Supporting Information

Albumin modified cationic nanocarriers to potentially create a new platform for drug delivery systems

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Materials and methods

Drug loading and Controlled Release

A drug stock solution in acetone was added to an empty glass vial. After evaporation of the solvent, 10 mL of polyurethane micellar solution was transferred into the glass vial and ultrasonated for 2 h. Then the result solution was passed through a 0.45 μmpore-sized syringe filter (Millipore, Carrigtwohill, Co. Cork, Ireland).

The release of PTX was conducted using a dialysis method in phosphate buffer solution (PBS, 10 mM, pH 7.4) containing 1 M sodium salicylate at 37 °C with shaking. The sodium salicylate to maintain a sink condition. At desired time intervals, 1 mL of release media was sampled and replenished with an equal volume of fresh media. The release experiments were conducted in triplicate.

The concentration of PTX in the samples was measured by HPLC system (Agilent 1260 series, USA) equipped with a reverse-phase C18 column (4.6 × 100 mm). The flow rate was 1.0 mL/min, and the mobile phase consisted of acetonitrile/water (60/40 v/v). The detection of PTX was performed by UV absorption at 227 nm.

Results and discussion

In Vitro Cellular Uptake of Micelles-Albumin Complex

In vitro cellular imaging of MACs and naked micelles was studied by confocal laser scanning microscopy (CLSM) and flow cytometry. Hela cells were treated without serum for 12 h in advance to avoid interference. As shown in Figure S2 and Figure S3, G8mE1900 and G8mE1900-LB both have intense green fluorescence in the cytoplasms by CLSM (Figure S3A). The fluorescence signal of G8mE1900-LB was stronger than that of naked micelles in 30 min, and both have the same stronger fluorescence intensity after 1 h incubation. BSA as the encapsulation matrix can efficiently enhance the intracellular uptake. In addition, cationic micelles bearing GQA inherently have an excellent cellular uptake, so G8mE1900 and G8mE1900-LB have a similar degree of internalization after 1 h. However, G8mE1900-HB is hardly observed with fluorescence signals both during 0.5 h and 1 h, indicating that high BSA concentration would decrease cell uptake. This phenomenon may be caused by two reasons, one is G8mE1900-HB containing excessive free BSA protein, which would be preferentially internalized by the tumor cells treated by serum free culture medium; the other one is that the surface of G8mE1900-HB has a higher negative charge, which will block the electrostatic interaction between the cell and MACs.

Table S1. The size, size distribution and zeta potential of polyurethane micelles and MACs.

sample	size (d.nm)	PDI	zeta potential (mV)
G8mE1900	75.15±1.48	0.416	-6.68±0.17
G8mE1900 + 0.001mg/mlBSA	74.11±0.52	0.429	31.97±1.44
G8mE1900 + 0.005mg/mlBSA	74.97±0.94	0.434	30.9±0.78
G8mE1900 + 0.01mg/mlBSA	71.26±0.48	0.395	25.83±0.49
G8mE1900 + 0.05mg/mlBSA	77.25±0.72	0.359	24.33±1.64
G8mE1900 + 0.1mg/mlBSA	137.05±16.25	0.774	22.23±1.92
G8mE1900 + 0.5mg/mlBSA	172.15±6.95	0.874	3.03±0.1
G8mE1900 + 1mg/mlBSA	101.78±5.48	0.58	-3.33±0.03
G8mE1900 + 2mg/mlBSA	135.2±1.012	0.63	-8.29±0.75

