Porphyrin-grafted Lipid Microbubbles for the Enhanced Efficacy of Photodynamic Therapy in Prostate Cancer through Ultrasound-controlled *In Situ* Accumulation

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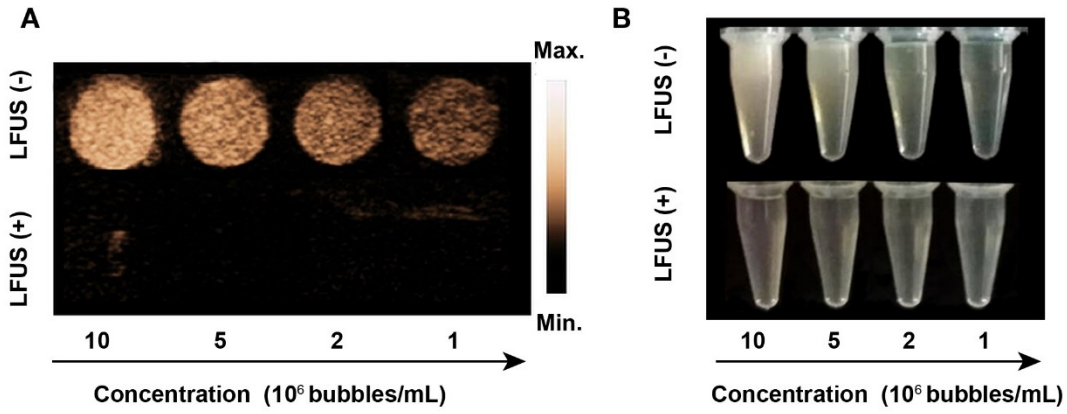
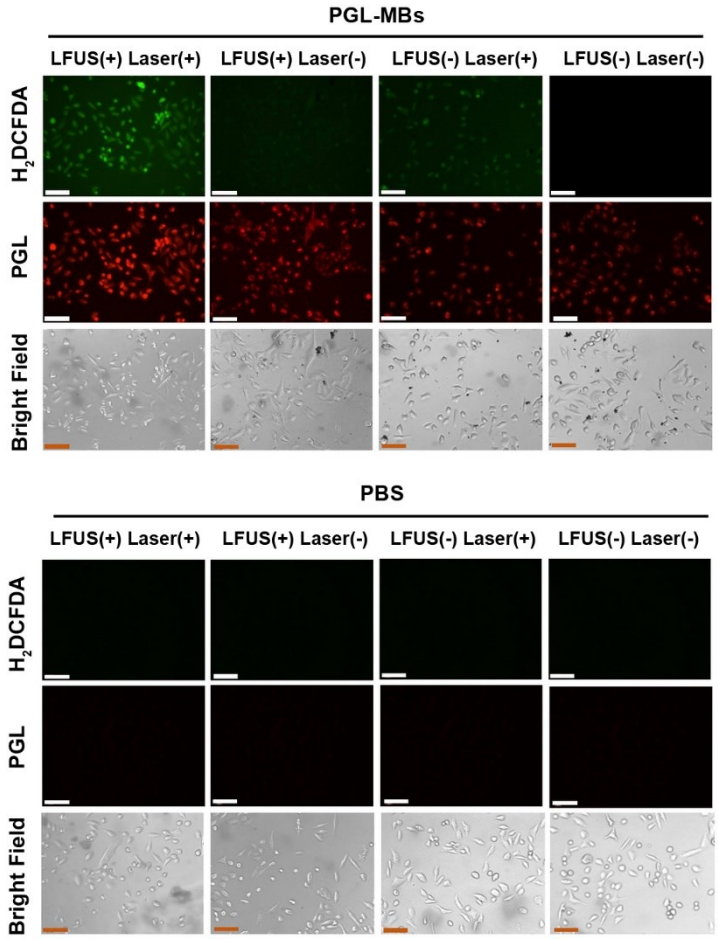
Keywords: porphyrin-grafted lipid, microbubbles, photosensitizer, ultrasound-targeted microbubble destruction, photodynamic therapy

