Supporting Information for

ORIGINAL ARICLE

Escape from abluminal LRP1-mediated clearance for boosted nanoparticle brain delivery and brain metastasis treatment

Naveed Ullah Khan[a], Jiang Ni[a,b], Xiufeng Ju[a], Tongtong Miao[a], Haiyan Chen[a], Liang Han[a,*]

[a]*Jiangsu Key Laboratory of Neuropsychiatric Diseases Research and College of Pharmaceutical Sciences, Soochow University, Suzhou 215123, China*

[b]*Department of Pharmacy, Affiliated Hospital of Jiangnan University, Wuxi 214000, China*

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*Corresponding authors. Tel./fax: +86 512 65882089.

E-mail address: hanliang@suda.edu.cn (Liang Han).

Running title: Escape from abluminal LRP1-mediated clearance for boosted brain targeting

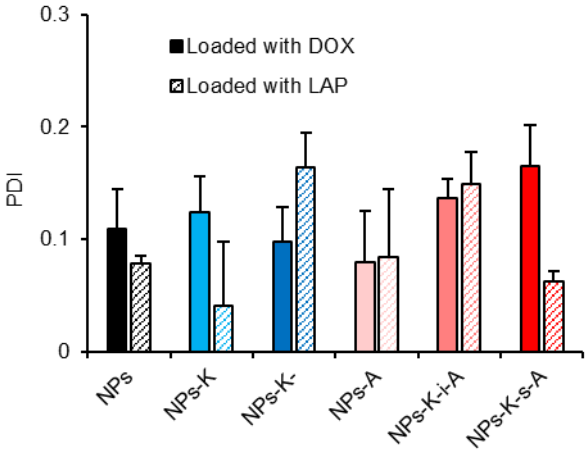

Figure S1 The polydispersity indices for the hydrodynamic size of DOX-loaded NPs and LAP-loaded NPs by dynamic light scattering. Data are presented as mean±SD (*n*=3).

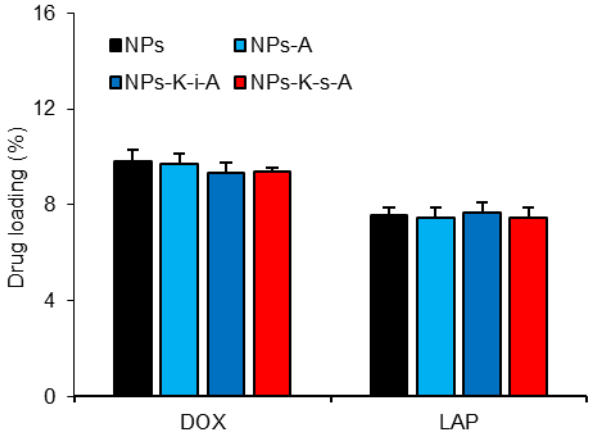

Figure S2 The loading efficiency of DOX and LAP in various NPs. Data are presented as mean±SD (*n*=3).

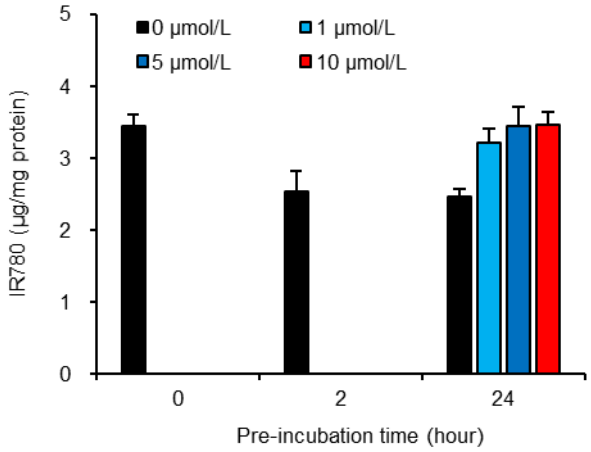

Figure S3 In vitro uptake of IR780-loaded NPs-K-s-A in bEnd.3 cells. The uptake parameter was set at 1.8 μg IR780/mL for 2 h. The NPs were pre-incubated with MMP1 (7.8 ng/mL) for different time with different concentration specific MMP1 inhibitor FN439. Data are presented as mean ± SD (n=4). ***P < 0.001.

