

## Supplementary information

### Mitochondria-targeting near-infrared light-triggered thermosensitive liposomes for localized photothermal and photodynamic ablation of tumors combined with chemotherapy

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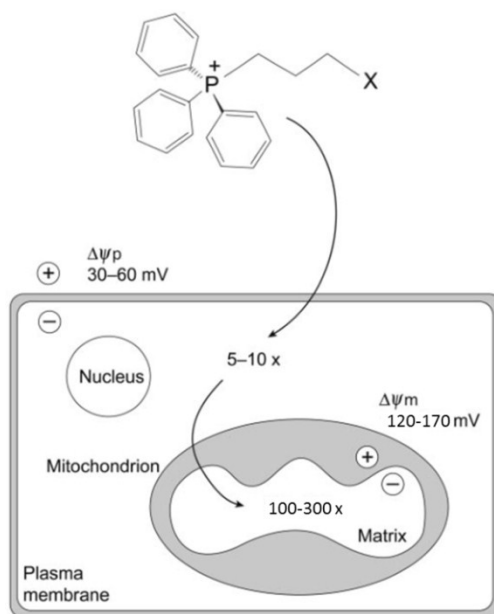


Fig.S1 Uptake of alkyl triphenylphosphonium cations by mitochondria within cells. The lipophilic triphenylphosphonium cation is covalently attached to a biologically active molecule (X). The lipophilic cation is accumulated 5- to 10-fold into the cytoplasm from the extracellular space by the plasma membrane potential ( $\Delta\Psi_p$ ) and then further accumulated 100- to 300-fold into the mitochondrial matrix by the mitochondrial membrane potential ( $\Delta\Psi_m$ ).

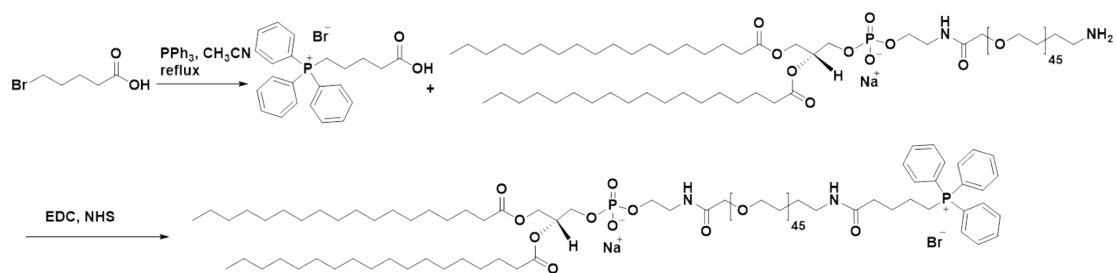


Fig. S2 Synthesis of the DSPE-PEG<sub>2K</sub>-TPP. The triphenylphosphine was abbreviated as PPh<sub>3</sub>.

