

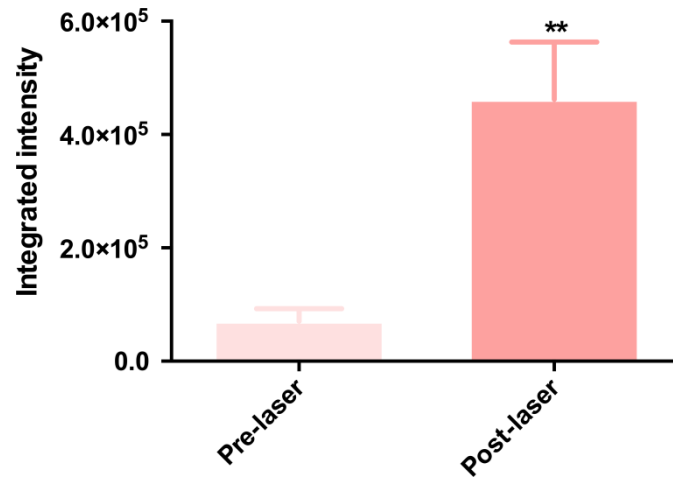
**Dissolving microneedles with spatiotemporally controlled pulsatile  
release nanosystem for synergistic chemo-photothermal therapy of  
melanoma**

Wanbing Qin<sup>1#</sup>, Guilan Quan<sup>2#</sup>, Ying Sun<sup>1</sup>, Minglong Chen<sup>1</sup>, Peipei Yang<sup>3</sup>, Disang  
Feng<sup>2</sup>, Ting Wen<sup>1</sup>, Xinyu Hu<sup>1</sup>, Xin Pan<sup>1</sup>✉, Chuanbin Wu<sup>1,2</sup>

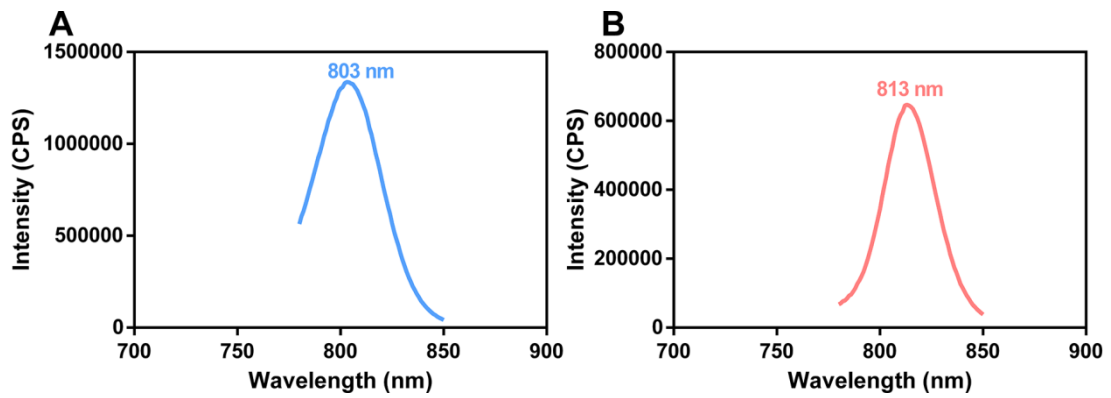
1. School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006,  
China
2. College of Pharmacy, Jinan University, Guangzhou, 510632, China
3. Department of Pharmacy Guangzhou Women and Children's Medical Center,  
Guangzhou Medical University, Guangzhou 510623, China

# These authors contributed equally to this work.

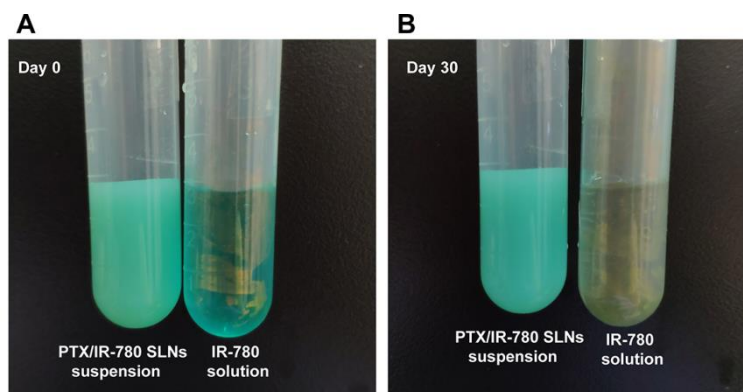
✉ Corresponding author: Xin Pan (panxin2@mail.sysu.edu.cn)



