Supporting Information

Clean Photothermal Heating and Controlled Release From Near Infrared Dye Doped Nanoparticles Without Oxygen Photosensitization

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Contents

Methods.

Absorption Spectroscopy. Absorption spectra were recorded on a PerkinElmer Lambda-25 spectrometer.

Fluorescence Spectroscopy. Fluorescence spectra were obtained at a Jobin Yvon Horiba FluoroMax-4 under temperature control using a thermostat equipped with a magnetic stirrer.

Dynamic Light Scattering. Dynamic light scattering experiments were performed using Malvern instrument (Malvern, Nano ZS, He-Ne laser wavelength at 633 nm) to examine the hydrodynamic diameters of the lipid-polymer hybrid nanoparticles and liposomes at pH 7.4. All measurements were conducted at a backscattering angle 173° and a temperature of 25°C. Three runs were conducted per measurement and the average values were calculated.

Ultrasonic Processor. A 130 Watt ultrasonic processor with pulsing button (Cole Parmer, USA, Model CPX130PB, S/N 78926W-02-14, frequency 20 kHz) was used for lipid-polymer hybrid nanoparticle preparation.

Differential Scanning Calorimetry (DSC). The glass transition temperature of solid PLGA [poly(D, L-lactide-*co*-glycolide); lactide:glycolide 50:50, ester terminated, M_w 7000-17000] and the phase transition temperature of liposomes were measured using a DSC1 STAR^e System (Mettler Toledo, USA) operating under N_2 flow.

Transmission Electron Microscopy (TEM). TEM was carried out to investigate the morphology of the Croc/LP-hybrid-NP. TEM images *(Titan 80-300, FEI, USA)* were recorded *with o*perating voltage of 300 kV and a Gatan 4x4k bottom-mount CCD camera. An aqueous solution of Croc/LP-hybrid-NP was localized on a carbon coated copper grid (300 mesh) and the samples were stained with 2% (w/v) phosphotungstic acid.

Laser Photothermal Heating. Lipid-polymer hybrid nanoparticles and Croc loaded liposomes were added to appropriate amount of 20 mM HEPES, 150 mM NaCl, pH 7.4 in a 1 cm quartz cuvette equipped with a magnetic stirrer. An Omega hypodermic thermocouple needle (HYPO-33-1-T-G-60-SMPW-M, USA) was placed in the solution and the temperature was recorded in a continuous fashion (1 sec intervals) using the associated USB converter. A continuous wave diode laser (Thorlab, USA) beam was aligned to pass through the solution (above the magnetic stirring bar and avoiding close contact with the thermocouple) in an identical manner in every experiment. The laser wavelength was 808 nm in all cases and unless stated otherwise, the laser power was set at 250 mW to give a fluence of 3.5 W/cm^2.

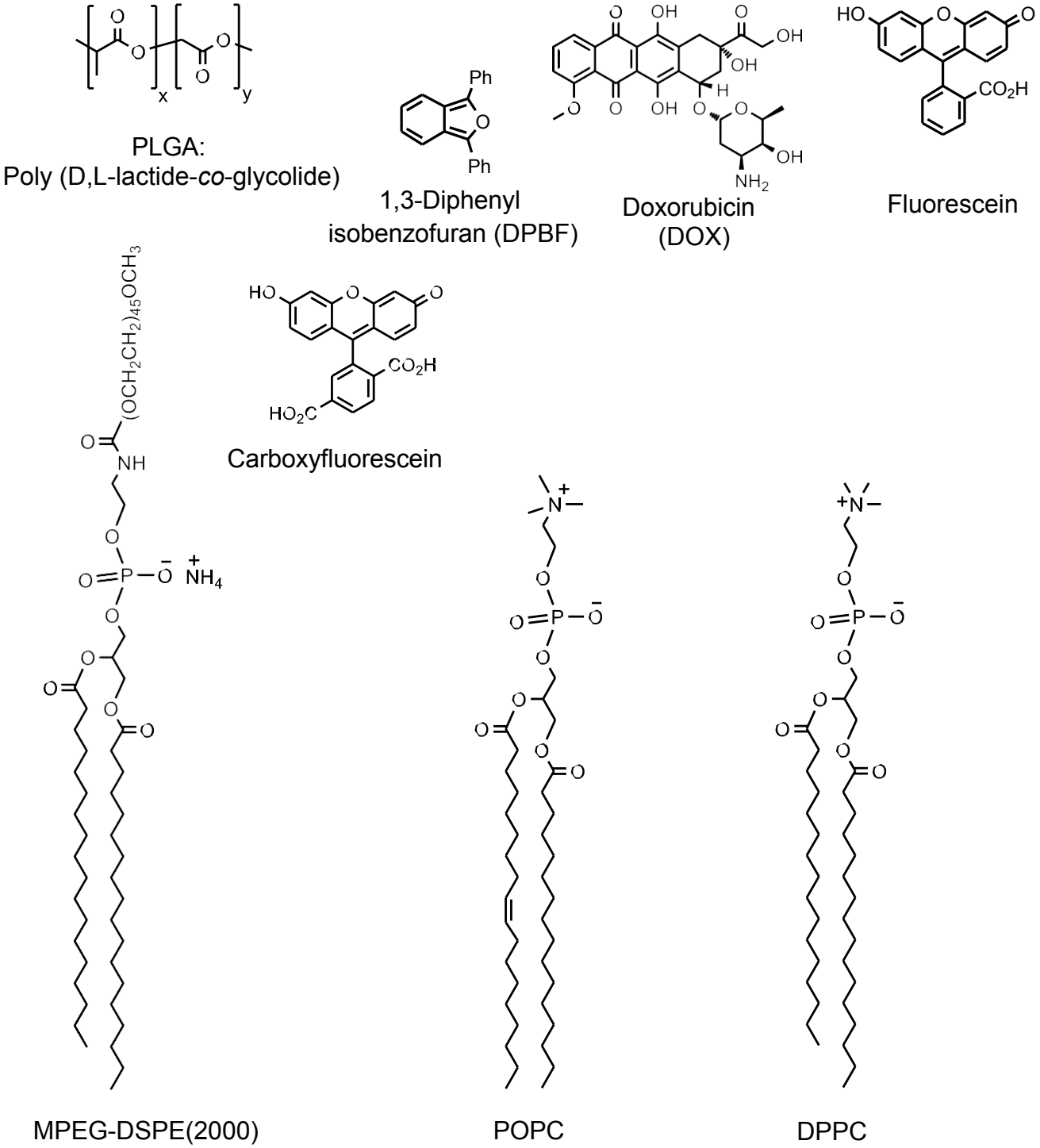

Figure S1: Molecular structures of PLGA, DPBF, DOX, fluorescein, carboxyfluorescein, and the lipid MPEG-DSPE(2000), POPC, and DPPC.