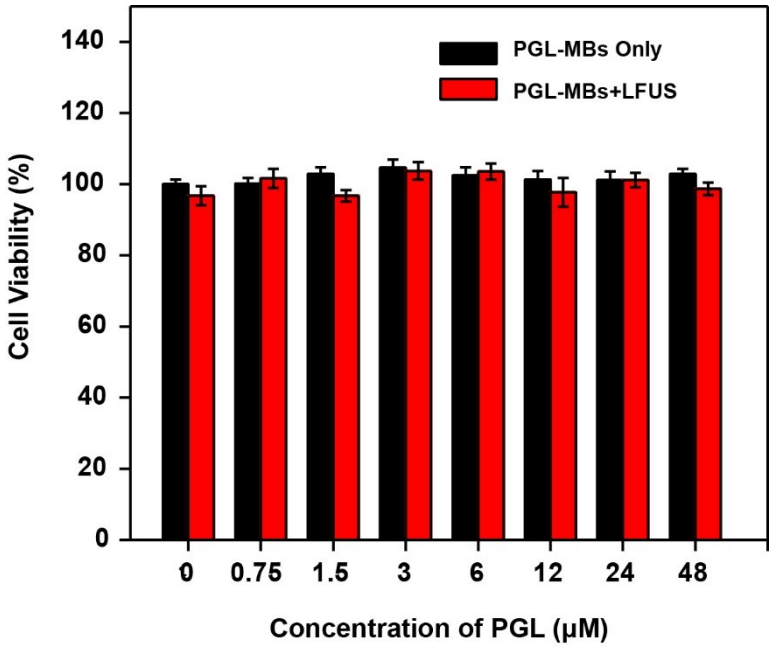
Supplementary Data



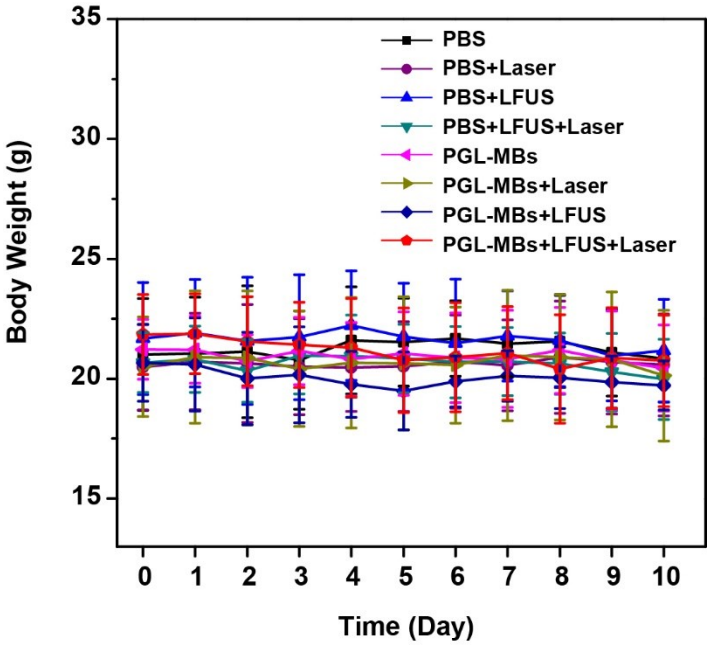
Supplementary Figure S1. Characterizations of porphyrin-grafted lipid microbubbles (PGL-MBs) before and after low-intensity ultrasound (LFUS) irradiation. (A) Contrast-enhanced ultrasound (CEUS) images at different PGL-MBs concentrations; (B) Appearance change PGL-MBs before and after LFUS irradiation.