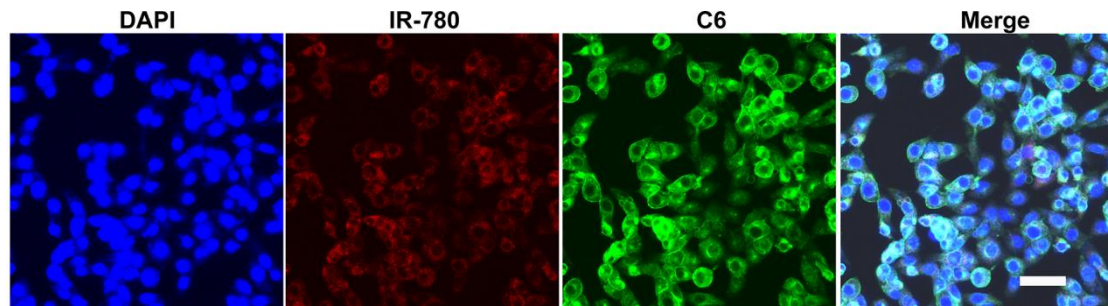
**Figure S1.** Quantitative analysis of fluorescence intensity of C6 before and after laser treatments.



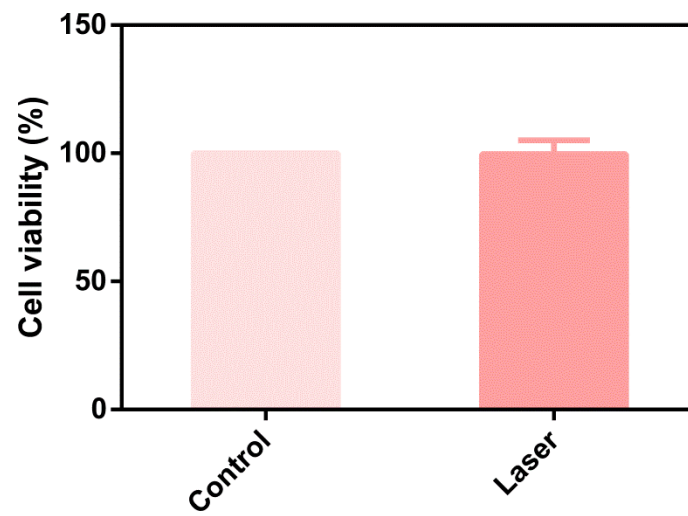
**Figure S2.** Fluorescence spectra of (A) IR-780 solution and (B) IR-780 SLNs suspension.