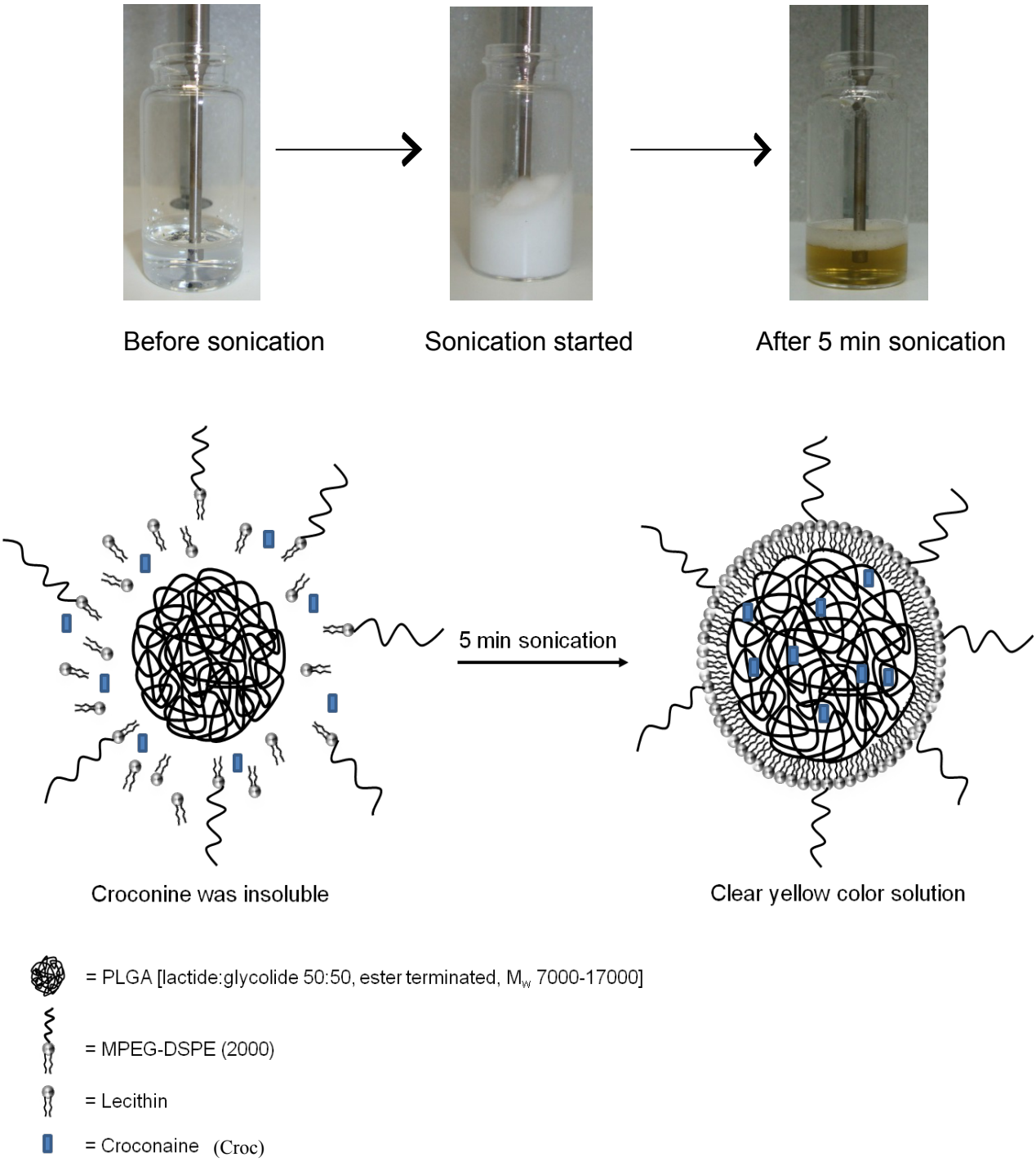

Figure S2: Schematic representation of Croc/LP-hybrid-NP formation using single step sonication method. Lecithin, MPEG-DSPE(2000), Croc, and PLGA polymer, are mixed together as a cocktail. After 5 min of sonication, it forms a clear yellow color solution. These compounds are self-assembled into core- shell structured hybrid nanoparticles.

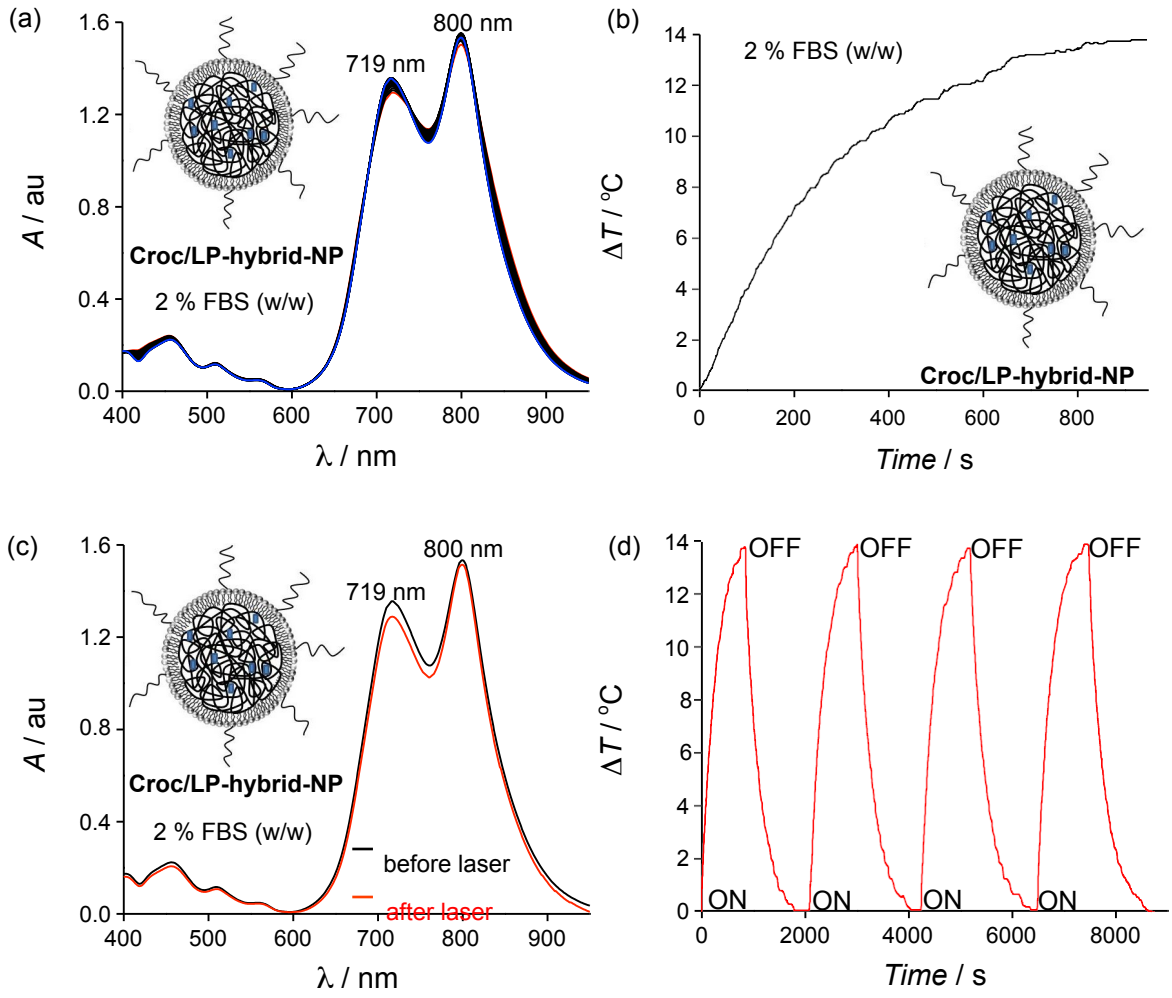

Figure S3: (a) UV/Vis absorption of Croc/LP-hybrid-NP in 2% FBS (w/w) at pH 7.4 (HEPES buffer) over 24 h. (b) Temperature change profile of Croc/LP-hybrid-NP in 2% FBS (w/w) at pH 7.4 (HEPES buffer) during laser (15 min, 808 nm) irradiation. (c) UV/Vis absorption plot of Croc/ LP-hybrid-NP in 2% FBS (w/w) at pH 7.4 (HEPES buffer) before (black) and after laser (15 min, 808 nm) irradiation. (d) Multiple heating cycles (4 cycles) of Croc/LP-hybrid-NP in 2 % FBS (w/ w) at pH 7.4 (HEPES buffer) during laser (15 min, 808 nm) irradiation.

