Supporting Information

Photoacoustic-imaging-guided therapy of functionalized melanin nanoparticles: combination of photothermal ablation and gene therapy against laryngeal squamous cell carcinoma

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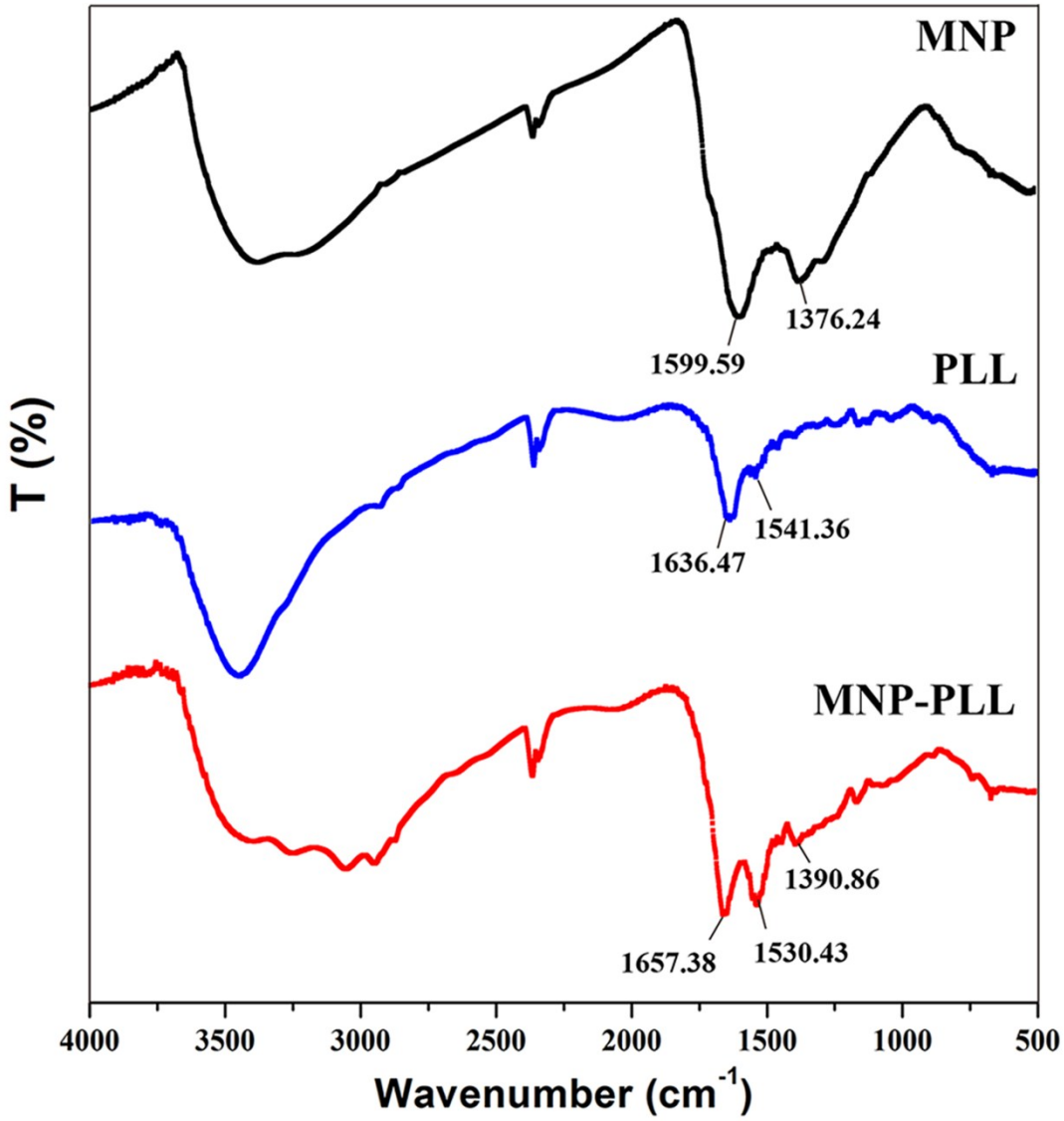

Fig. S1. FT-IR spectra of MNP, PLL and MNP-PLL.