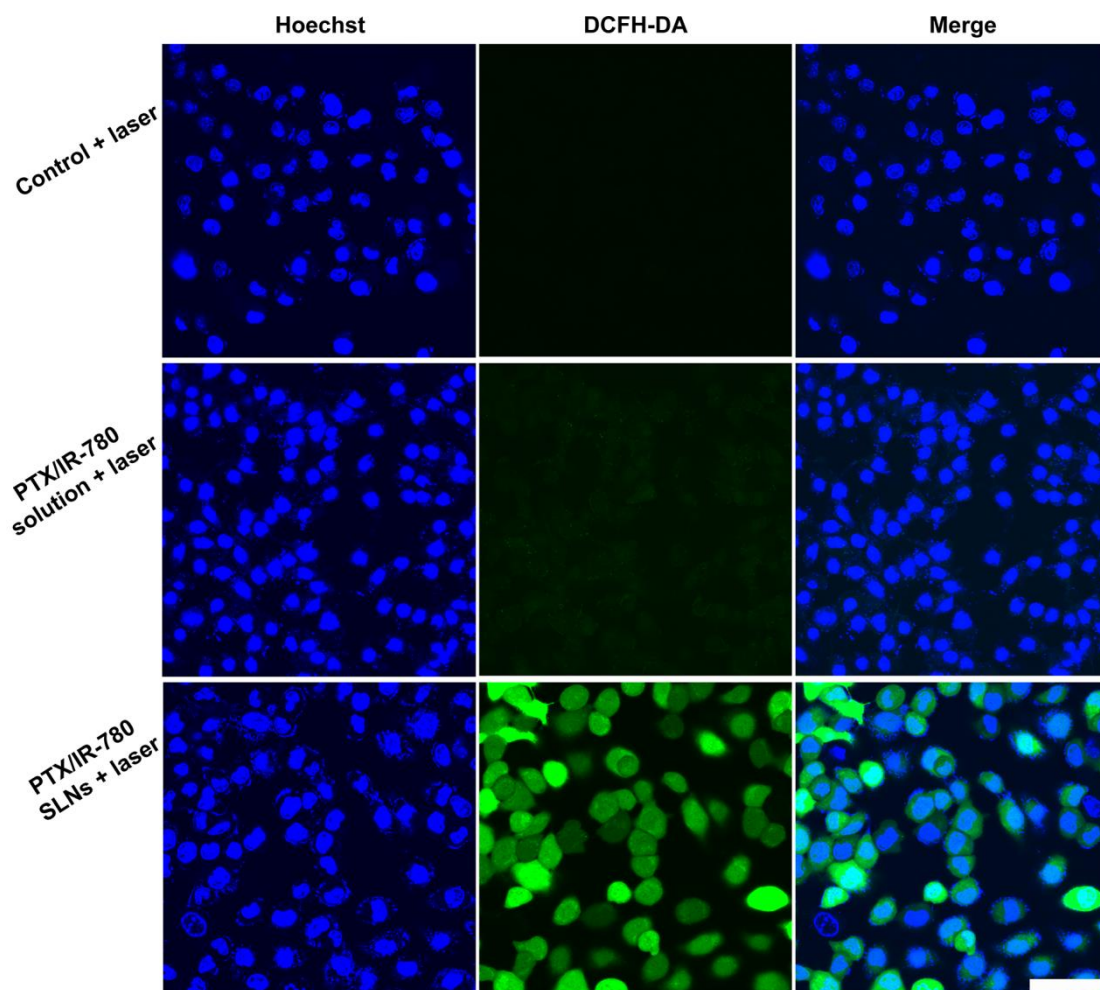
**Figure S3.** The picture of PTX/IR-780 SLNs suspension and IR-780 solution placed at 4 °C for (A) 0 day and (B) 30 days, respectively.



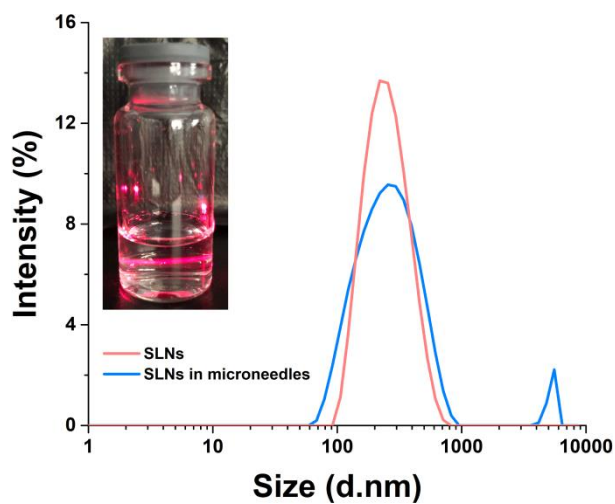
**Figure S4.** The CLSM images of B16 cells incubated with C6/IR-780 SLNs for 2 h (IR-780: 10 µg/mL, C6:1 µg/mL). The scale bar is 50 µm.



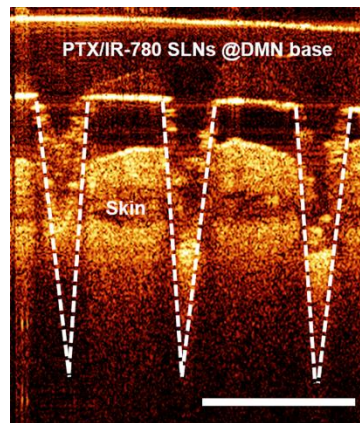
**Figure S5.** Viability of B16 cells treated with or without laser irradiation ( $n = 3$ ).