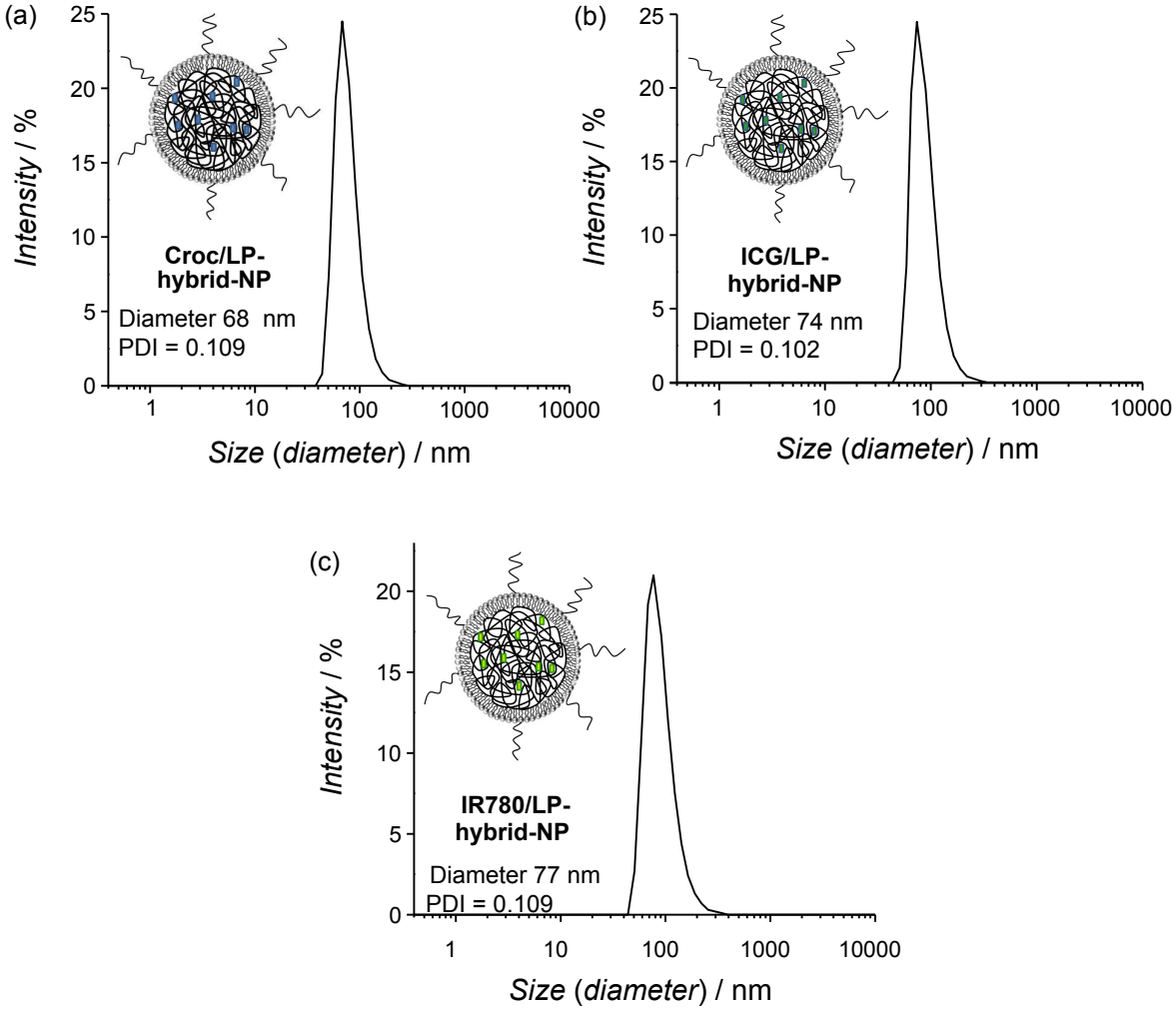

Figure S4: DLS study of (a) Croc/LP-hybrid-NP, (b) ICG/LP-hybrid-NP), and (c) IR780/LP-hybrid- NP in HEPES buffer at pH 7.4.

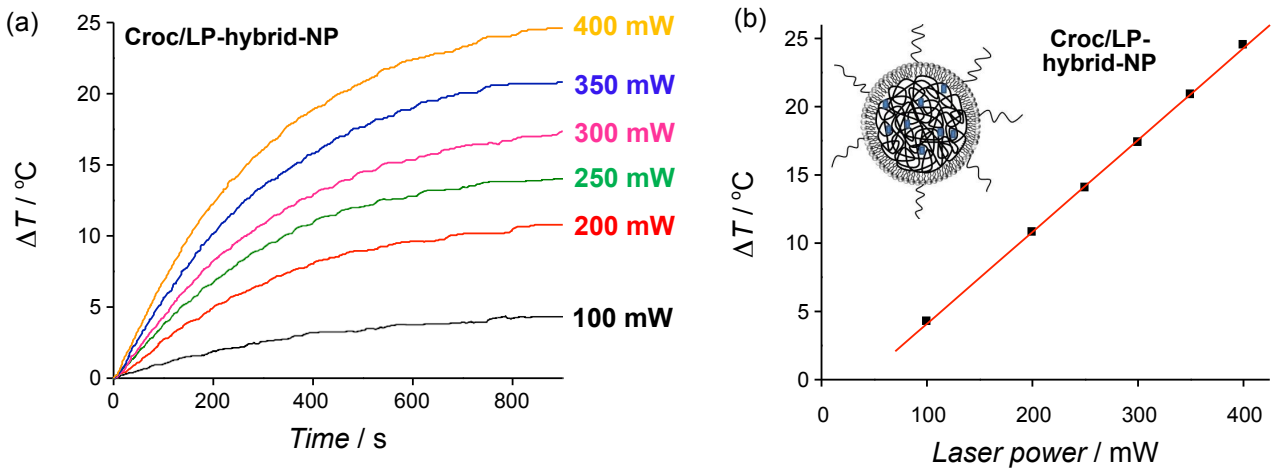

Figure S5: (a) Temperature change profiles of Croc/LP-hybrid-NP at pH 7.4 (HEPES buffer) as a function of laser power for 15 min at 808 nm laser irradiation. (b) Linear response with the incident laser power.

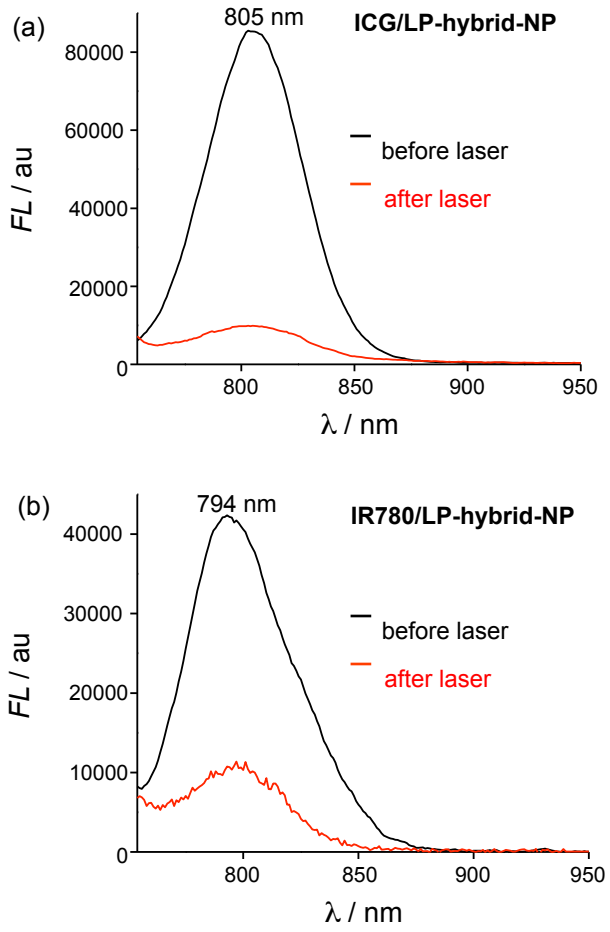

Figure S6: Fluorescence plots of (a) ICG/LP-hybrid-NP and (b) IR780/LP-hybrid-NP at pH 7.4 (HEPES buffer) before (black) and after (red) laser (15 min, 808 nm) irradiation, λ_{ex} = 740 nm. Control experiments showed no change in fluorescence upon sitting for 15 min in the dark.

