Supporting Information

for

Photoresponsive hydrogel networks using melanin nanoparticle photothermal sensitizers

By

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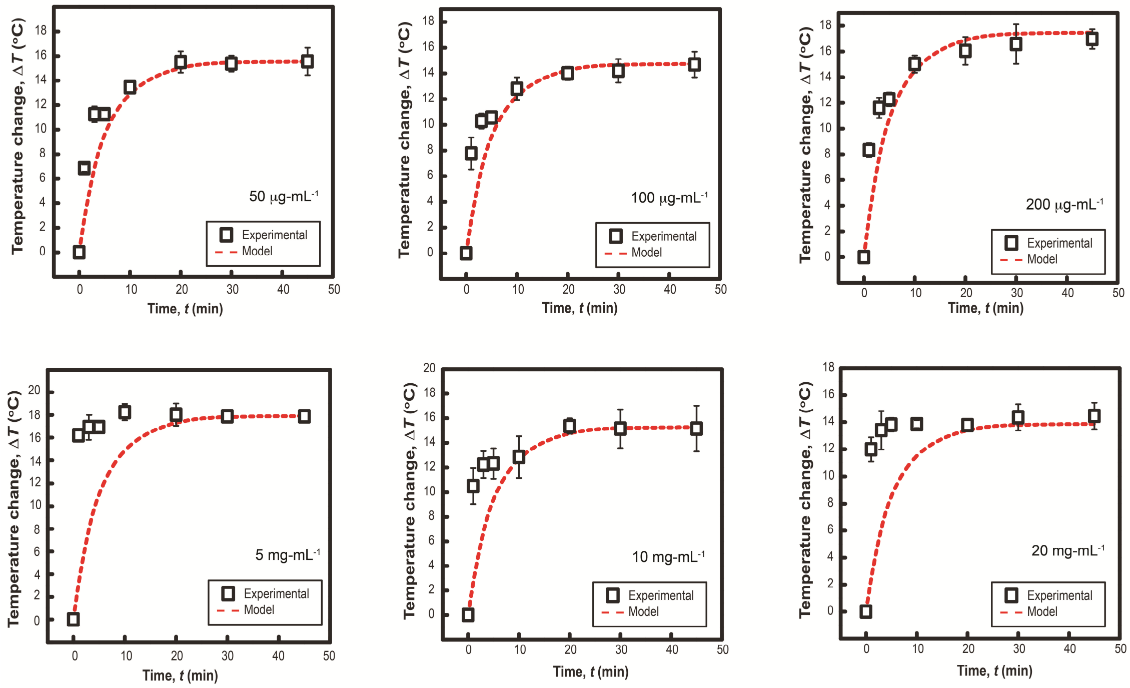

Figure S1. Temporal evolution of photothermal heating of MelNP dispersions with different concentrations ranging from 50 µg-mL^{-1} to 20 mg-mL^{-1}. The predicted transient temperature profiles matched that of experimentally determined values at low concentrations of MelNP ($\leq$ 5 mg-mL^{-1}). However, the temporal temperature profiles deviated significantly from experimental observations as the MelNP concentration was increased (See Text).

Detailed Calculations of Photo-Induced Heating of Melanin Nanoparticle Dispersions

MelNPs dispersions and MelNP-loaded hydrogels are prepared in scintillation vials to facilitate formation and optical thermal characterization. The heating rate of photo-induced aqueous melanin nanoparticle dispersions was determined by

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{in} - Q_{out} \qquad \text{Eqn. S1}$$

In this equation, m_i and $C_{p,i}$ represent the mass and heat capacity of component i, T represents the temperature of the aqueous dispersion. The value of m_{H2O} and $C_{p,H2O}$ were taken as 1 g per mL and 4.18 J-g^{-1}K^{-1} respectively. The value of m_{MelNP} varies with MelNP concentration while 2.51 J-g^{-1}K^{-1} was used as the value of $C_{p,MelNP}$. The rate of energy supplied was calculated using Eqn 2.

$$Q_{in}(z) = \frac{dI(z)}{dz} \qquad \text{Eqn. S2}$$

The absorbed light intensity is calculated using the following relationship derived from the Beer-Lambert law.