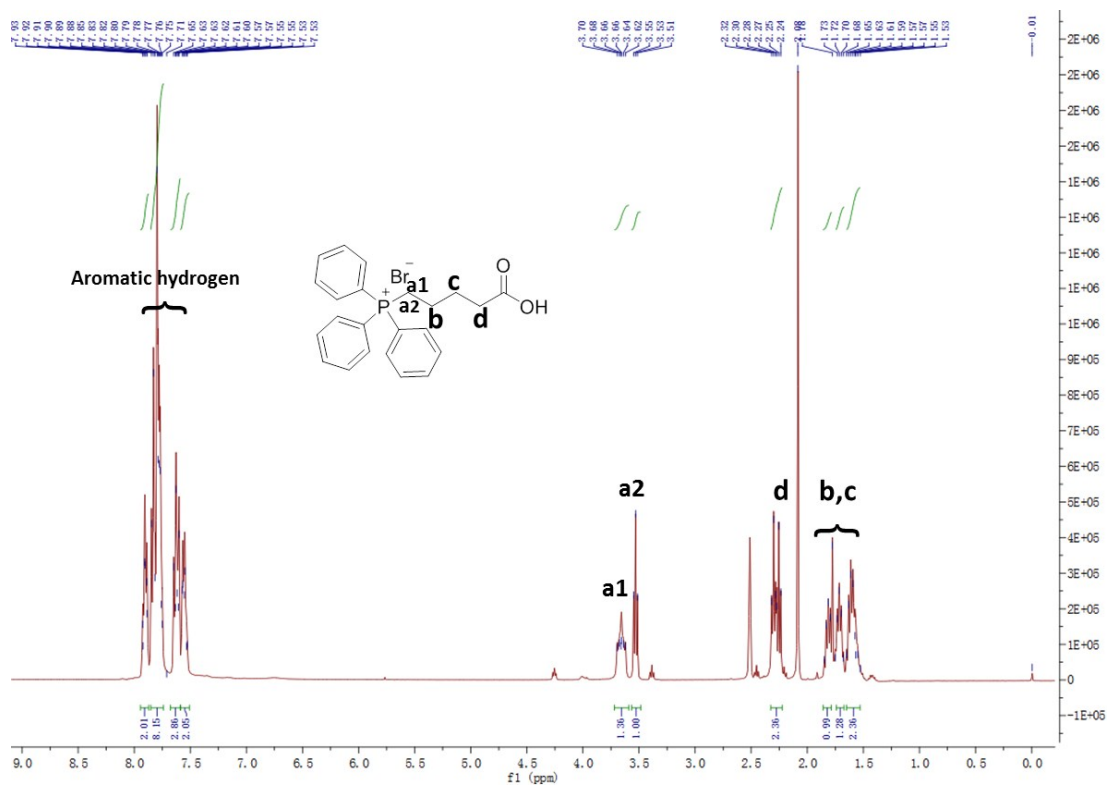


Fig.S3<sup>1</sup>H-NMR spectrum of PPh<sub>3</sub>Br-(CH<sub>2</sub>)<sub>4</sub>-COOH (TPP) in DMSO-*d*<sub>6</sub>.

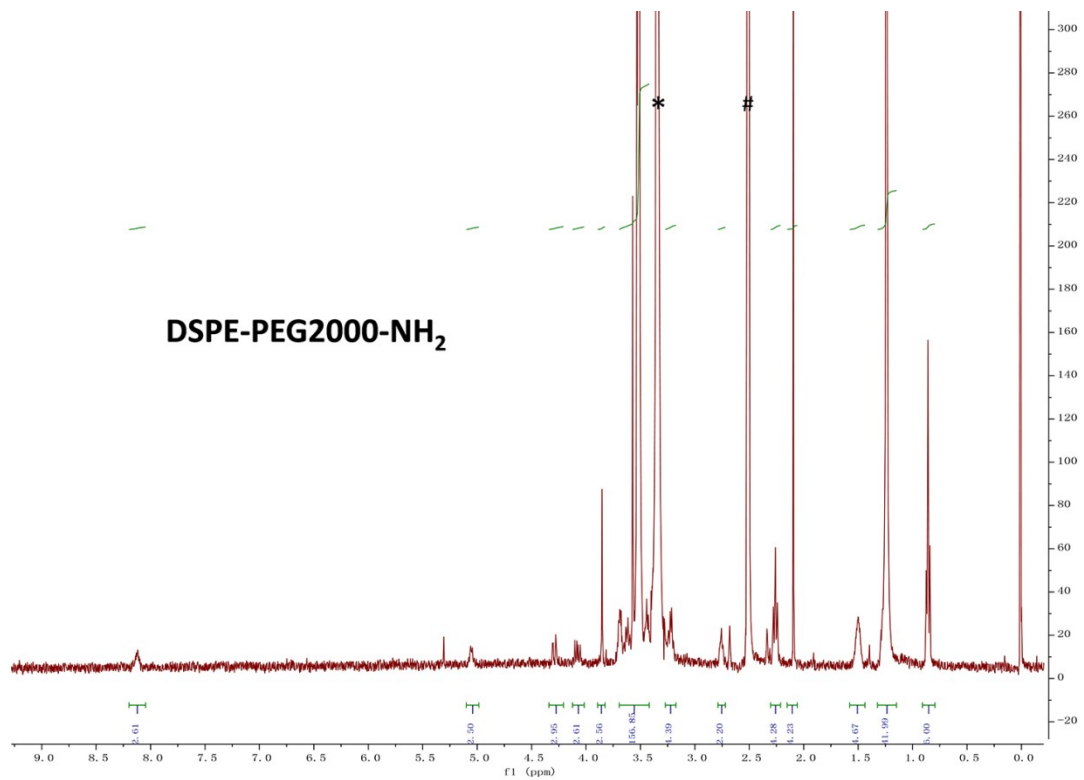


Fig.S4 <sup>1</sup>H-NMR spectrum of DSPE-PEG2000-NH<sub>2</sub> in DMSO-*d*<sub>6</sub>.