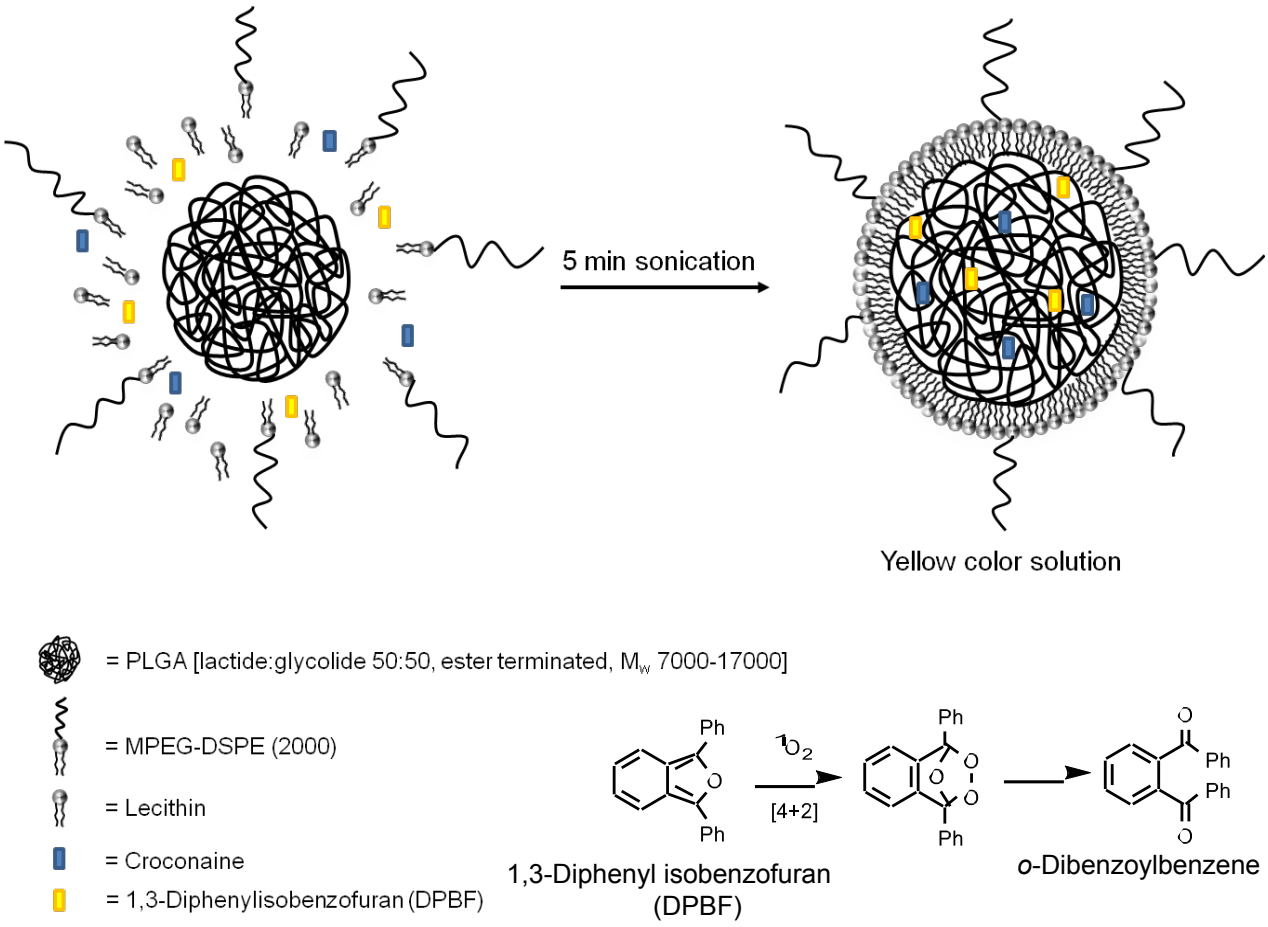

Figure S7: Schematic representation of Croc/DPBF/LP-hybrid-NP formation using single step sonication method. Lecithin, MPEG-DSPE(2000), Croc, DPBF, and PLGA polymer, are mixed together as a cocktail. After 5 min of sonication, a clear yellow solution forms and the dyes are self-assembled into core of the nanoparticles.

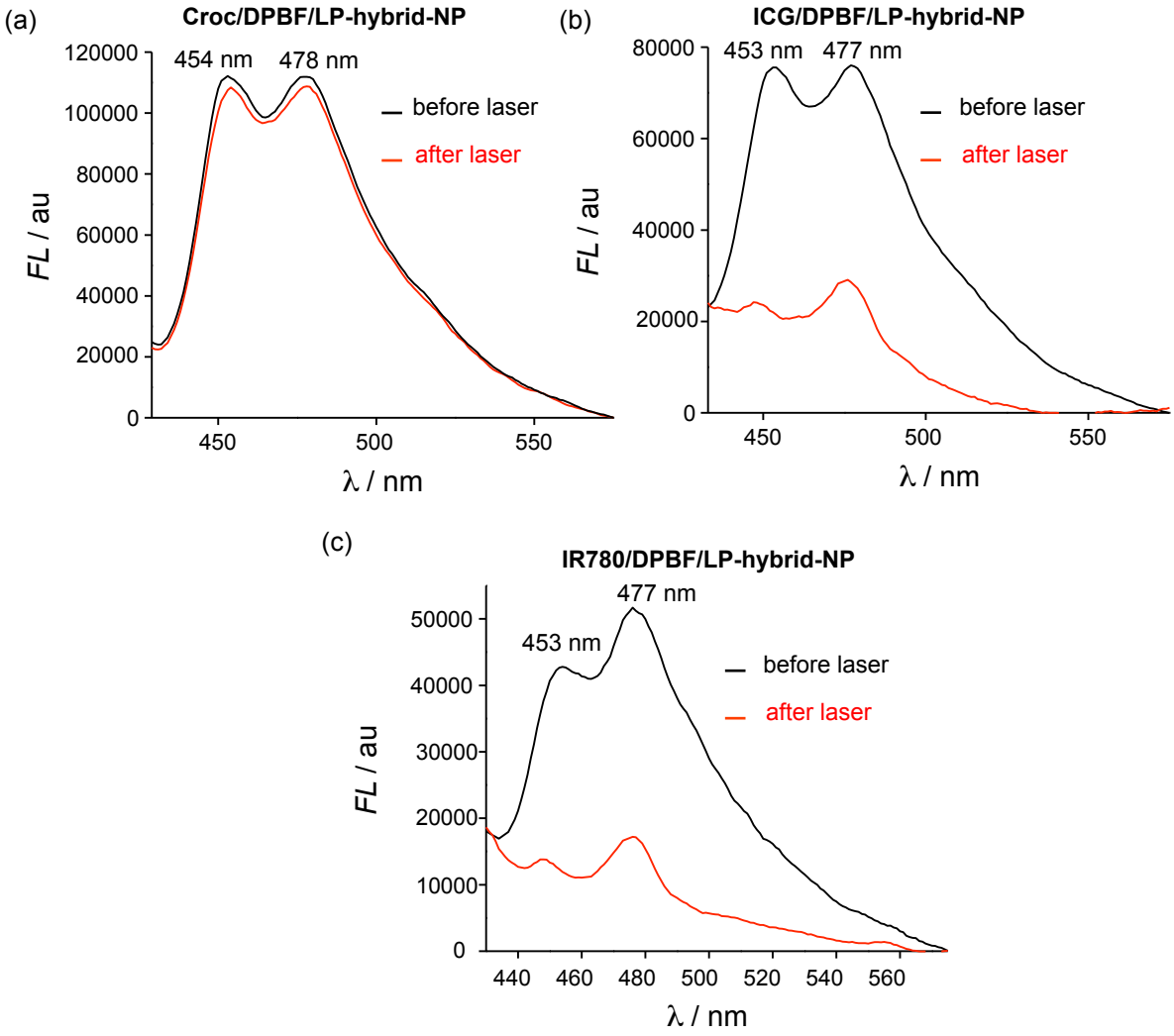

Figure S8: Plots of DPBF fluorescence in (a) Croc/DPBF/LP-hybrid-NP, (b) ICG/DPBF/LPLP-hybrid-NP, and (c) IR780/DPBF/LP-hybrid-NP at pH 7.4 (HEPES buffer) before (black) and after (red) laser (15 min, 808 nm) irradiation, λ_{ex} = 410 nm. Significant laser induced quenching of DPBF fluorescence was observed in the samples of ICG/DPBF/LPLP-hybrid-NP and IR780/DPBF/LP-hybrid-NP.