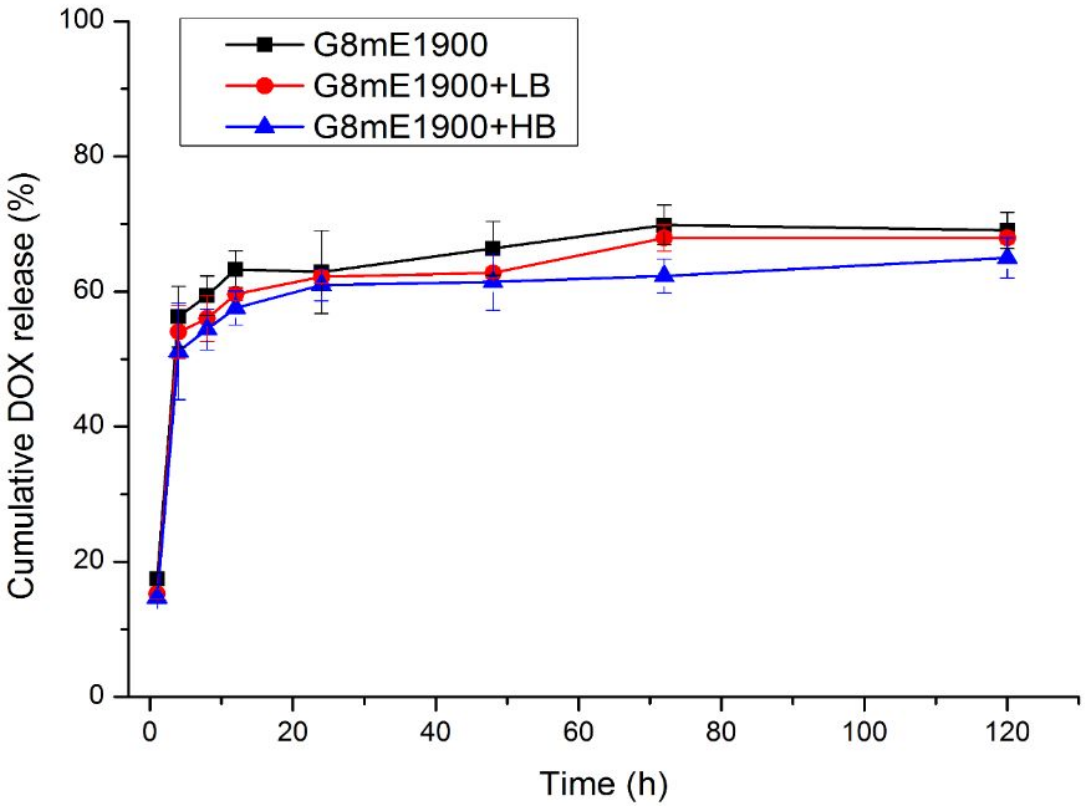

Figure S1. Drug release profile of naked micelles and MACs during 120 h. Albumin corona have almost no effect to the drug release property.