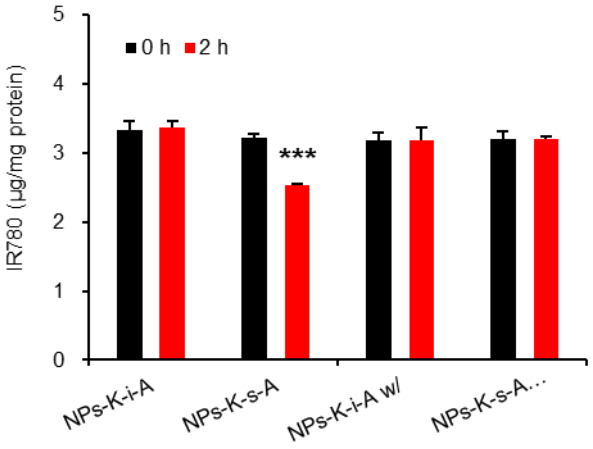

Figure S4 In vitro uptake of IR780-loaded NPs-K-s-A and NPs-K-i-A in bEnd.3 cells. The uptake parameter was set at 1.8 μg IR780/mL for 2 h. The NPs were pre-incubated with MMP1 (7.8 ng/mL) for 2 h with or without 1 μmol/L FN439. Data are presented as mean ± SD (n = 4). ***P < 0.001.

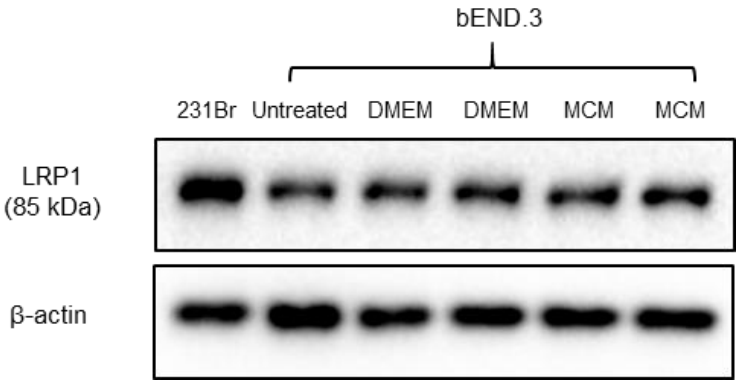

Figure S5 Representative image of LRP1 expression determined by Western blotting on bEND.3 cells, which were treated with DMEM, or MDA-MB-231Br-HER2 conditioned medium (MCM) for 24 h. 231Br cells were used as control.

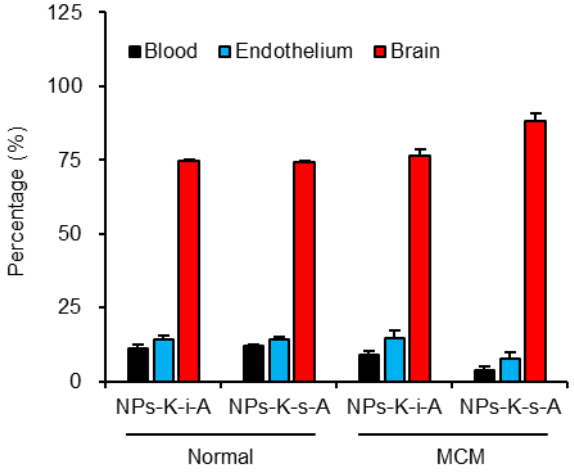

Figure S6 The distribution percentage of DOX-loaded NPs-K-i-A and NPs-K-s-A in blood side, brain endothelium and brain side on an in vitro BBB model. Amounts of DOX were measured after 6 h incubation in DMEM or MCM. Data are presented as mean ± SD (*n*=3).