$$I = I_0(1 - e^{-\beta z}) \quad \text{Eqn. S3}$$

I_0 was measured to be 10.8 mW-m^{-2}. The value of β was estimated using the following input parameters for Mie scattering (reference 34 in main text). Briefly, the refractive index mismatch ratio (n_{MelNP}/n_{water}) and the size parameter ($x = 2\pi D_{MelNP}/(\lambda/n_{water})$) were calculated. The indices of refraction of melanin and water are given by n_{MelNP} = 1.3 and n_{water} = 1.33, respectively. The value N_{MelNP} represents the number density of MelNP nanoparticles in solution assuming a spherical particle of diameter $D_{MelNP} = 2R_g$ = 200 nm. This calculation uses a melanin mass density of 1.68 g-cm^{-3} (reference 28 in main text). We used an algorithm to calculate the efficiency of scattering Q_s (reference 40 in the main text). Briefly, the algorithm was based on the following equation:

$$Q_s = \frac{2}{x^2}\sum_{n=1}^{N}(2n+1)(|a_n|^2 + |b_n|^2) \quad \text{Eqn. S4}$$

where the complex Mie coefficients a_n and b_n were functions depending on x and the complex refractive index[1]. The output values of β ($Q_s SA_{MelNP} N_{MelNP}$) are summarized in **Table S1**.

Table S1. Scattering coefficients used for aqueous melanin dispersions as a function of melanin nanoparticle concentration.

MelNP conc, c_{MelNP} (mg-mL^{-1})	0.05	0.1	0.2	1	5	10	20
Scattering coefficient β x 10^{-2} (cm^{-1})	0.1090	0.1109	0.1330	0.160	0.747	1.254	2.259

Heat loss was dominated by radial thermal conduction through the walls of the glass vials. The rate of heat loss Q_{out} is calculated using Eqn 4:

$$Q_{out} = -k_{SiO_2} S \frac{dT}{dr_{shell}} \qquad \text{Eqn. 4}$$

In this expression, k_{SiO2} represents the heat transfer coefficient of silicon oxide (1 W-m^{-1}-K^{-1})[2], S is the surface area of conduction and r_{shell} is the coordinate within the silicon oxide shell between the inner (R_{in}) and outer radii (R_{out}) of the conduction path where $|R_{out} – R_{in}| << R_{in}$. The symbol k_{SiO2} represents the heat transfer coefficient of silicon oxide (1 W-m^{-1}-K^{-1}). The inner (R_{in}) and outer (R_{out}) radii was measured to be 1.59 cm and outer radii (R_{out}) was 1.68 cm.

