Supporting Information

Delicately Designed Cancer Cell Membrane-Camouflaged Nanoparticles for Targeted ^{19}F-MR/PA/FL Imaging-Guided Photothermal Therapy

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Experimental Methods:

Cancer Cell Membrane Proteins Characterization: SDS-PAGE (Sodium dodecyl sulfate-polyacrylamide gel electrophoresis) assay was carried out to depict proteins species on cancer cell membrane. A549 cells were trypsinized and suspended in PBS. AM vesicles and AM-PPNPs samples were purified and stored in PBS. A549 cells, AM vesicles and AM-PPNPs samples plus the SDS-PAGE gel loading buffer were heated in boiling water bath for 10 min. Each sample (10 μL) was loaded into the bottom of wells of Mini-PROTEAN Tetra System (BIO-RAD, CA, USA). Coomassie Blue protocols were utilized to accomplish protein staining, after that the gel was washed to reduce background before FL imaging.

Cell Culture: A549 lung cancer cells and MRC-5 lung fibroblast cells were both cultured in complete MEM medium in the presence of 10% foetal bovine serum and 1% antibiotics (100 μg/mL penicillin and 100 μg/mL streptomycin) at 37 °C in a humidified environment with 5% CO_2.

Stability Experiment of AM-PP@ICGNPs: AM vesicles extracted from cells were labeled with 0.2 mmol membrane tracker DiI. AM@DiI vesicles were coated onto PP@FITCNPs cores to form the final nanoparticles. A549 cells were plated in a 6-well plate with a coverslip placed in the bottom, control the cell concentration to be 2×10^4 /well. When cells reached 60%–70% confluence, fresh medium dissolving the double-tagging AM@DiI-PP@FITCNPs were added for further 4 h incubation. After washed three times by PBS, DAPI was used to stain cell nuclei. The DiI (561 nm excitation and 565 nm emission) and FITC (488 nm excitation and 500-550 nm emission) fluorescence signals were observed by confocal laser scanning microscope (A1R/A1, Nikon, Japan).

Cell Experiment for ^{19}F-MRI: A549 cells and MRC-5 cells were cultured in T75 culture flask with complete MEM medium. When the cells reached to confluence 90-100%, aspirate the regular culture medium. Serum-free medium dissolved with

AM-PP@ICGNPs (C_F=15 mM) and bare PP@ICGNPs (C_F=15 mM) were added for 6 h incubation, 9×10^7 cells were trypsinized and collected. After purification, the cells were suspended in PBS and transfered to a 5 mm NMR tube for ^{19}F-MRI assessment on 9.4 T Micro-imaging system (Bruker Avance 400, Ettlingen, Germany).

Pharmacokinetic Study of AM-PP@ICGNPs: To study the blood circulation behavior of AM-PP@ICGNPs, balb/c mice were intravenous injected with AM-PP@ICGNPs, bare PP@ICGNPs and ICG molecules. About 100 μL blood were withdrawn through the retro orbital sinus bleeding at fixed times after injection. Blood samples were then dissolved in 900 μL radio immunoprecipitation assay (RIPA) lysis buffer. The fluorescence spectra of ICG was then tested to determine the blood circulation of nanoparticles.

Animals and Tumor Model： Twenty male Balb/c nude mice (5–6 weeks of age, weighing 18-21 g) were obtained from Beijing Vital River Laboratory Animal Technology Co., Ltd.. All experimental protocols in this study were approved by Animal Care and Use Committees at the Innovation Academy for Precision Measurement Science and Technology, the Chinese Academy of Sciences. To establish A549 tumor xenografts models, mice were subcutaneously inoculated on the left hind leg with 100 μL 1×10^8 cells/mL of A549 cells suspended in PBS. The tumor size was recorded at specific time points after inoculation.

MRI Experiments Parameters: ^{1}H-MRI was carried out by using the RARE (rapid acquisition with refocused echoes) method. The imaging parameters were set as follows: number of average is 4 times, repetition time (TR) is 6381 ms, effective time (TE) is 56 ms, field of view (FOV) is 30 mm × 30 mm, slice thickness (SI) is 1.5 mm, matrix size is 256 × 256. ^{19}F-MRI were acquired using RARE sequence. The parameters were set as follows: number of average is 1024 times, repetition time (TR) is 2500 ms, effective time (TE) is 3 ms, matrix size is 32 × 32, field of view (FOV) is 37 mm × 37 mm, slice thickness (SI) is 1.5 mm, the total scan time was approximately 2h50min.