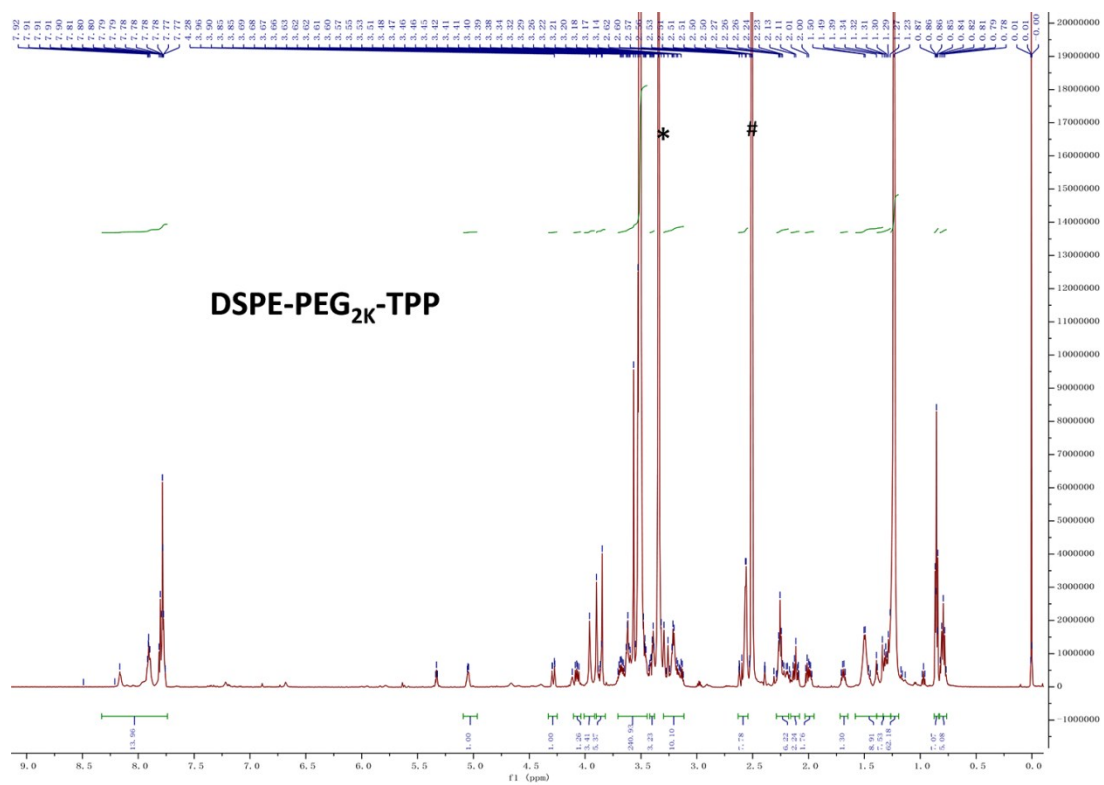


Fig.S5 <sup>1</sup>H-NMR spectrum of DSPE-PEG<sub>2K</sub>-TPP in DMSO-*d*<sub>6</sub>.

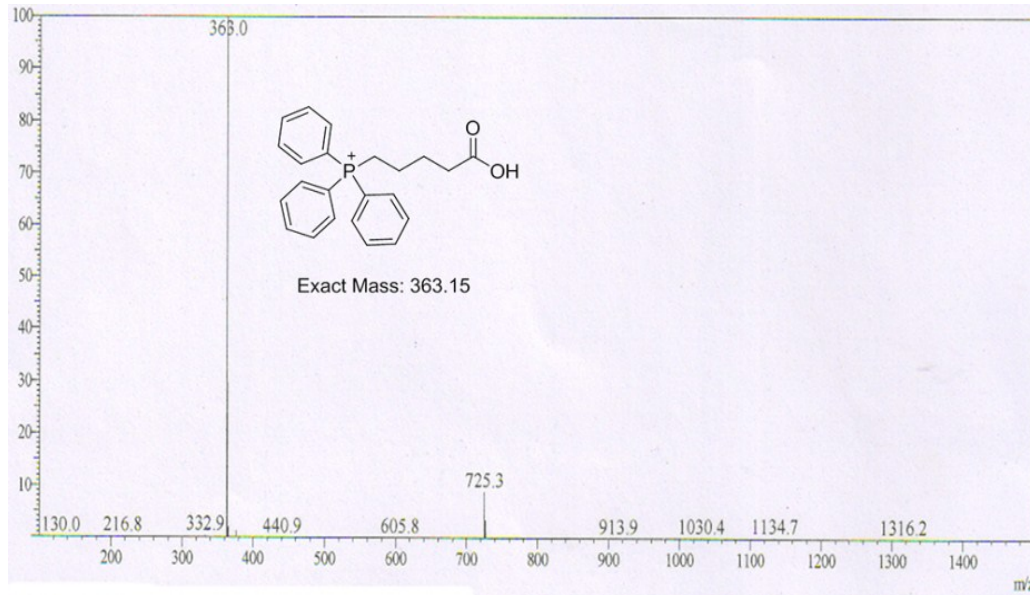


Fig.S6 Mass spectrum of mitochondria targeted small molecule PPh<sub>3</sub>Br-(CH<sub>2</sub>)<sub>4</sub>-COOH (TPP).

