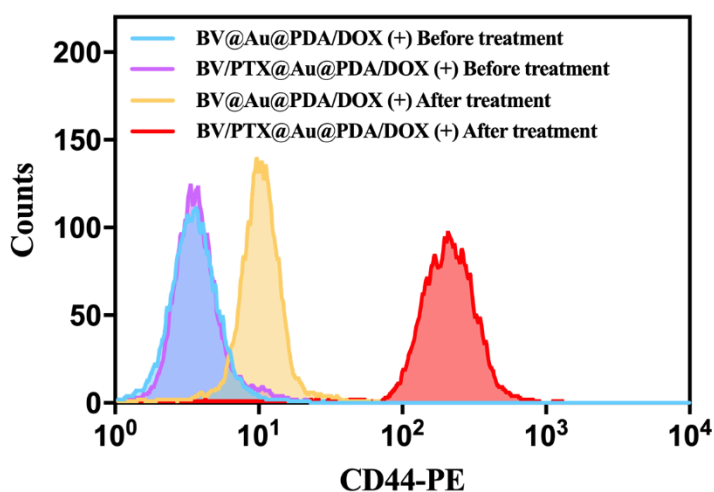


Figure S11. CD44 expression of BV@Au@PDA/DOX with laser irradiation and BV/PTX@Au@PDA/DOX with laser irradiation before and after first treatment by FCM analysis.

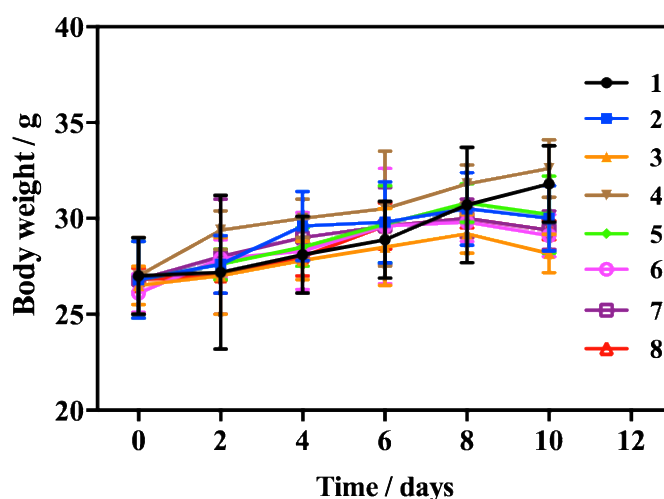


Figure S12. Body weight changes of different groups in the therapeutic period. Group 1: saline, 2: BV/PTX, 3: BV/PTX@Au, 4: BV/PTX@Au with laser irradiation, 5: BV@Au@PDA/DOX, 6: BV@Au@PDA/DOX with laser irradiation, 7: BV/PTX@Au@PDA/DOX, 8: BV/PTX@Au@PDA/DOX with laser irradiation.

Tables

Table S1 IC50 value of PTX with different formulations and incubation time

IC50 value ($\mu\text{g/mL}$)	24 hours	48 hours	72 hours
Free PTX	22.51	25.50	25.32
BV/PTX@Au	34.34	41.14	48.72
BV/PTX@Au (+)	2.07	1.90	1.93
BV/PTX@Au@PDA/DOX	14.16	14.77	14.64
BV/PTX@Au@PDA/DOX (+)	0.97	1.22	1.12

Table S2 IC50 value of DOX with different formulations and incubation time

IC50 value ($\mu\text{g/mL}$)	24 hours	48 hours	72 hours
Free DOX	11.15	10.57	11.76
BV/PTX@Au@PDA/DOX	7.93	6.86	6.74
BV/PTX@Au@PDA/DOX (+)	0.58	0.55	0.56