Biosafety of AM-PP@ICGNPs: The mice were sacrificed after the whole treatment (18 d). Tumors and major organs such as liver, spleen, kidneys, heart, lung were harvested and fixed by using 4% paraformaldehyde for later paraffin embedding. Tissue sections were then prepared for H&E staining, followed by histology evaluation. Tumor tissues were also stained with Ki-67 to observe cell proliferation. The blood biochemistry indicators of liver and spleen, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine (CRE) and blood urea nitrogen (BUN), were measured by Zokoyo Biotech, Wuhan.

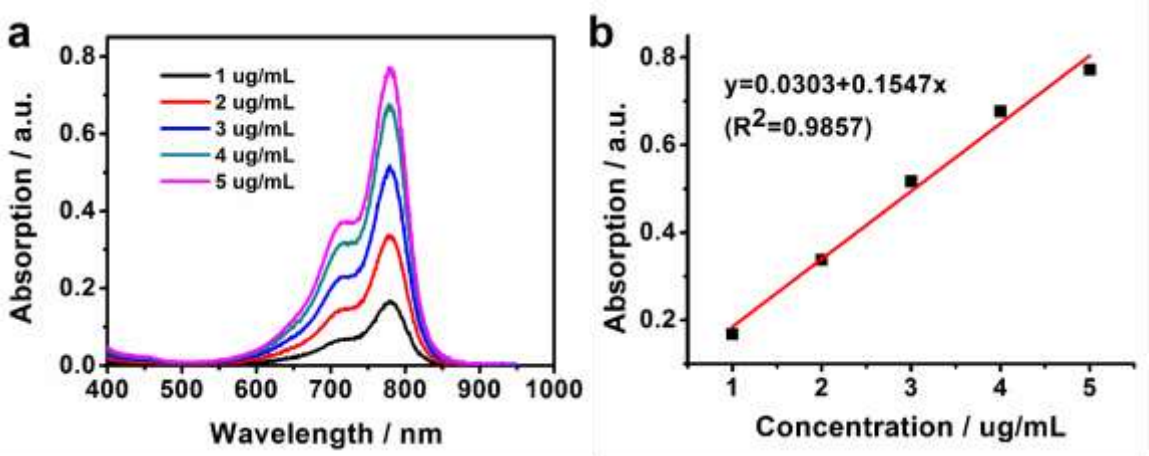

Figure S1 (a) The UV-vis absorbance spectrum of ICG with different concentrations. (b) The standard curve of UV-vis absorption spectrum of ICG.

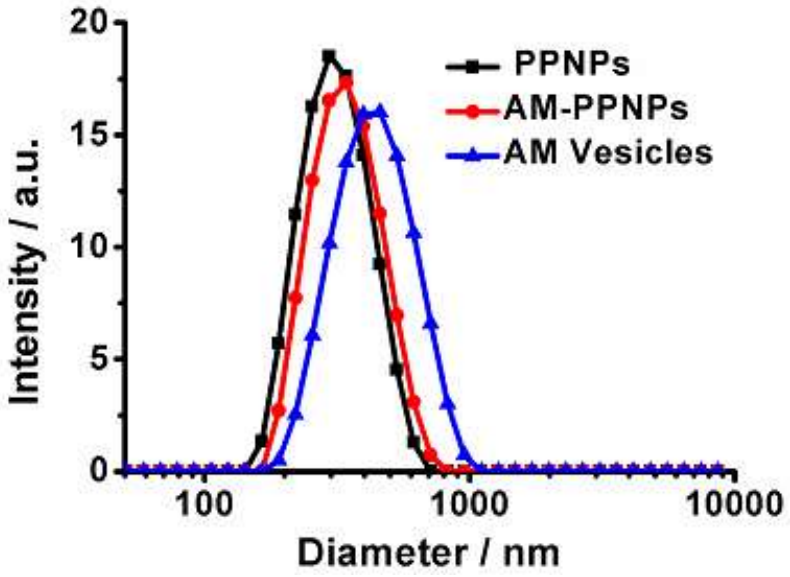

Figure S2 DLS diameter distribution of AM vesicles, PPNPs and AM-PPNPs.