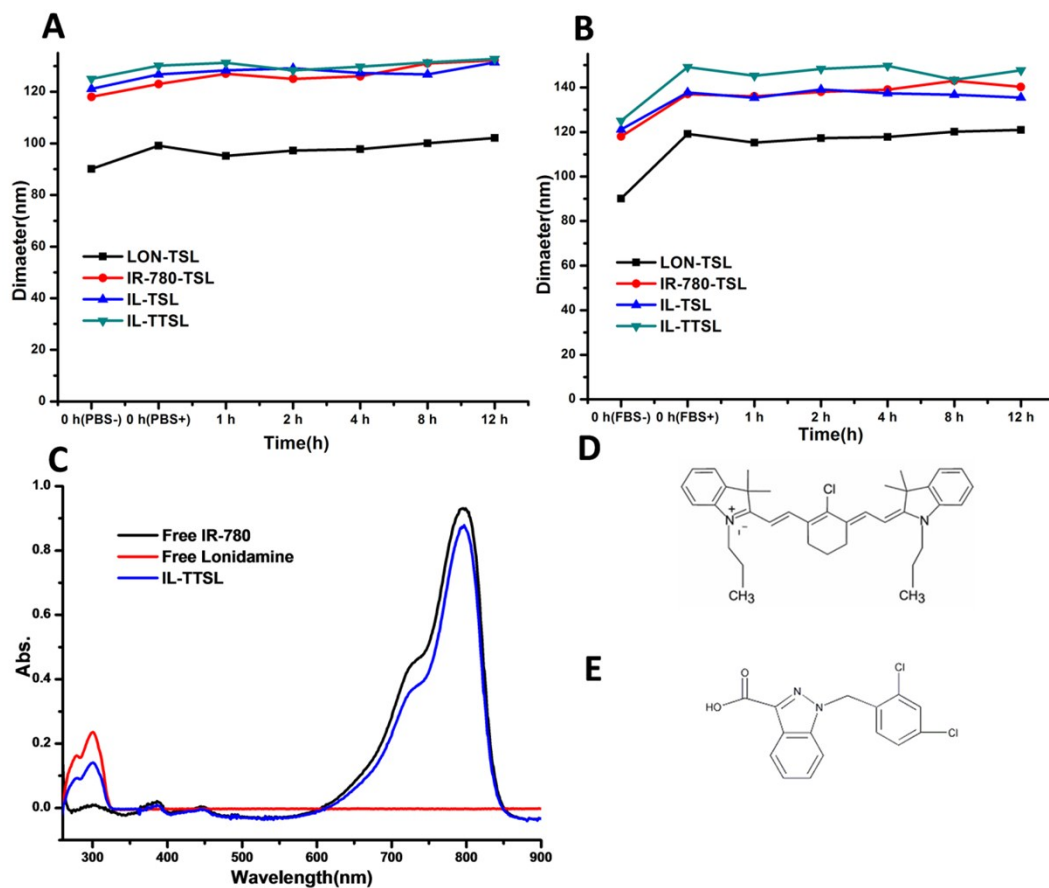


Fig.S7 Characteristics of liposomes. (A) Colloid stability test of different liposomes at room temperature in PBS. (B) Colloid stability test of different liposomes at room temperature in DMEM supplemented with 10% FBS. (C) Normalized UV/Vis absorption spectra of IL-TTSL. Free IR-780, free Lonidamine and IL-TTSL were detected in DMSO solution. (D) and (E) Chemical structural formula of IR-780 and Lonidamine.