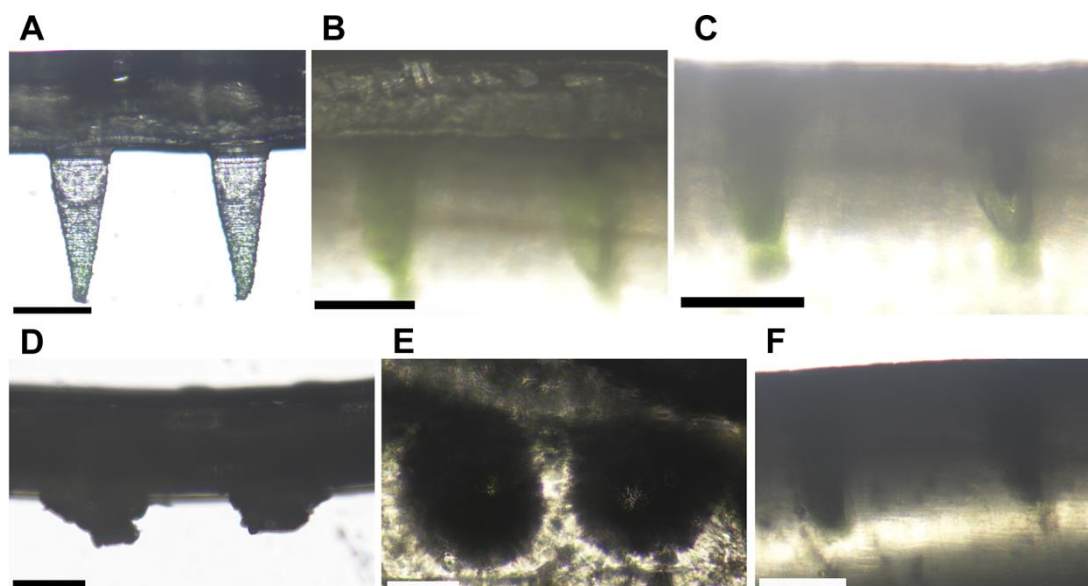
**Figure S6.** The CLSM images of ROS generation in B16 cells after treated with different treatments with laser (808 nm, 1W/cm<sup>2</sup>). The scale bar is 50  $\mu$ m.



**Figure S7.** The particle size of SLNs before and after dissolving PTX/IR-780 SLNs @DMNs

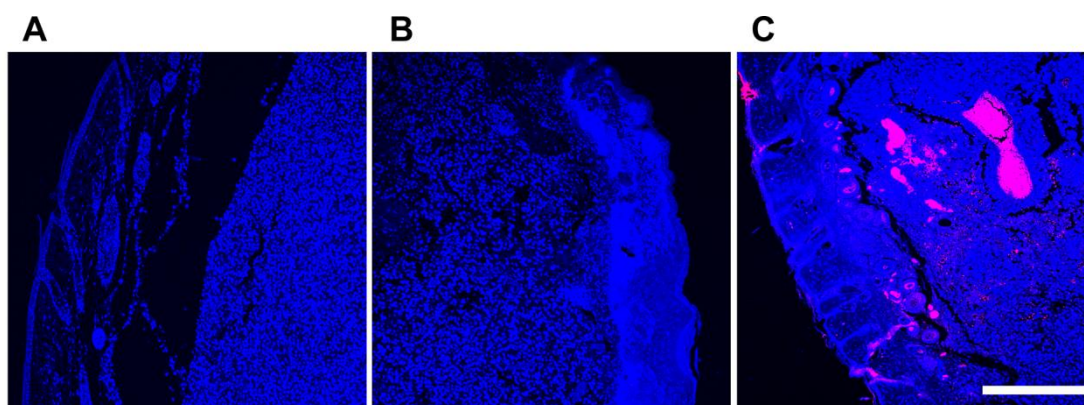


**Figure S8.** Two-dimentional OCT image of rat skin after inserted with PTX/IR-780 SLNs @DMNs. The scale bar is 500  $\mu$ m.