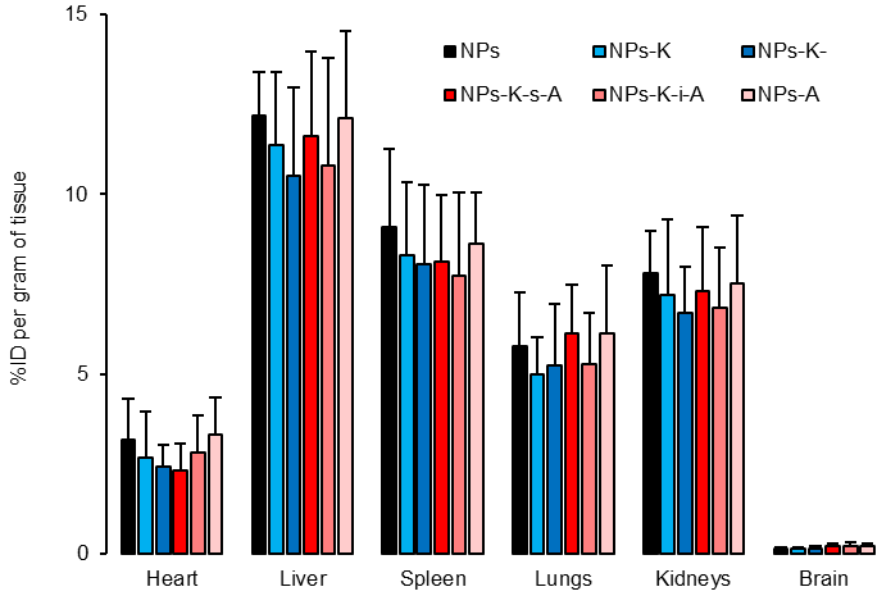

Figure S7 Quantitative biodistribution (% ID/g) of intravenously injected various IR780-loaded NPs (0.75 mg IR780/kg) in normal mice. Data are presented as mean ± SD (*n*=5).

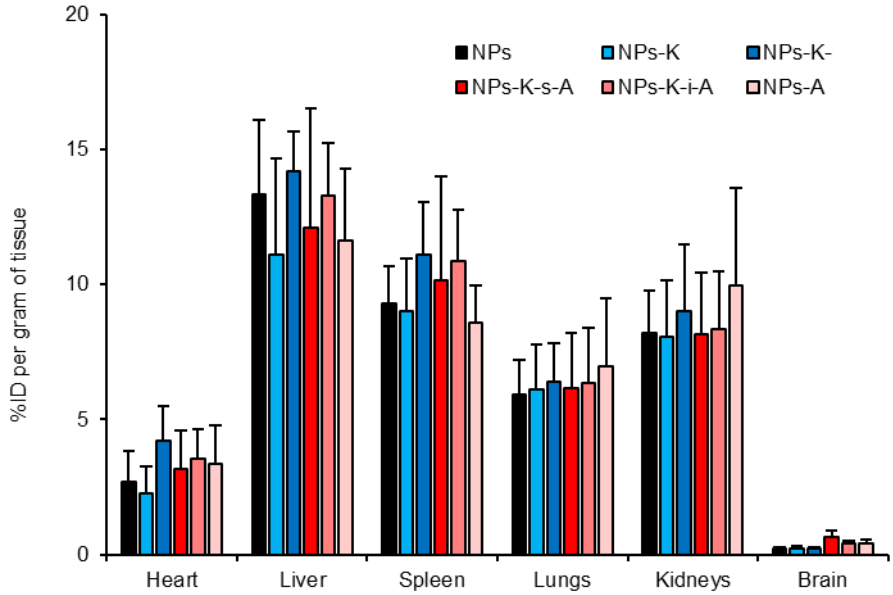

Figure S8 Quantitative biodistribution (% ID/g) of intravenously injected various IR780-loaded NPs (0.75 mg IR780/kg) in BCBM-bearing mice. Data are presented as mean ± SD (*n*=6).

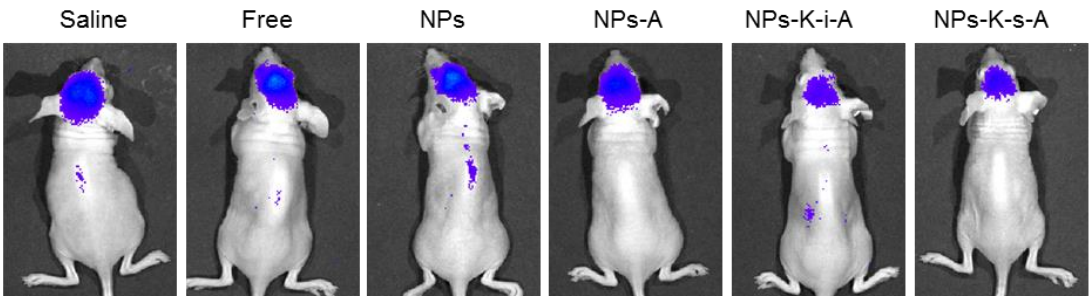

Figure S9 Representative bioluminescence images of chosen mice for *in vivo* antitumor evaluation. Bioluminescence imaging was performed by IVIS imaging system on Day 1 after intracardiac injection to screen successful animal models.