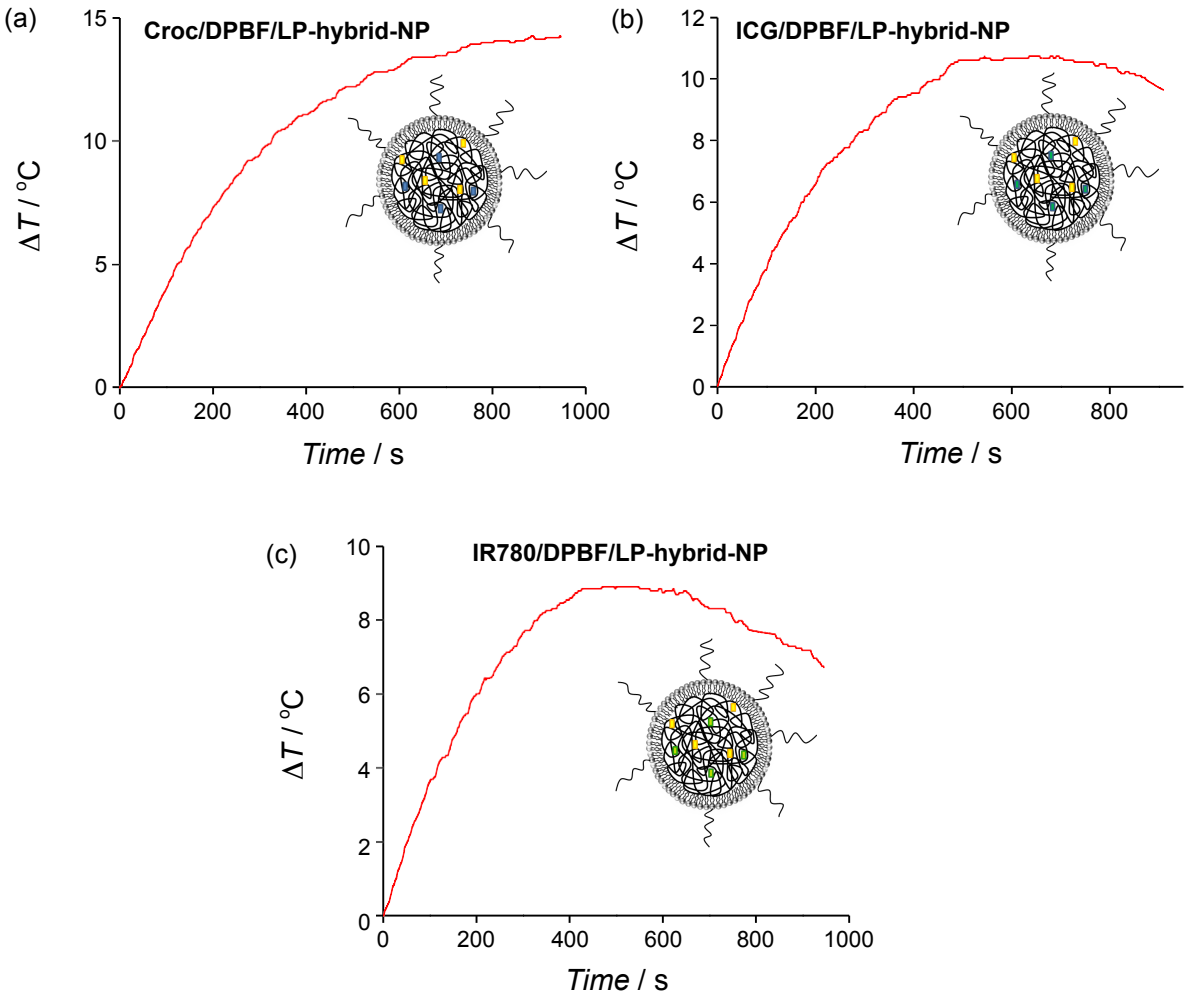

Figure S9: (a-c) Temperature change profiles during laser (15 min, 808 nm) irradiation for Croc/ DPBF/ LP-hybrid-NP, ICG/DPBF/LP-hybrid-NP, and IR780/DPBF/LP-hybrid-NP, respectively, at pH 7.4 (HEPES buffer).

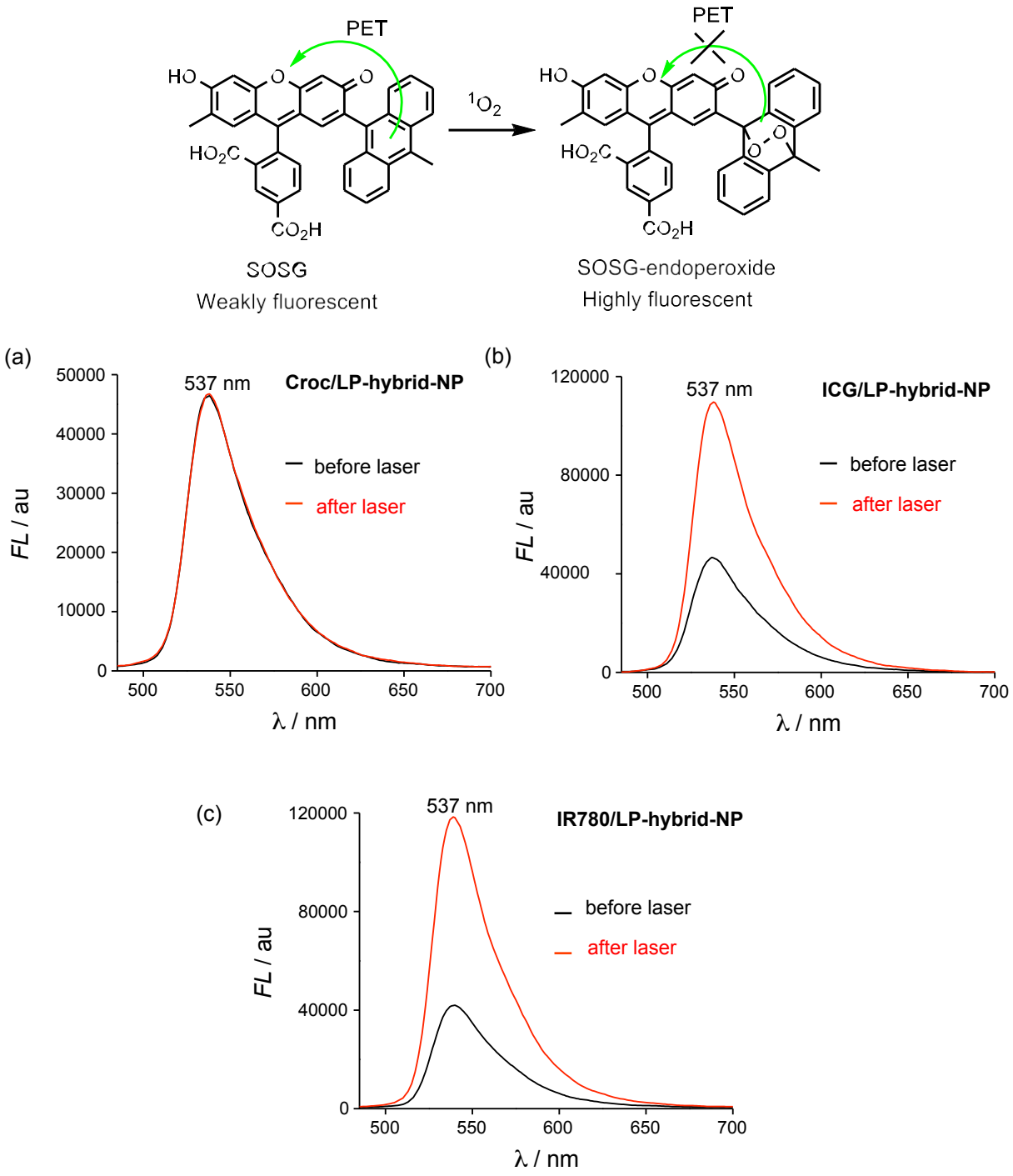

Figure S10: (a) Fluorescence plot of (a) Croc/LP-hybrid-NP, (b) ICG/LP-hybrid-NP, and (c) IR780/ LP-hybrid-NP in presence of SOSG (40 ∝g/mL) at pH 7.4 (HEPES buffer) before (black) and after (red) laser (15 min, 808 nm) irradiation, λ_{ex} = 475 nm. Significant fluorescence enhancement of SOSG reagent is observed for ICG/LP and IR780/LP hybrid-NPs at pH 7.4 which indicates $^1O_2$ generation.