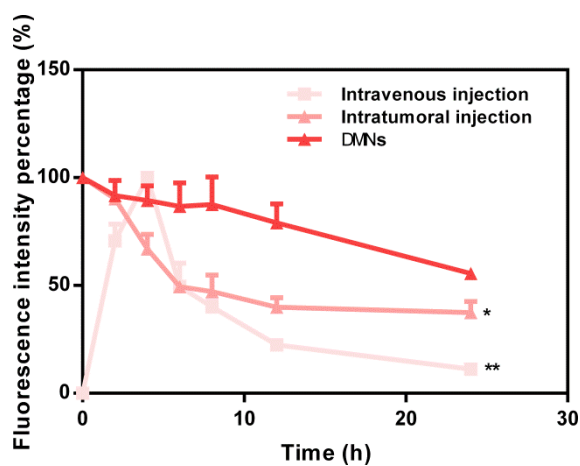


**Figure S9.** Bright field micrographs of PTX/IR-780 SLNs @DMNs inserted into the gelatin gel. (A) The picture of PTX/IR-780 SLNs @DMNs before insertion. (B) The picture of PTX/IR-780 SLNs @DMNs inserted into the gelatin block. (C) The picture

of PTX/IR-780 SLNs accumulated in the gelatin block after the DMNs base part was removed. (D) The picture of PTX/IR-780 SLNs @DMNs after removed from gelatin block. (E) The surface of the gelatin block after removed PTX/IR-780 SLNs @DMNs. (F) PTX/IR-780 SLNs accumulated in the gelatin block after sealed for 24 h. The scale bar is 400  $\mu\text{m}$ .