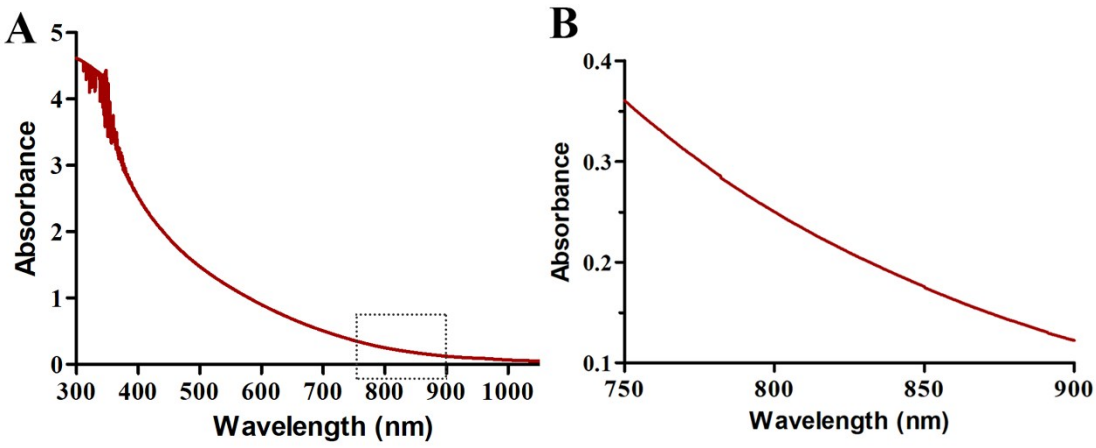

Fig. S2. UV-vis-NIR spectra of MNP-PLL. The left graph (A) indicates the whole absorption profiles ranged from 300 nm to 1000 nm, while the right graph (B) magnifies the absorption portion between 750 nm and 900 nm.

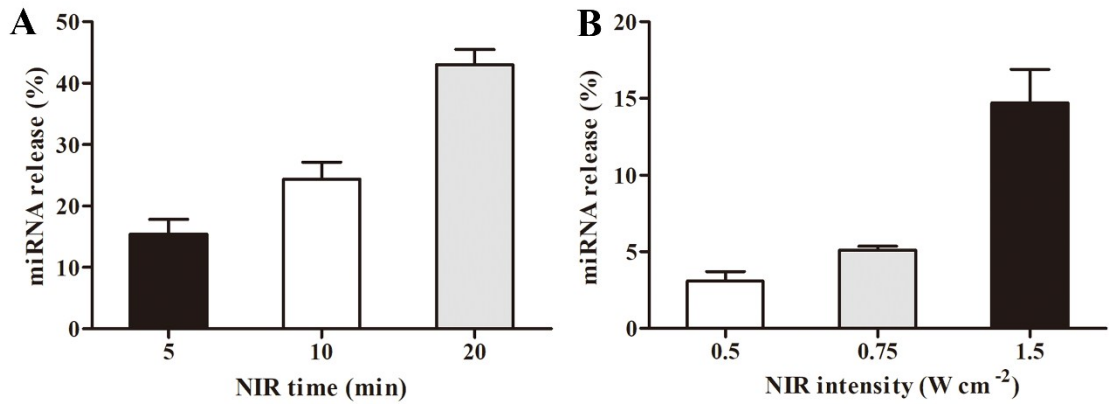

Fig. S3. Accumulative miRNA release from MP-miRNA triggered by NIR irradiation for different times (A) and at various power density (B).

The photothermal stability of MNP-PLL

To investigate the photothermal stability, the solution of MNP-PLL（1.5 mg/ml）was irradiated with NIR laser (808 nm laser at 1.5 W/cm^2 for 300 s) and then cooled naturally. The indocyanine green (ICG) solution (0.05 mg/ml), which has been widely used as an FDA-approved NIR dye, was used as a control. This process was performed under five cycles and temperatures of each cycle were monitored during heating. As shown in **Fig. S4**, after five cycles of NIR irradiation, MNP-PLL remained excellent photo-thermal stability and no distinct temperature decrease could be observed between each cycle. On the contrast, ICG suffered rapidly decreased photothermal conversion capability after multiple rounds of NIR irradiation.