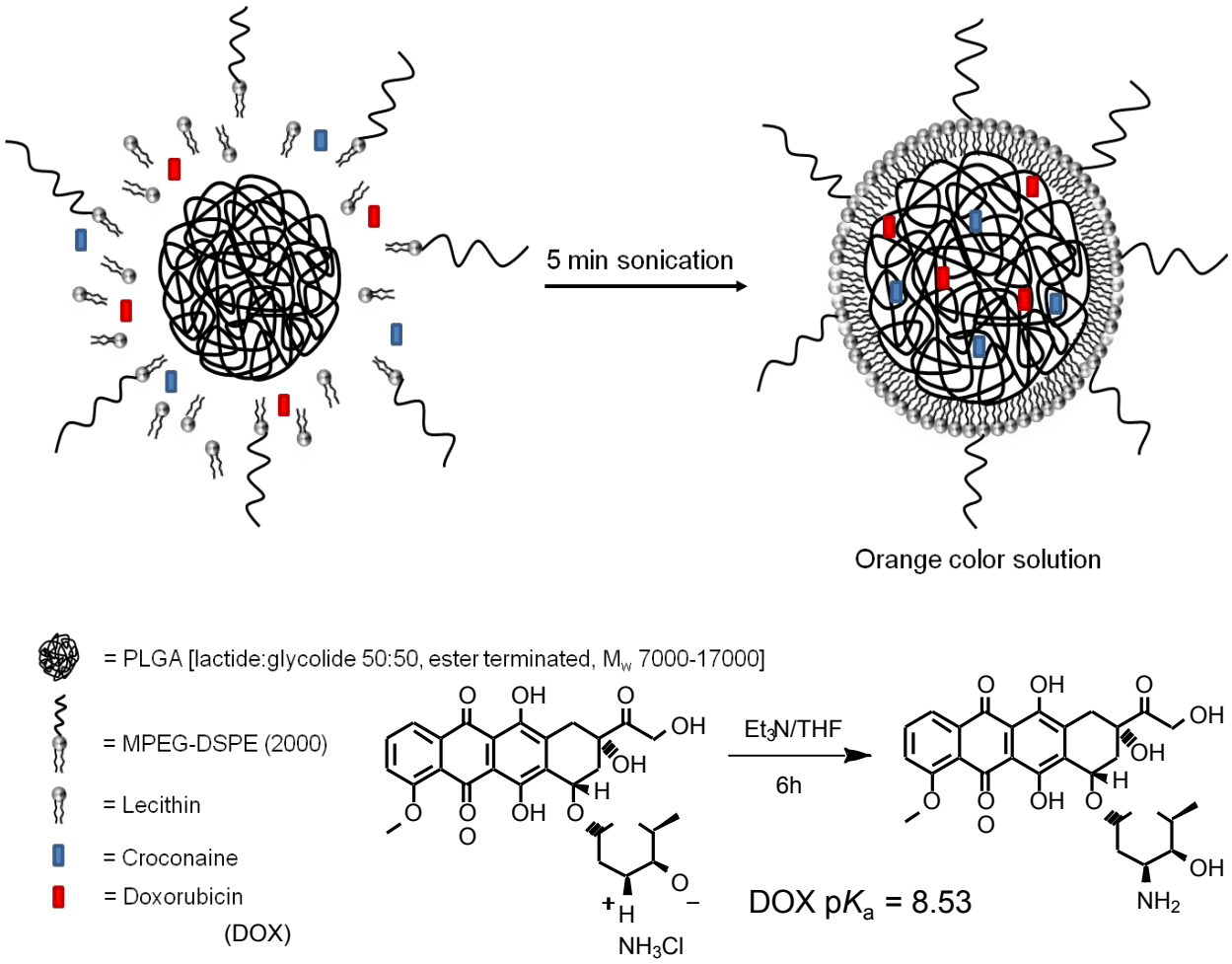

Figure S11: Schematic representation of Croc/DOX/LP-hybrid-NP formation using single step sonication method. Lecithin, MPEG-DSPE(2000), Croc, DOX, and PLGA polymer, are mixed together as a cocktail. After 5 min of sonication, it forms a clear orange color solution. These compounds are self-assembled into core-shell structured hybrid nanoparticles.

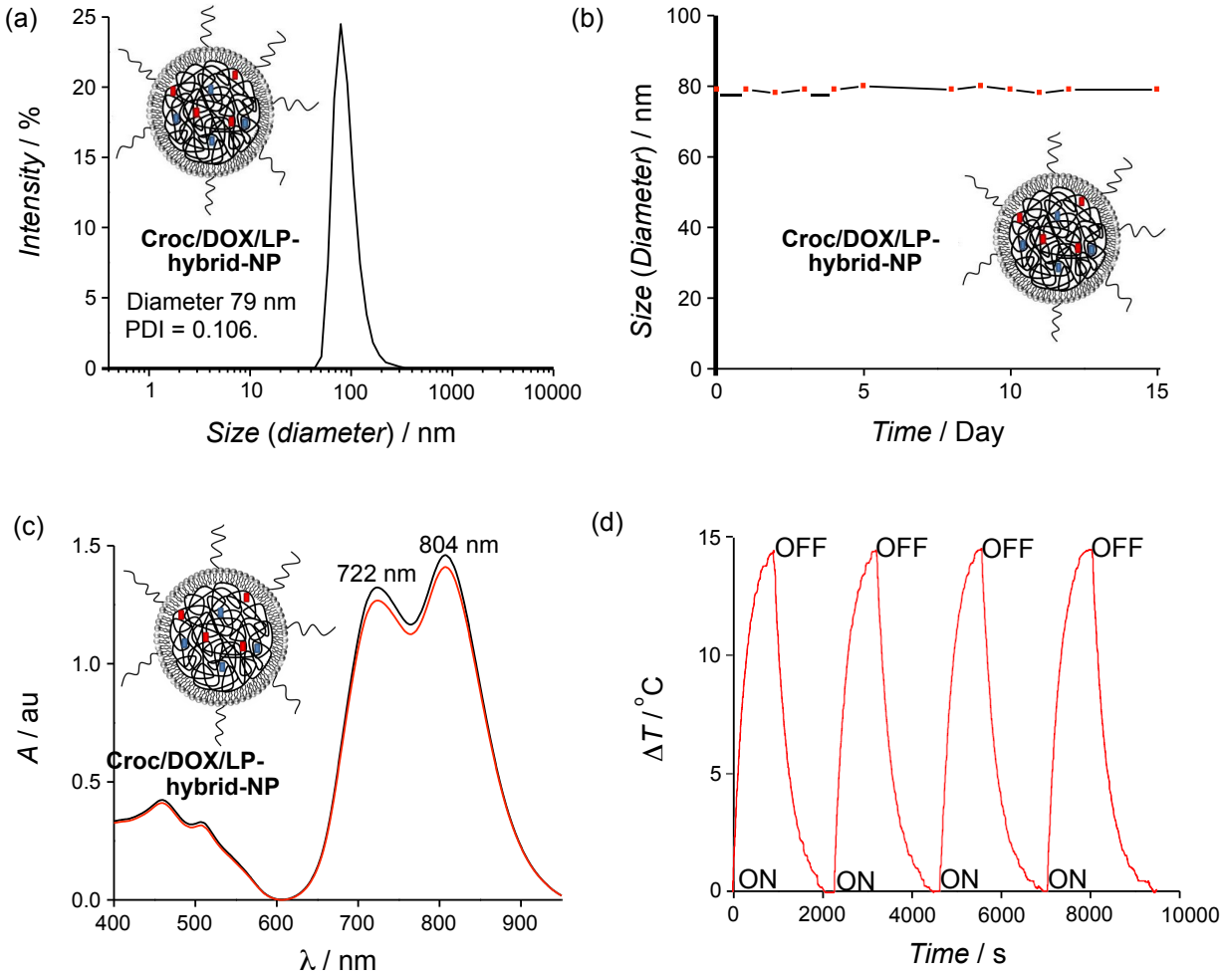

Figure S12: (a) DLS study of Croc/DOX/LP-hybrid-NP in HEPES buffer at pH 7.4. (b) Size of Croc/DOX/LP- hybrid-NP doe not change over 15 days. (c) UV/Vis absorption of Croc/DOX/LP-hybrid-NP at pH 7.4 (HEPES buffer) before (black) and after (red) laser (15 min, 808 nm) irradiation. (d) Multiple heating cycles (4 cycles) of Croc/DOX/LP-hybrid-NP at pH 7.4 (HEPES buffer) caused by laser irradiation.