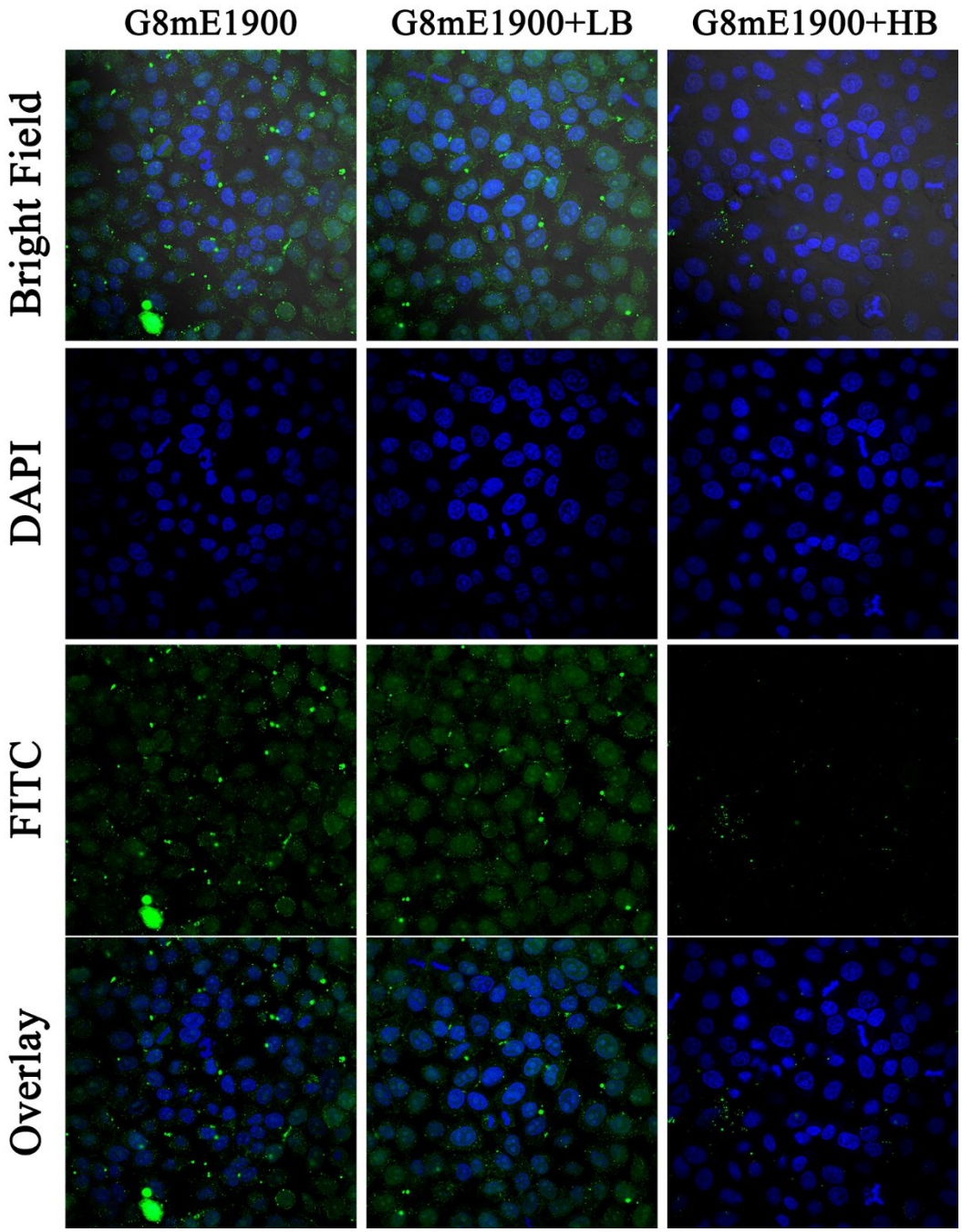

Figure S2. CLSM images of HeLa cells incubated with cationic micelles modified by different BSA concentration for 0.5 h.

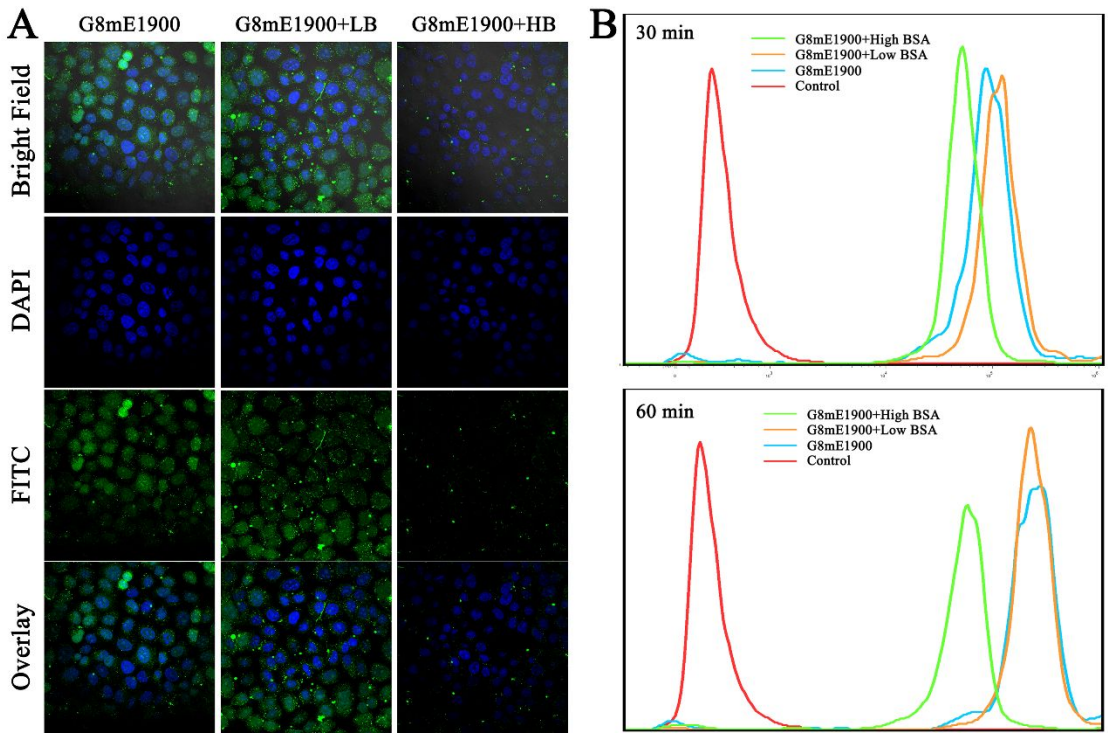

Figure S3. CLSM images (A) and Flow cytometry (B) of HeLa cells incubated with cationic micelles modified by different BSA concentration for 0.5 h (B) and 1 h (A, B).