Supplementary Figure S2. Detection of singlet oxygen in human prostate cancer PC-3 cells. H_2DCFDA showed green fluorescence in the presence of singlet oxygen. Cell uptake of PGL-MBs was observed by the red channel, which showed the fluorescence of PGL. (Scale bar: 20 μm)

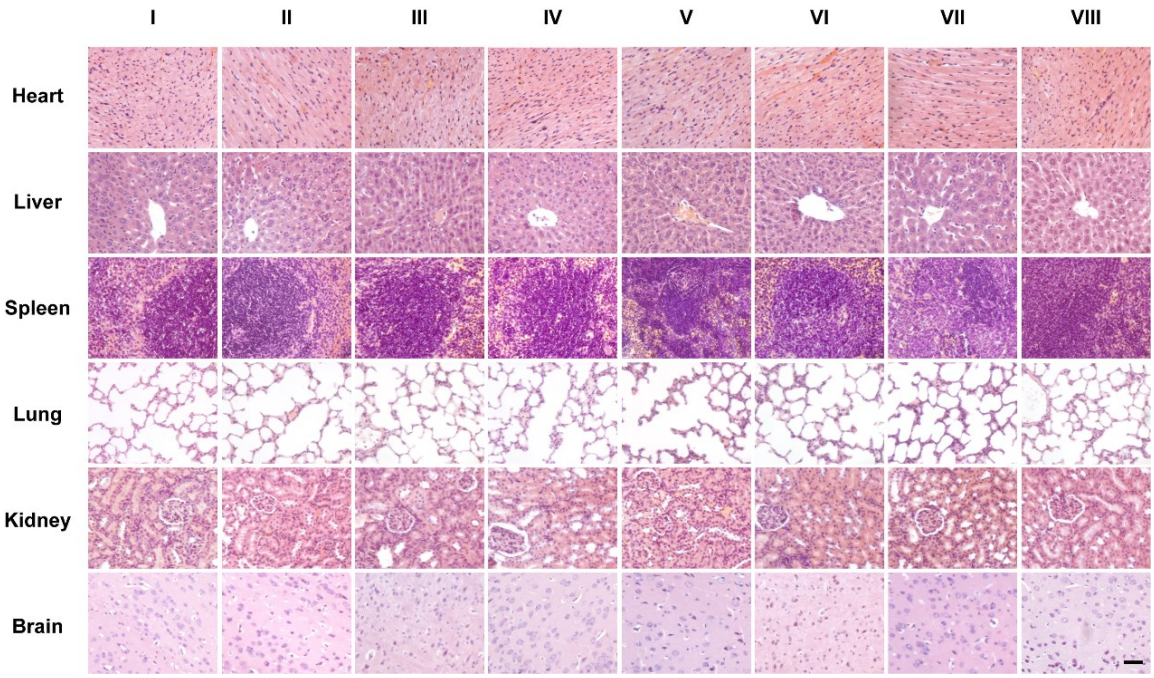


Supplementary Figure S3. Evaluation of the biocompatibility of PGL-MBs using human umbilical vein endothelial cells (HUVECs). Cell viability of HUVECs incubated with PGL-MBs (combined with LFUS or not) for 24 h were measured by CCK-8 test.