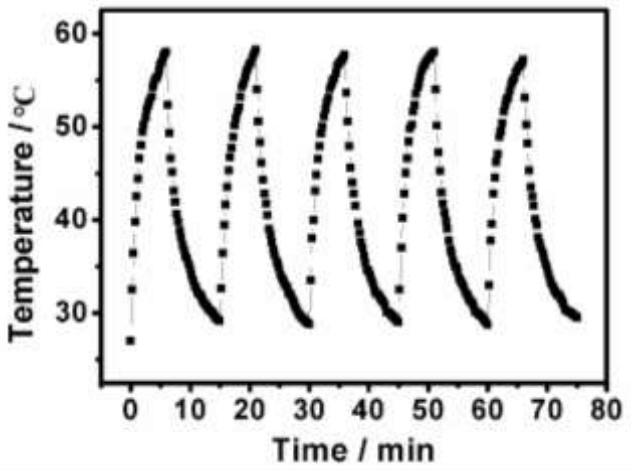

Figure S3 Temperature change of AM-PP@ICGNPs over five cycles of repeated laser irradiation (765 nm , 400 mW/cm^2, 6 min on and 9 min off).

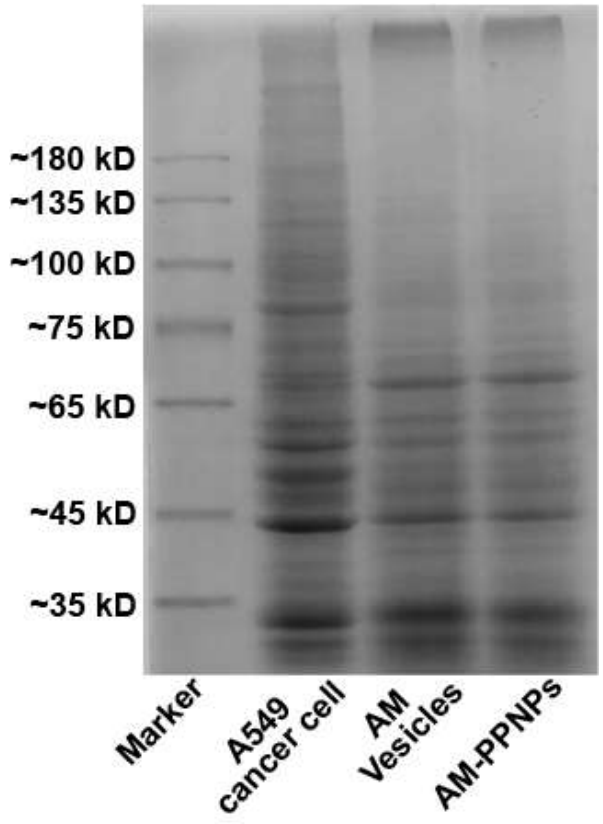

Figure S4 SDS-PAGE protein analysis of A549 cancer cell, A549 cell membrane vesicles, AM-PPNPs.