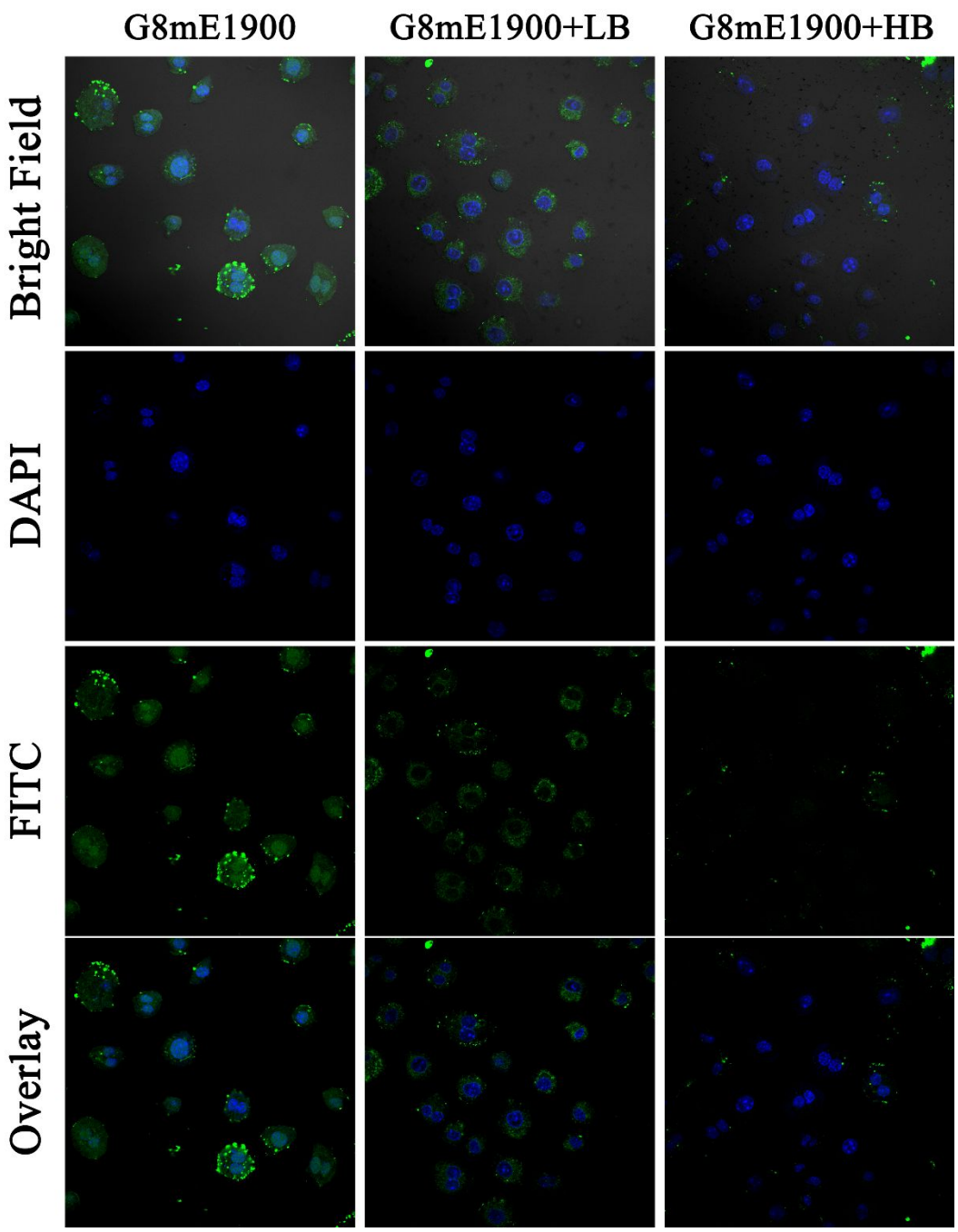

Figure S4. CLSM images of Raw 264.7 cells cells incubated with cationic micelles modified by different BSA concentration for 0.5 h.