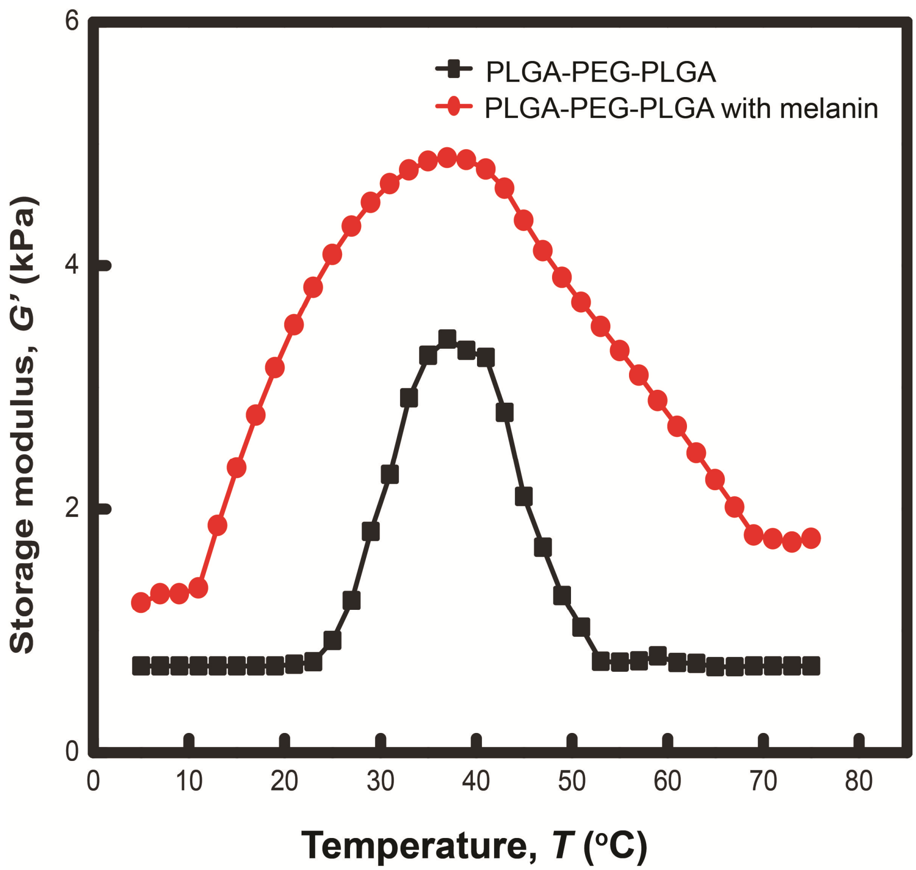

Figure S2. Phase transition behavior of hydrogel formed from 200 mg-mL^{-1} PLGA-PEG-PLGA concentrations. Loading MelNP expands the gel transition of the hydrogel by accelerating sol-gel transition and retarding precipitation (See Text).

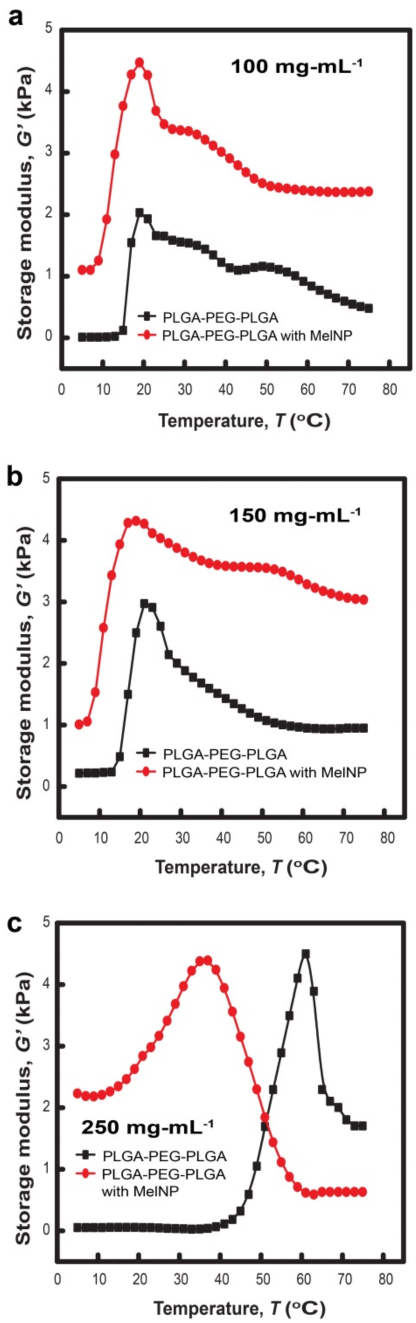

Figure S3. Phase transition behavior of hydrogel formed from different PLGA-PEG-PLGA concentrations: a) 100 mg-mL^{-1}, b) 150 mg-mL^{-1}, and c) 250 mg-mL^{-1} with and without 1 mg-mL^{-1} MelNP. Loading MelNP expands the gel transition of the hydrogel by accelerating sol-gel transition and retarding precipitation (See Text).