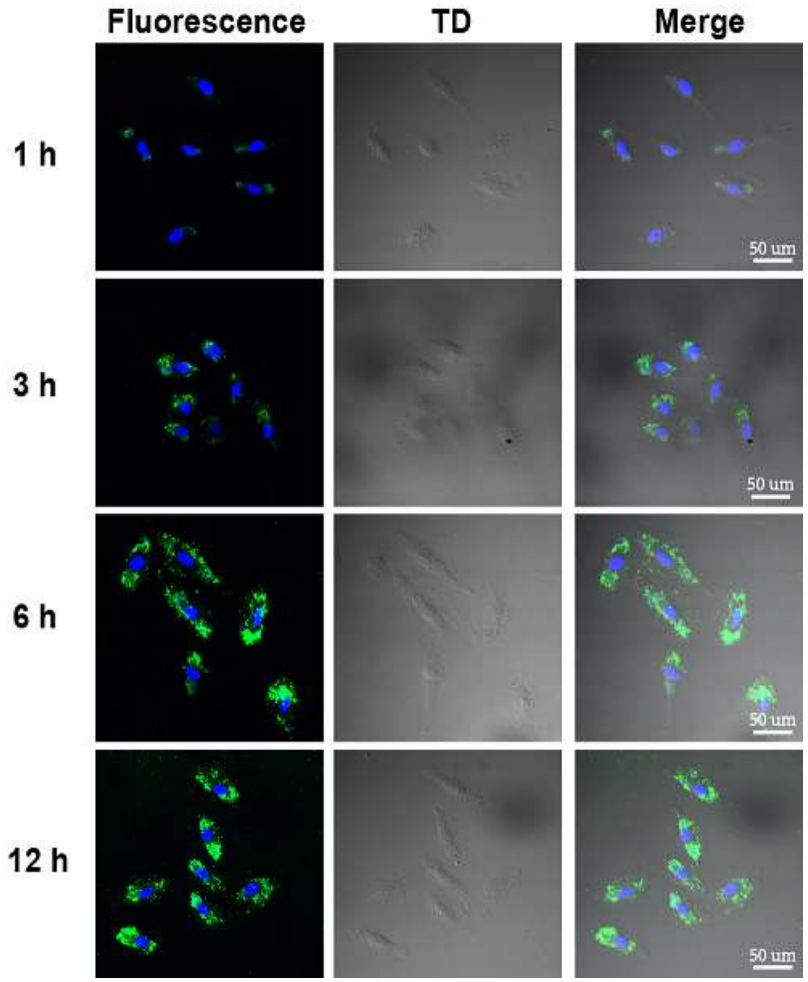

Figure S5 Fluorescence imaging of A549 cells incubated with AM-PP@FITCNPs for specific times captured by laser scanning confocal microscopy. Cell nuclei was stained by DAPI.

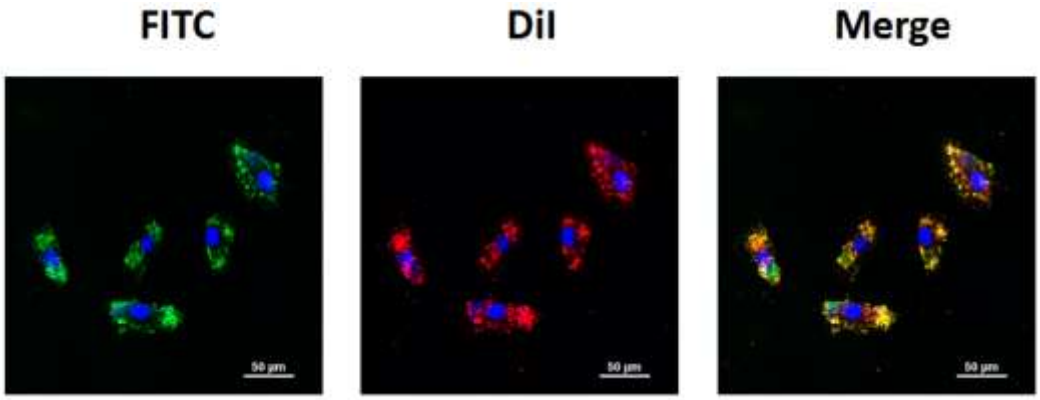

Figure S6 Fluorescence images of A549 cells treated with AM@DiI-PP@FITCNPs for 4 h captured by laser scanning confocal microscop. Colocalization of the A549 membranes (visualized with red DiI dyes) and polymeric cores (visualized with green FITC dyes) was demonstrated.

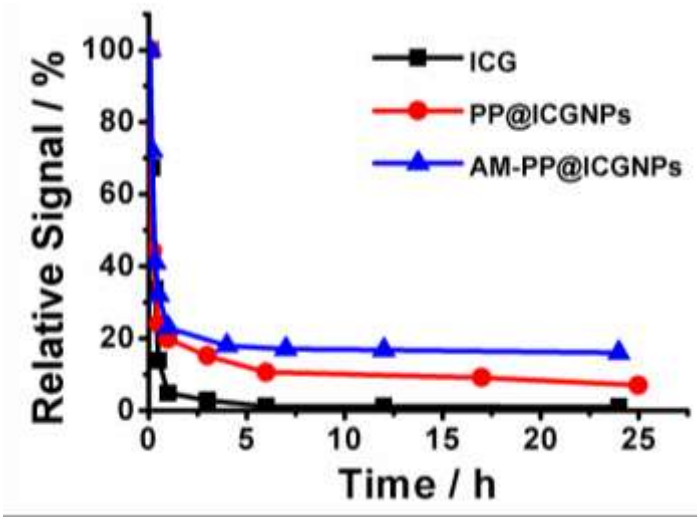

Figure S7 ICG-loaded nanoparticles were injected intravenously through the tail vein of Balb/c mice. Blood was withdrawn intraorbitally at various time points and measured for fluorescence at 765 nm excitation to evaluate the systemic circulation lifetime of the nanoparticles.