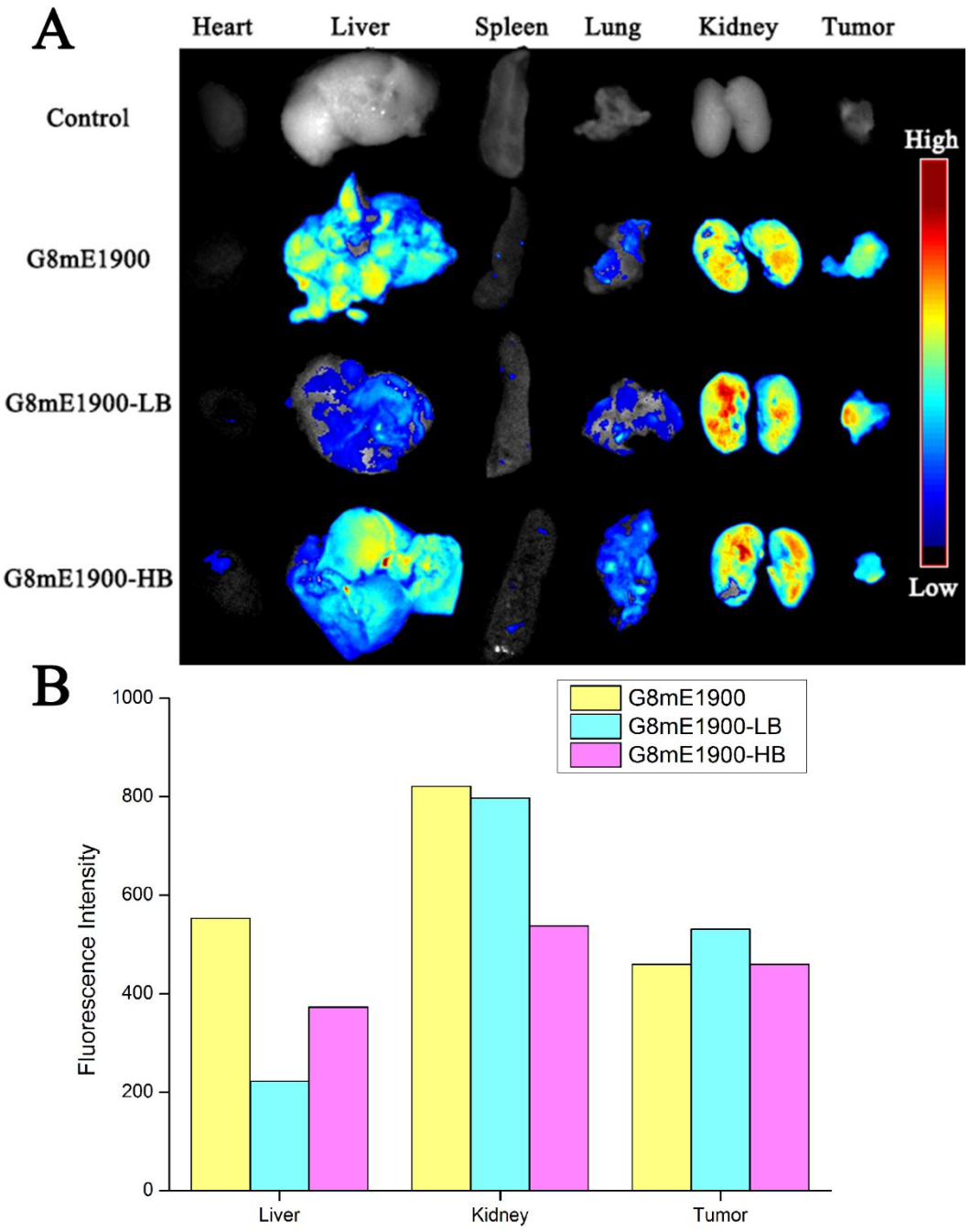

Figure S5. (A) In vivo fluorescence images of tumor-bearing nude mice receiving intravenous injection of fluorescent-labeled naked micelles and MACs after 6 h. (B) Quantification of the fluorescent in Liver, Kidney and Tumor after 6 h injection.