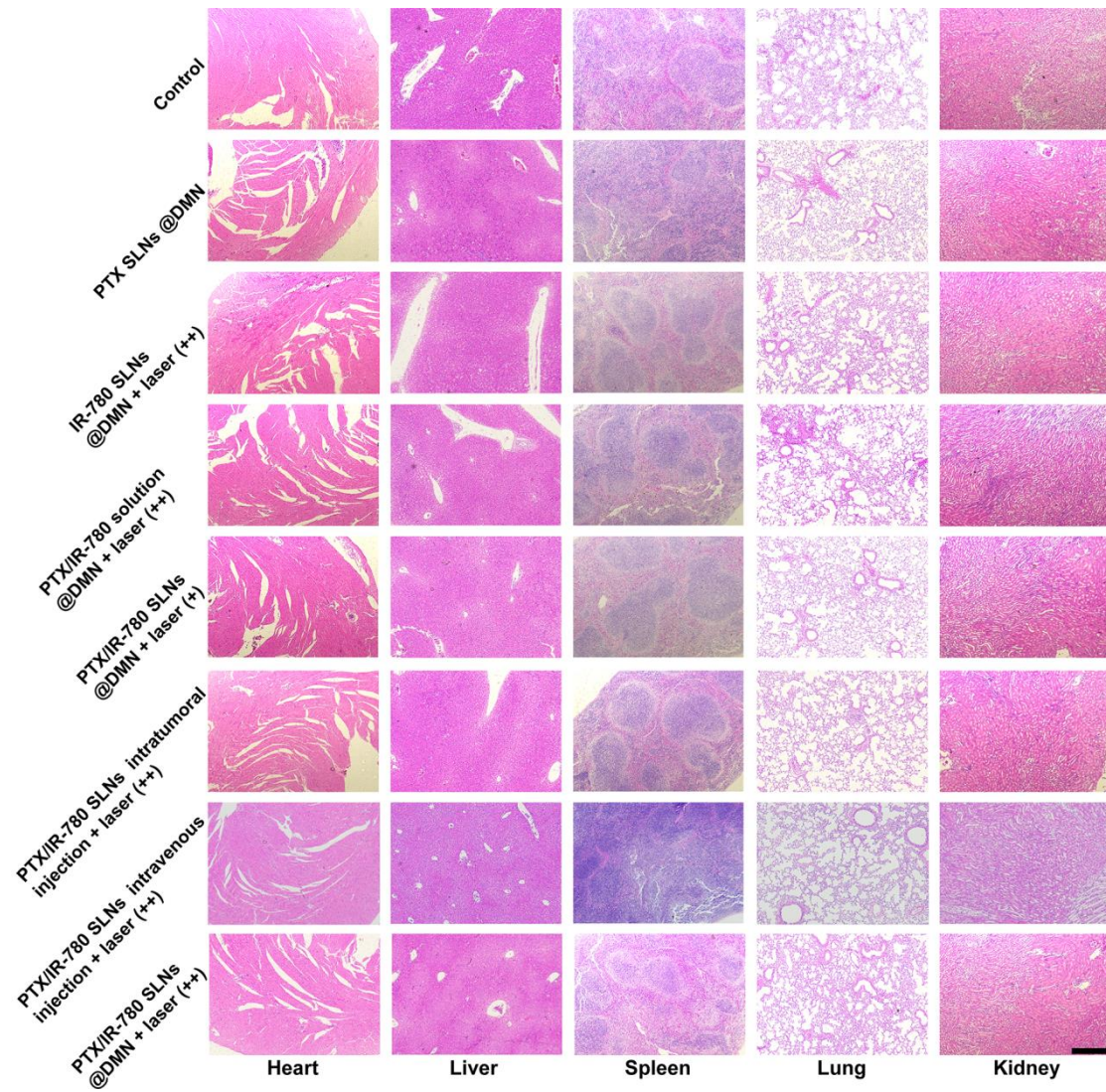


**Figure S10.** HSP 70 immunofluorescence staining of tumor after different treatments with or without laser (808 nm, 1 W/cm<sup>2</sup>). (A) No treatment. (B) PTX/IR-780 SLNs @DMNs without laser. (C) PTX/IR-780 SLNs @DMNs laser (++). The scale bar is 400  $\mu\text{m}$ .

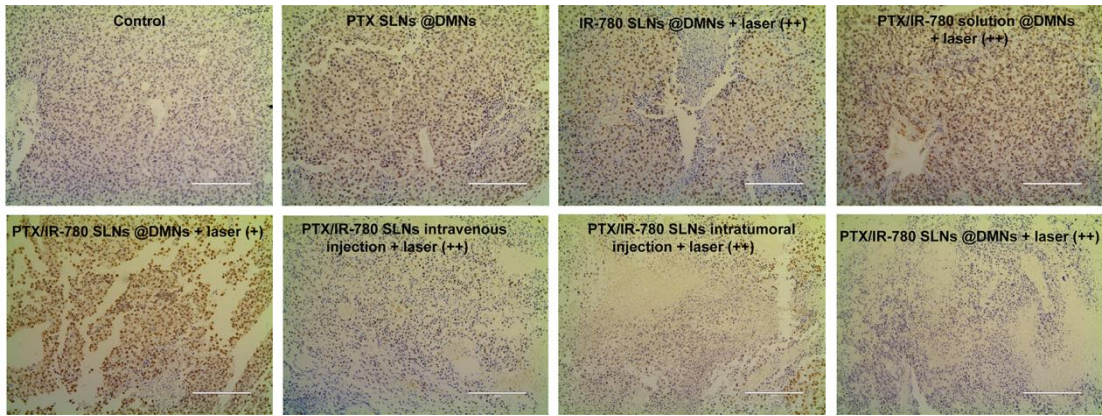


**Figure S11.** Normalized value of mean fluorescent intensity at different time intervals

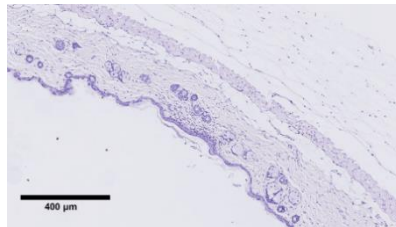
after administration of PTX/IR-780 SLNs by intravenous injection, intratumoral injection, and DMN, respectively ( $n = 3$ ). Data are expressed as the mean  $\pm$  SD, \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  versus DMNs.