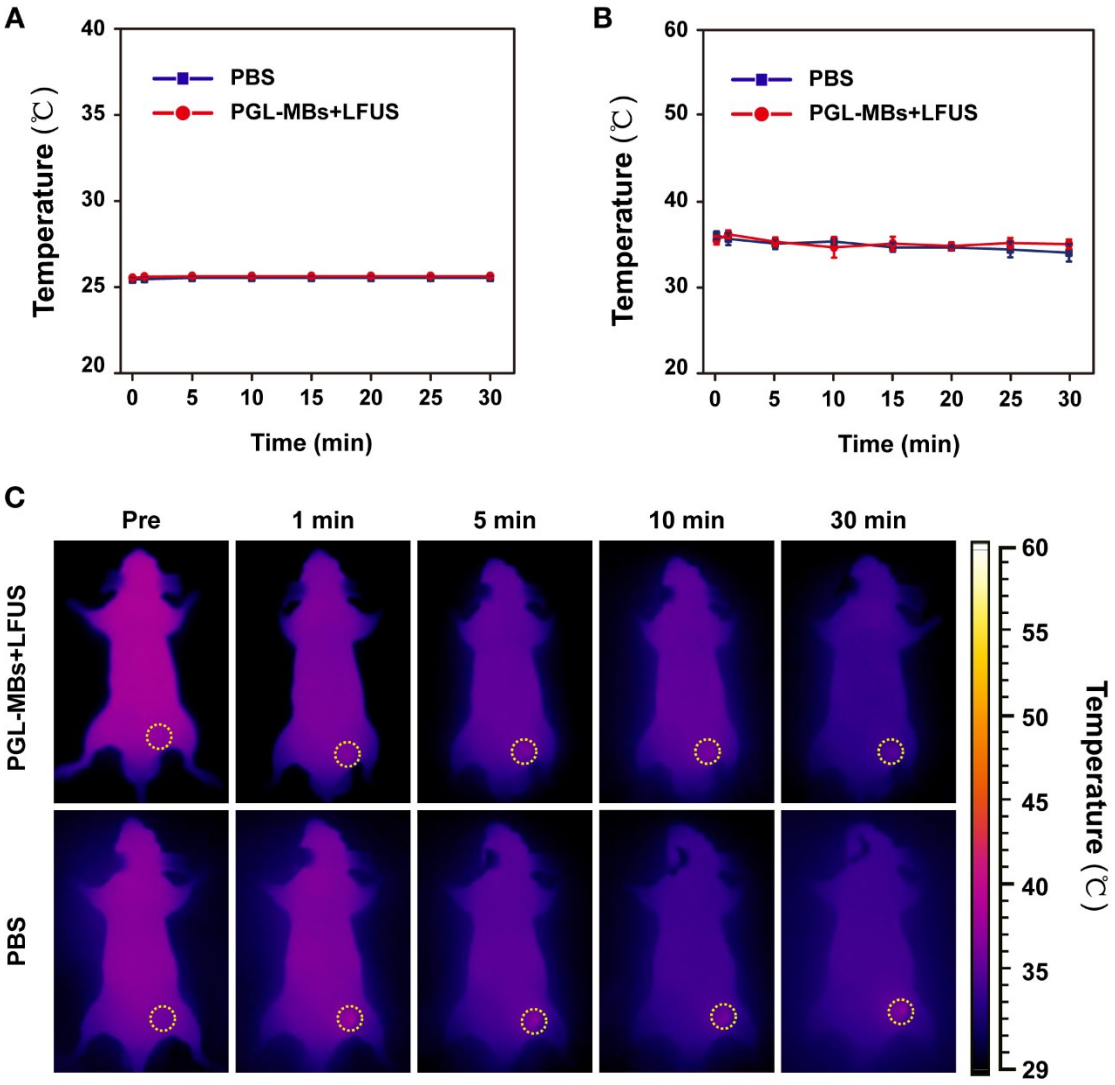


Supplementary Figure S4. Body weight curve measured every day after various

treatments.



Supplementary Figure S5. Representative hematoxylin and eosin (H&E) stained sections of major organs from mice after treatments up to 10 days. (Groups: I. PGL-MBs+LFUS+Laser; II. PGL-MBs+LFUS; III. PGL-MBs+Laser; IV. PGL-MBs only; V. PBS+LFUS+Laser; VI. PBS+LFUS; VII. PBS+Laser; VIII. PBS only. Scale bar: 50 μm)



Supplementary Figure S6. Temperature monitoring during PDT process. (A) *In vitro* temperature-time curves of PBS and PGL-MBs+LFUS solution (1 mg/mL). (n = 3) (B) *In vivo* temperature-time curves of the tumor site in the nude mice bearing subcutaneous PC-3 xenografts. PBS and PGL-MBs were injected intravenously and infrared camera was used to monitoring the temperature change. (n = 3) (C) Representative photographs taken by infrared camera. Tumors are circled with yellow dashed lines.