Supporting Information

Ultrasound triggered tumor oxygenation with oxygen-shuttle nano-perfluorocarbon to overcome hypoxia-associated resistance in cancer therapies

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Figure S1. Freeze-etching replication TEM image of as-made HSA-stabilized PFC nano-droplets after US treatment for 30 min.

Figure S2. Relative viabilities of 4T1 cells and CT26 cells incubated with PFC nanoemulsion for 24 h. Different volumes of PFC was added into 100 μl of cell culture for incubation.

Figure S3. Blood circulation profile of nano-PFC after intravenous (i.v.) injection into mice. The concentrations of PFC in blood were determined by gas chromatography–mass spectrometry (GC-MS) at various time points post injection.

Figure S4. Hypoxia inducible factor 1 alpha (HIF-1 α) staining used for evaluation of the tumor hypoxia state. Immunofluorescence imaging of tumor slices after various treatments including Ctrl + O₂ + US, PFC + O₂, PFC + O₂ + US. Blue, green, and red channels indicate DAPI, hypoxia region, and blood vessels with CD31 expression, respectively. The HIF-1 α expression level in PFC + O₂ + US treated tumors was dramatically decreased, suggesting their greatly relieved hypoxia conditions.

Figure S5. Tumor uptake of Liposome@Ce6. (a) The structure and composition of Liposome@Ce6. (b) Measurement of singlet oxygen by the SOSG test for different samples including free Ce6, Liposome@Ce6 and water under the 660 nm light exposure (5 mW cm^{-2}) for different periods of time. (c) Ex vivo fluorescence imaging of major organs/tissues including liver, spleen, kidney, heart, lung, and tumor, taken 24 h post i.v. injection of Liposome@Ce6. (d) Quantitative analysis of ex vivo Ce6 fluorescence intensity in different organs / tissues in (c).

Figure S6. Tumor growth curves of different groups of mice (five mice per group) after various treatments including untreated control (Ctr) and PFC + O₂+ US. For the later, tumor-bearing mice were i.v injected with 200 μ L of PFC nanoemulsion and treated with 30 min of tumor-focused US under hyperoxic breathing.