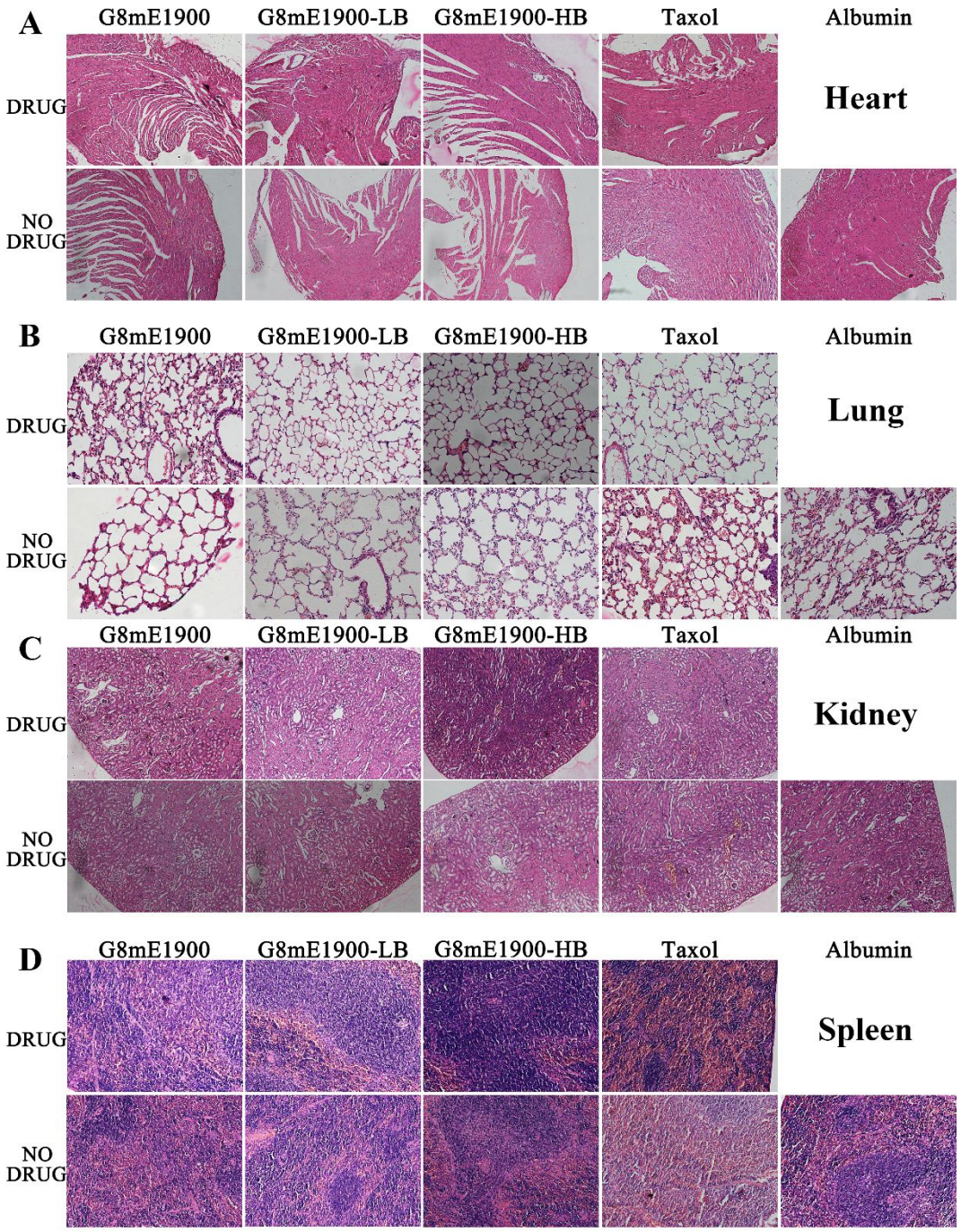

Figure S6. H&E staining of Heart (A), Lung (B), Kidney (C) and Spleen (D) sections separated from animals receiving different treatments.