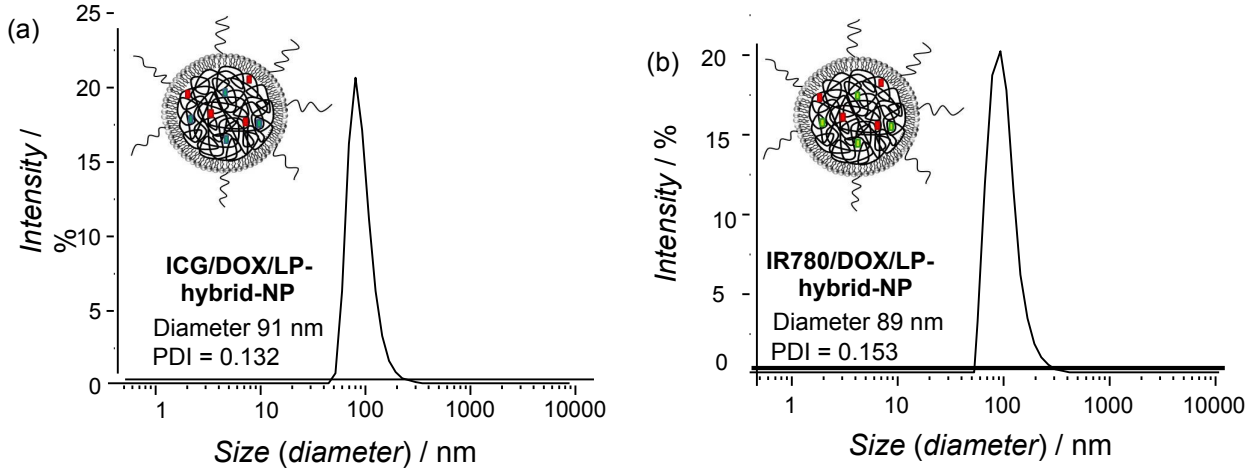

Figure S13: DLS study of (a) ICG/DOX/LP-hybrid-NP and (b) IR780/DOX/LP-hybrid-NP in HEPES buffer at pH 7.4.

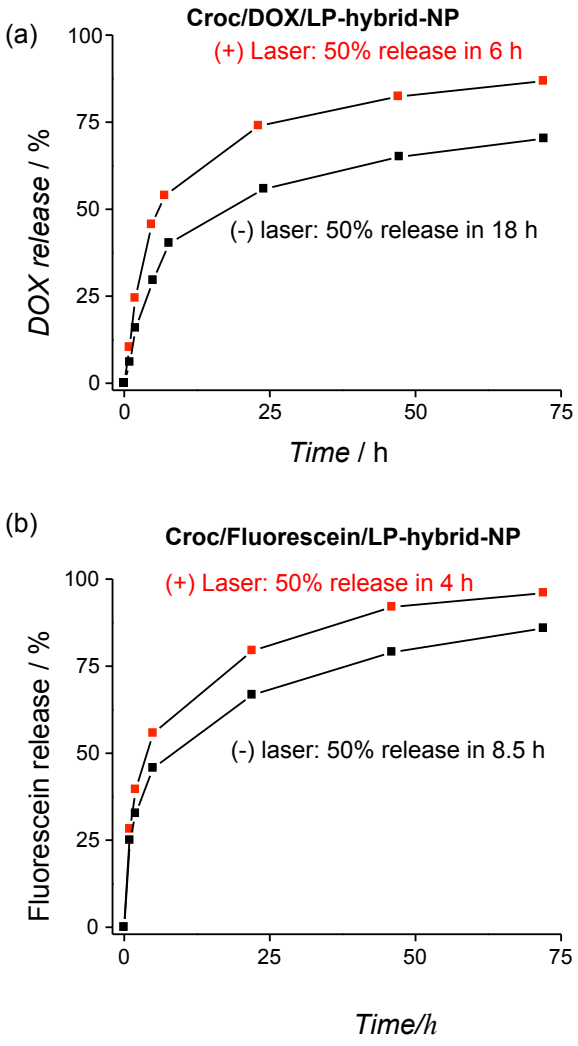

Figure S14. (a) DOX and (b) Fluorescein release from Croc/DOX/LP-hybrid-NP and Croc/ Fluorescein/ LP-hybrid-NP at pH 7.4 (HEPES buffer) and 37 °C, after either an initial laser irradiation (15 min) (red) or no laser irradiation (black).

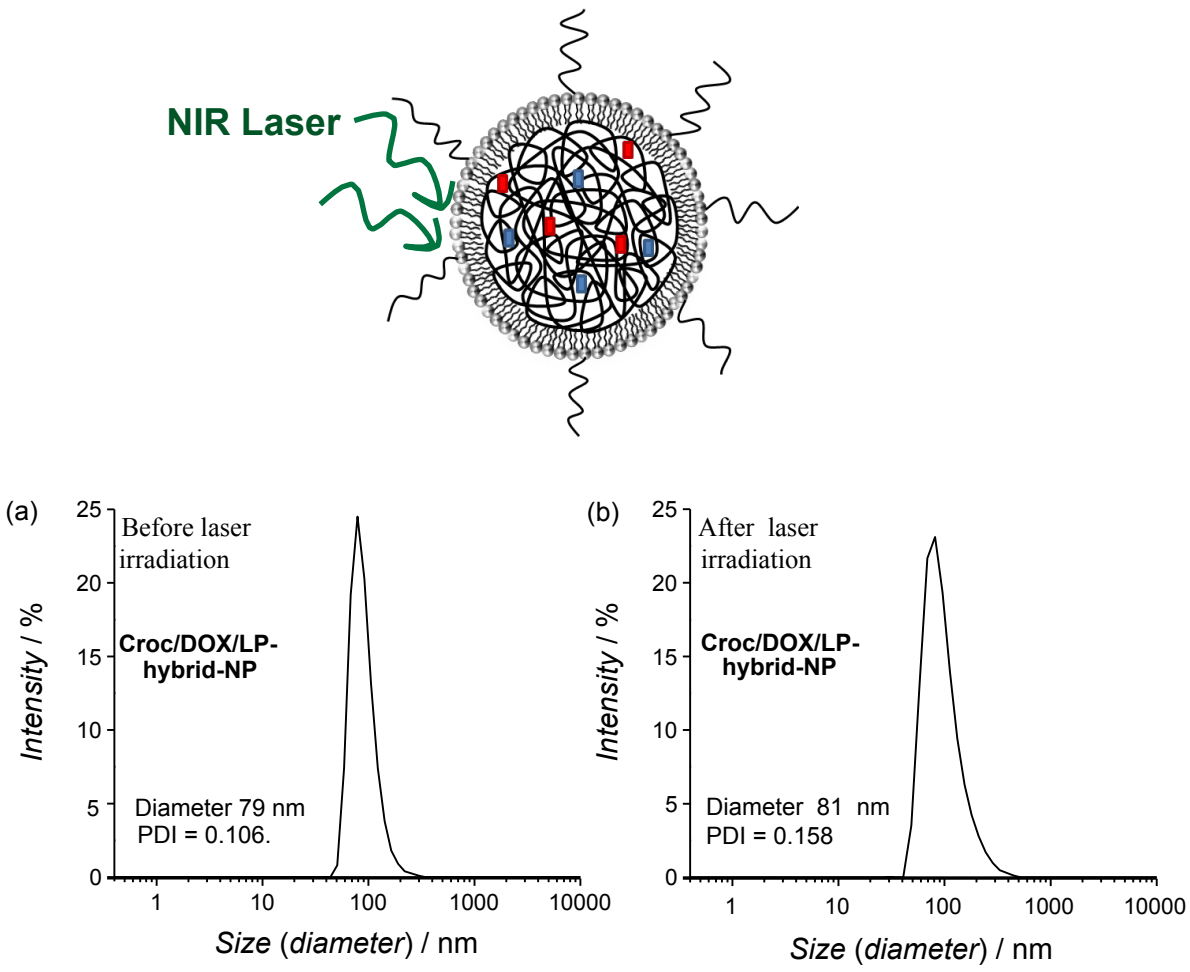

Figure S15: DLS study of Croc/DOX/LP-hybrid-NPs at pH 7.4 (HEPES buffer) before (a) and after (b) laser (15 min, 808 nm) irradiation.