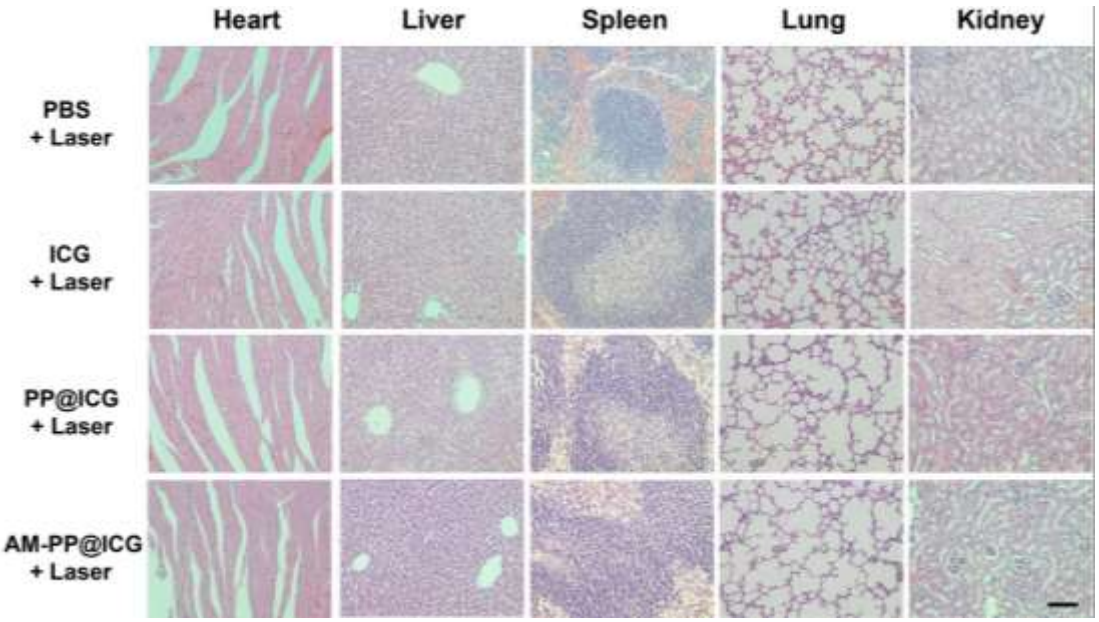

Figure S8 Histopathologic examination of the tissues including heart, liver, spleen, lung and kidney from Balb/c nude mice after intravenous administration of PBS, ICG, PP@ICGNPs and AM-PP@ICGNPs followed by NIR irradiation. Scale bar = 100 μm.

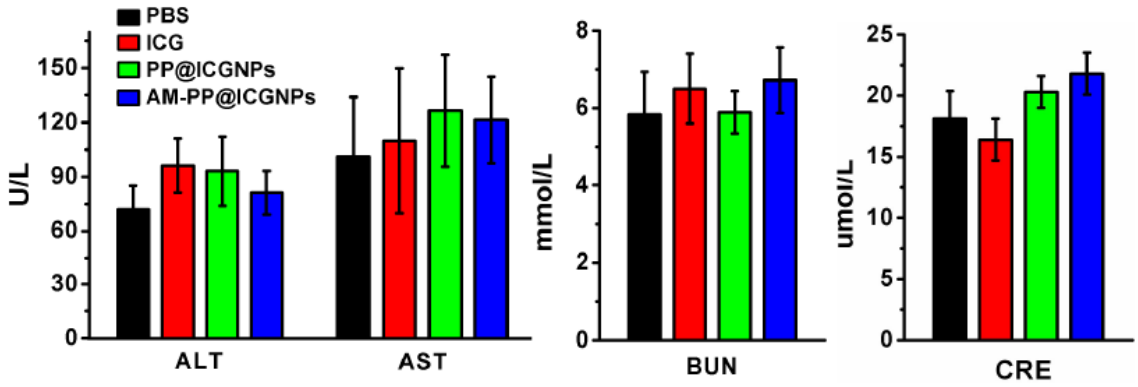

Figure S9 Blood biochemistry analysis of liver and kidney function markers (ALT, AST, BUN and CRE) after intravenous administration of PBS, ICG, PP@ICGNPs and AM-PP@ICGNPs followed by NIR irradiation.