**Figure S12.** H&E staining images of major organs after different treatments. The scale bar is 100  $\mu$ m.



**Figure S13.** Ki67 staining of tumors after different treatments for 12 days. The scale bar is 400  $\mu\text{m}$ .



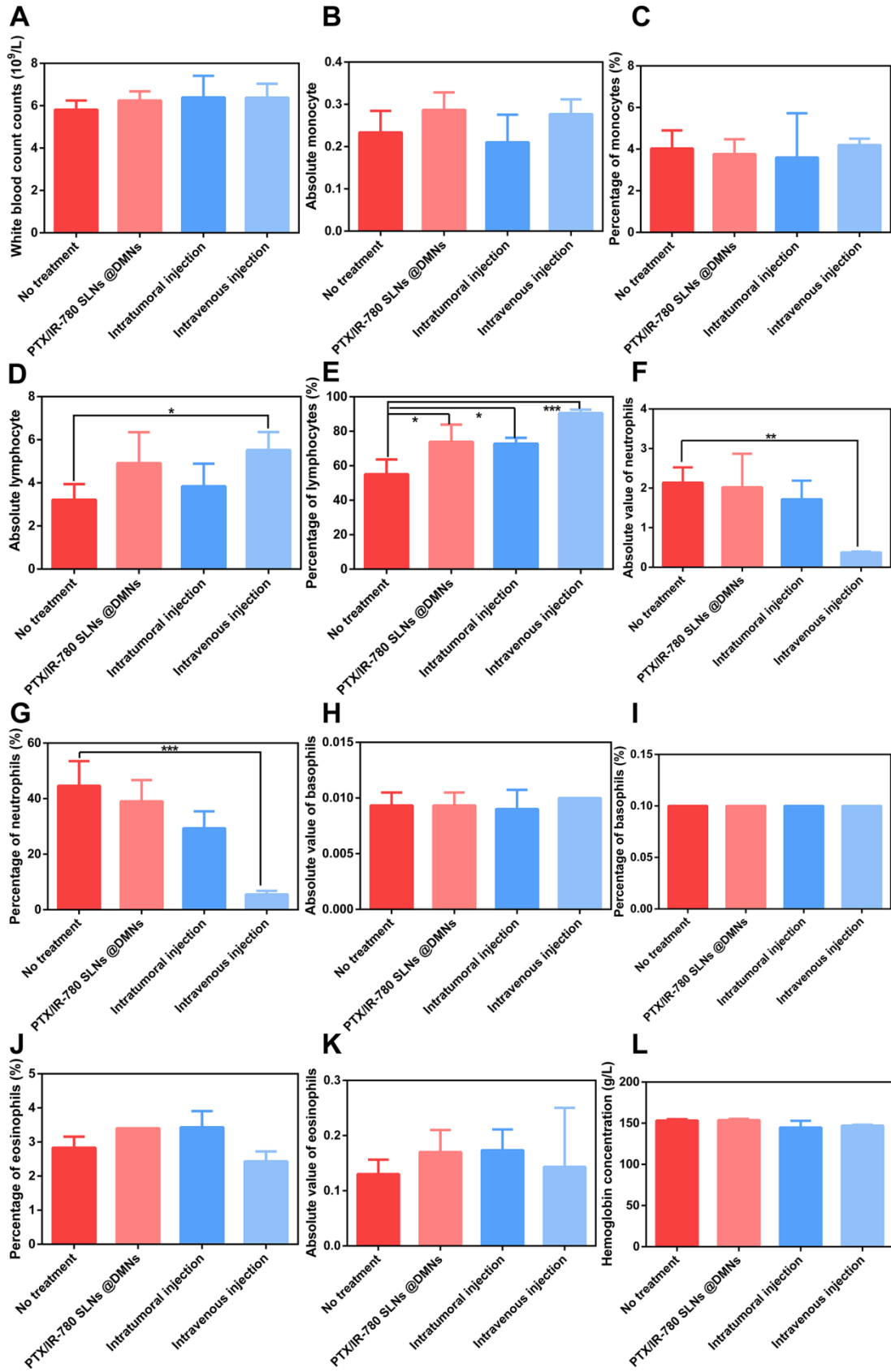
**Figure S14.** Ki67 staining of healthy mice skin.