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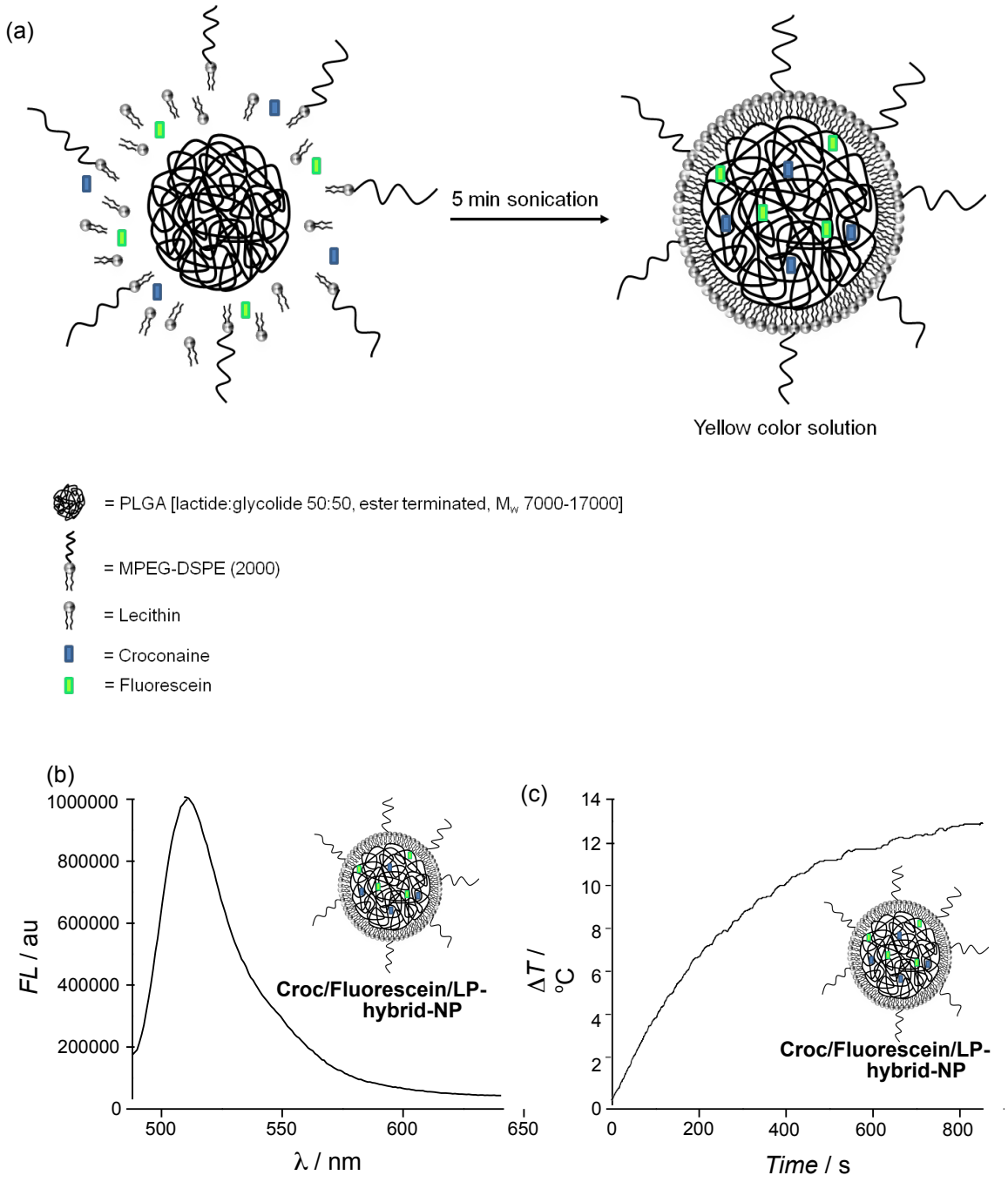

Figure S16: (a) Schematic representation of Croc/Fluorescein/LP-hybrid-NP formation using single step sonication method. (b) Fluorescence plot of Croc/Fluorescein/LP-hybrid-NP at pH 7.4 (HEPES buffer), λ_{ex} = 480 nm. (c) Temperature change profile of Croc/Fluorescein/LP-hybrid-NP at pH 7.4 (HEPES buffer) caused by laser (15 min, 808 nm) irradiation.

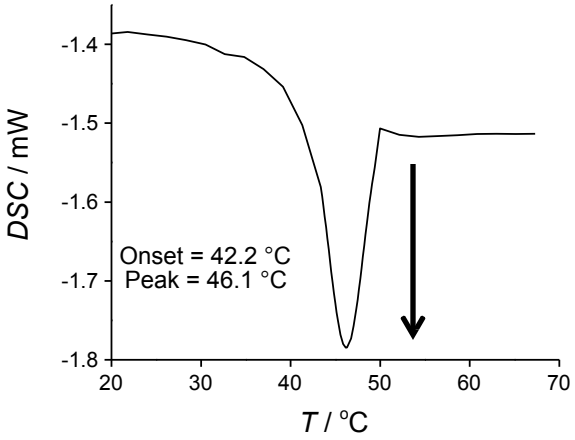

Figure S17: DSC of PLGA [poly(D, L-lactide-*co*-glycolide); lactide:glycolide 50:50, ester terminated, M_w 7000-17000].

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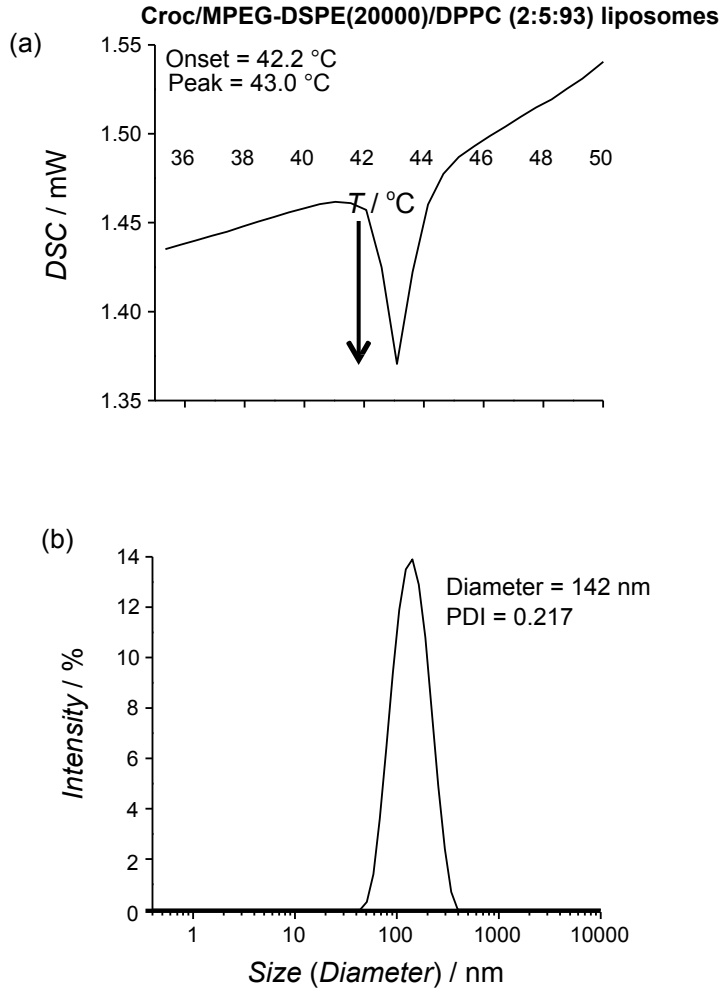

Figure S18: (a) DSC of Croc/MPEG-DSPE(20000)/DPPC (2:5:93) liposomes. (b) DLS study of Croc/MPEG-DSPE(20000)/DPPC (2:5:93) liposomes in HEPES buffer at pH 7.4.