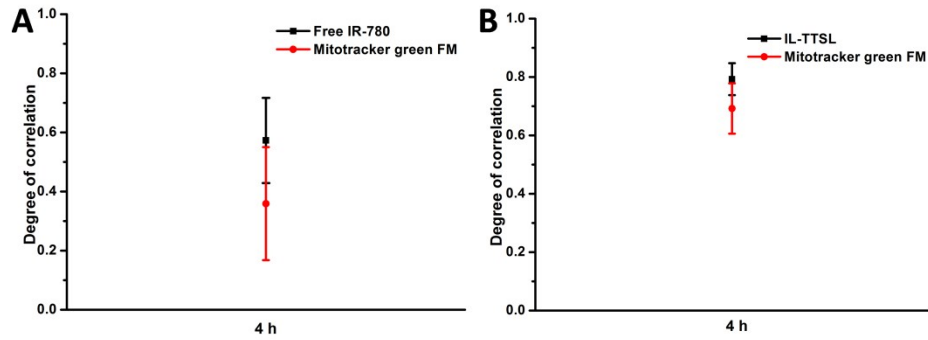


Fig.S8 (A) Co-localization quantitative analysis of free IR-780 with mitochondria from Fig.4(A). (B) Co-localization quantification of IL-TTSL with mitochondria from Fig.4 (A). Manders' coefficients  $M_1$  and  $M_2$  represent the correlation between the intracellular locations of IR-780 (red) and IL-TTSL (red) with mitochondria (green), respectively.

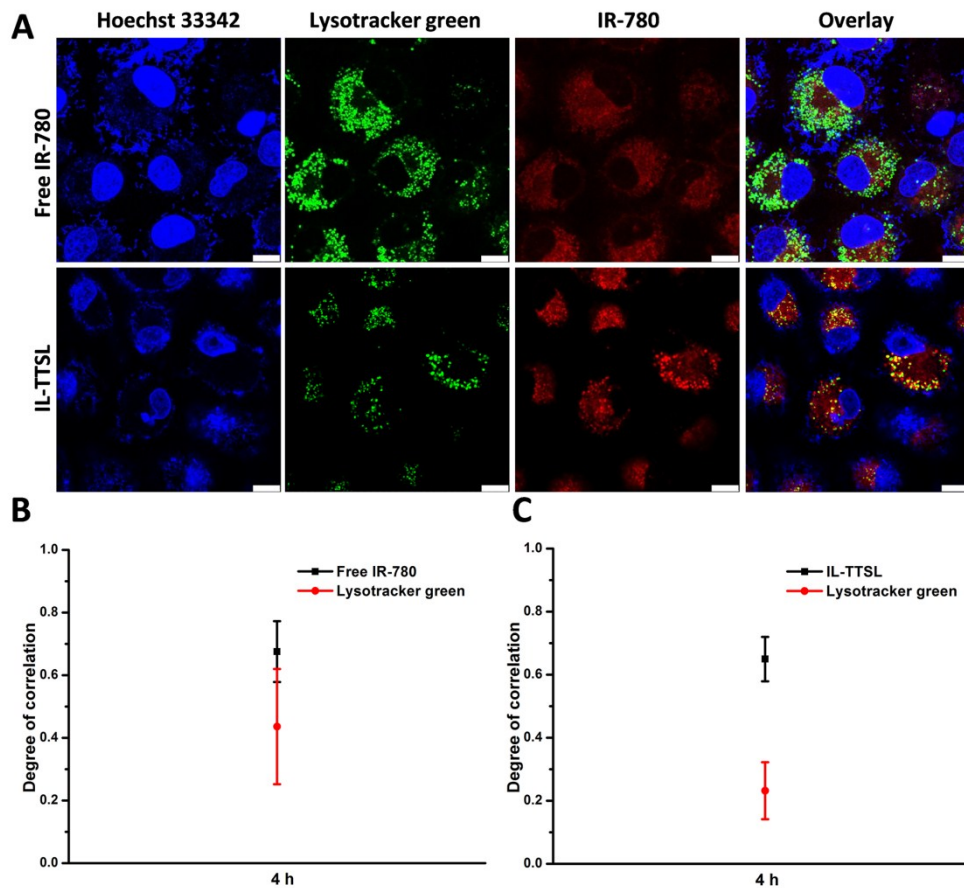


Fig.S9 (A) The *in vitro* cellular uptake of IL-TTSL and intracellular co-localization between lysosomes and liposomes IL-TTSL. Scale bar:10  $\mu$  m. IR-780 was excited at 638 nm and emission spectrum was collected from 650 to 800 nm. (B) Co-localization quantitative analysis of free IR-780 with lysosomes from (A). (C) Co-localization quantification of IL-TTSL with lysosomes from (A). (B) and (C) Quantification of co-localization of (A). Manders' coefficients  $M_1$  and  $M_2$  represent the correlation between the intracellular locations of IR-780 (red) and IL-TTSL (red) with lysosomes (green), respectively.



Fig. S10 Images of mice bearing LL/2 tumors after treatment.