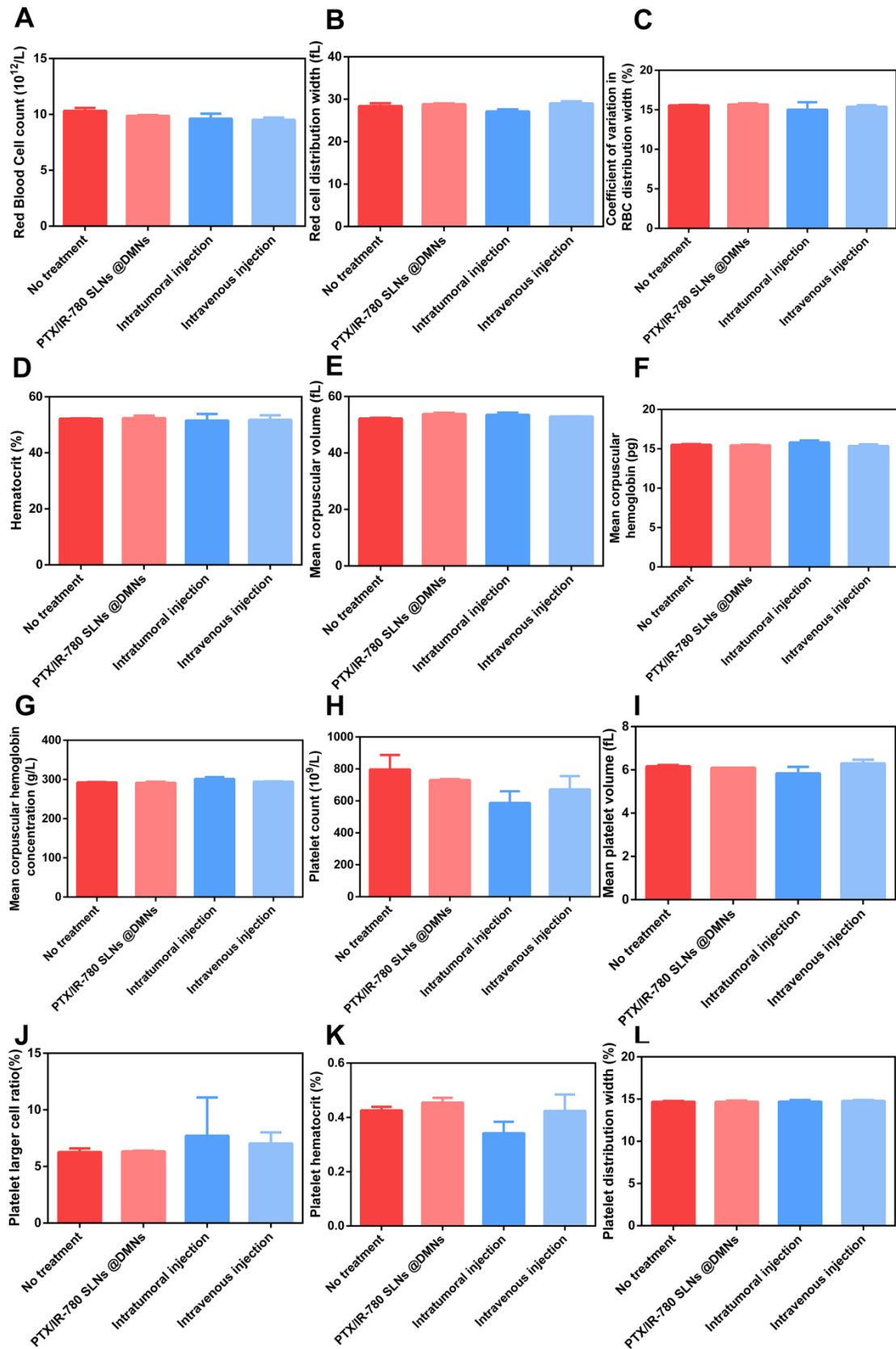
**Figure S15.** Pictures of mice back skin recovery after treated with PTX/IR-780 SLNs

@DMNs with or without laser (808 nm, 1 W/cm<sup>2</sup>).



**Figure S16.** Changes in blood routine examination parameters in various treatments.

Values are expressed as mean  $\pm$  S.D., \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  versus control ( $n = 3$ ).



**Figure S17.** Changes in blood routine examination parameters in various treatments.

Values are expressed as mean  $\pm$  S.D., ( $n = 3$ ).