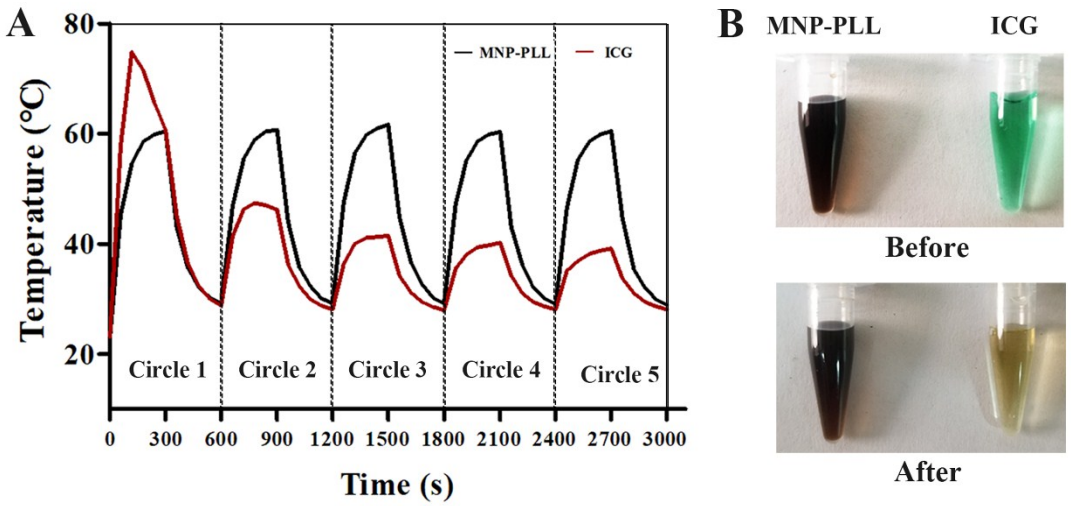

Fig. S4. (A) Temperature variations of MNP-PLL (0.15 mg/mL) and Indocyanine green (ICG) solution (0.05 mg/mL) under irradiation by an 808-nm laser at the power density of 1.5 W/cm^2 for five cycles (5 min of irradiation for each cycle). (B) Photos of MNP-PLL and ICG solution before and after five cycles of photothermal heating.

The physiological stability of MP-miRNA NPs

The physiological stability of the nanoparticle was evaluated by monitoring the change of the hydrodynamic sizes in the DMEM medium containing 10% FBS using the Nano-Zetasizer[1, 2]. Shortly, the MP-miRNA NPs was added to DMEM medium containing 10% FBS and incubated at 37℃ for 24 h. Then the sample was analyzed at 0 h, 2 h, 4 h, 6 h and 24 h post-incubation by dynamic light scattering.

After adding the nanoparticles in the serum-containing solution, the hydrodynamic size increased to around 80 nm (peak at 0 h post-incubation), which might occur as a result of association with proteins due to the positive potential of MP-miRNA NPs. However, after 24-h incubation, the main hydrodynamic size remained at about 80 nm. Thus, we concluded that the MP-miRNA NPs were stable in serum.

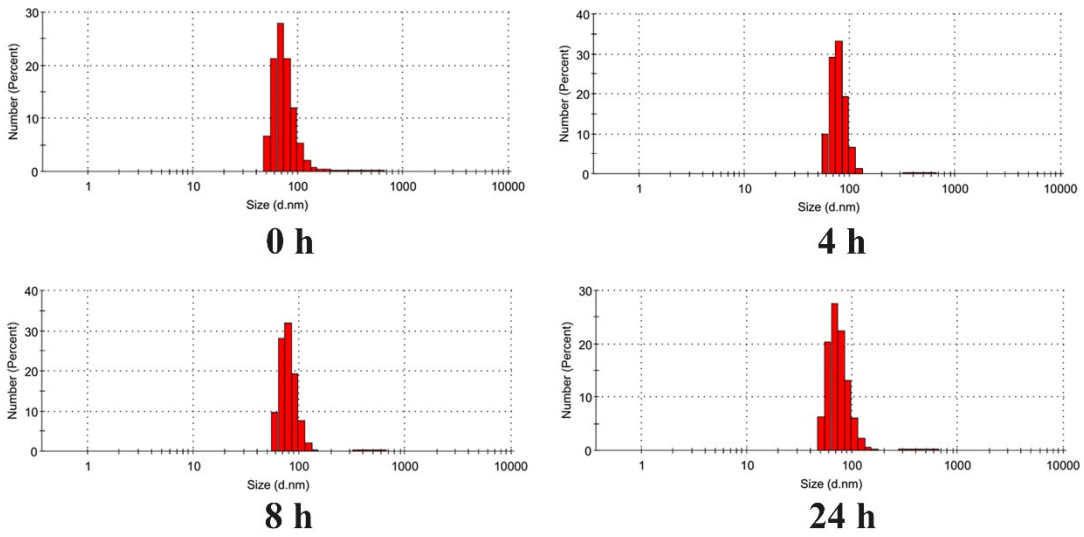

Fig. S5. Hydrodynamic size of MP-miRNA during different incubation time in the DMEM medium containing 10% FBS.

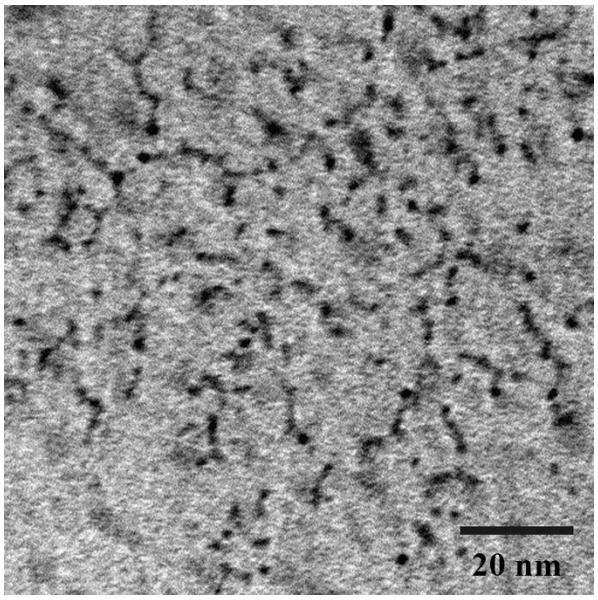

Fig. S6. TEM images of MP-miRNA NPs after NIR irradiation at 808-nm laser with the power density of 1.5 W/cm^2 for 5 mins.

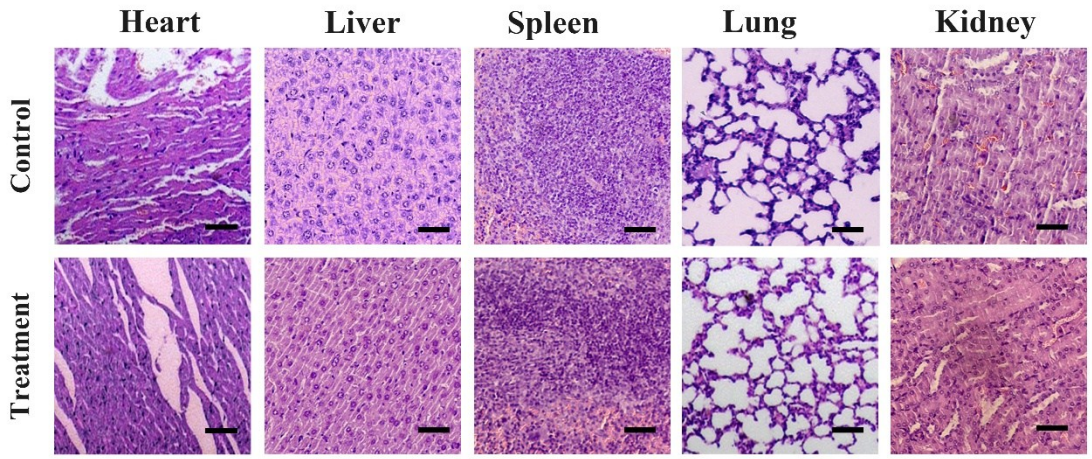

Fig. S7. The H&E images of major organs (heart, liver, spleen, lung and kidney) from the control of healthy mice and tumor-bearing mice received treatment of MP-miR-145-5p+laser. Scale bar =100 μm

References

1. Z. Zha, X. Yue, Q. Ren and Z. Dai, *Adv Mater*, 2013, **25**, 777-782.
2. P. Wang, L. Zhang, W. Zheng, L. Cong, Z. Guo, Y. Xie, L. Wang, R. Tang, Q. Feng, Y. Hamada, K. Gonda, Z. Hu, X. Wu and X. Jiang, *Angew Chem Int Ed Engl*, 2018, **57**, 1491-1496.