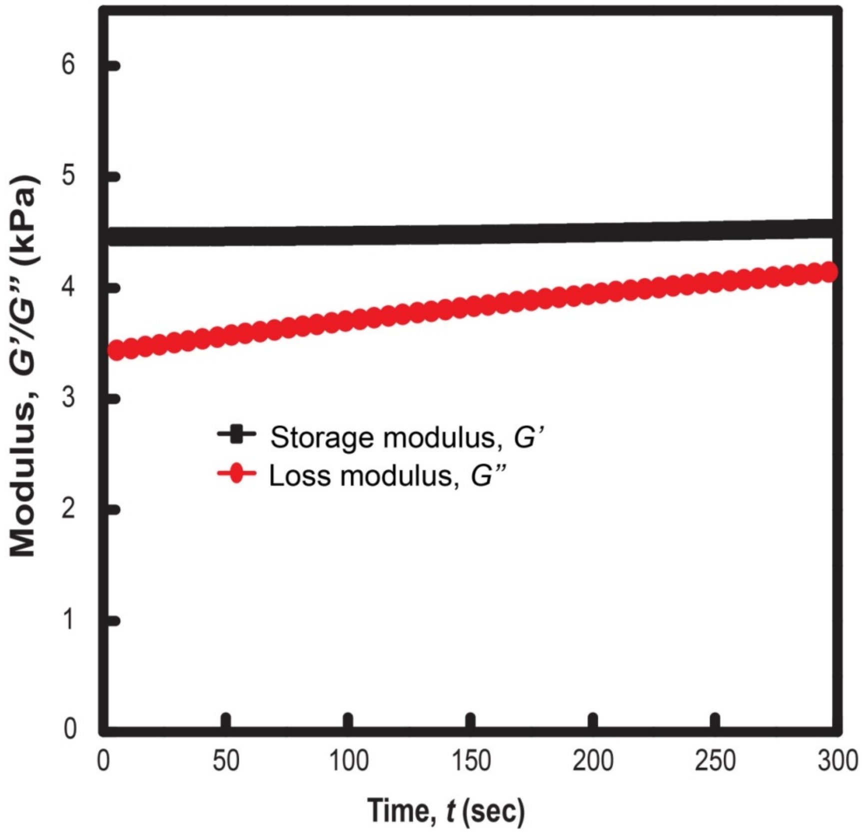

Figure S4. Hydrogel formed from 200 mg-mL^{-1} solution of PLGA-PEG-PLGA doped with 1mg-mL^{-1} MelNP was exposed to UV light. No change in *G'* was observed over irradiation time, suggesting that the decrease in *G'* of PLGA-PEGPLGA hydrogel with embedded MelNP (Fig. 7) resulted from the photothermal response of the MelNP. A slight increase of *G"* was observed possibly due to dehydration of the hydrogel during UV irradiation time.

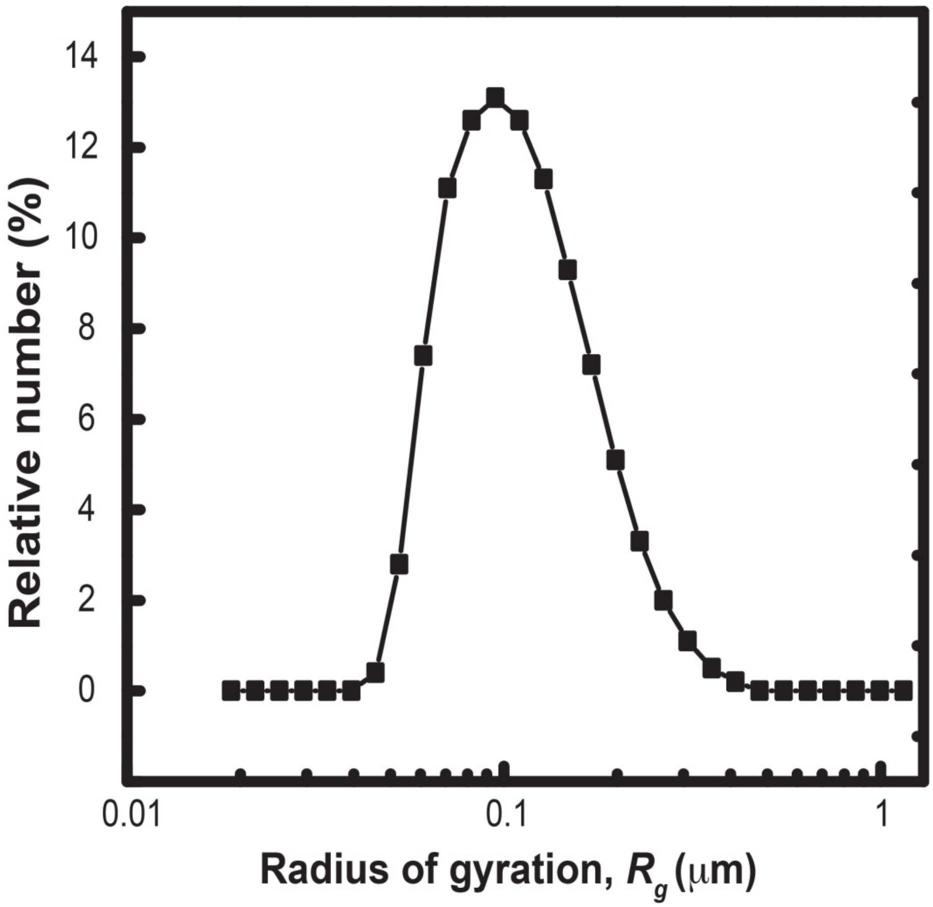

Figure S5. Size distribution of MelNP at concentration 1 mg-mL^{-1} was measured by dynamic light scattering.

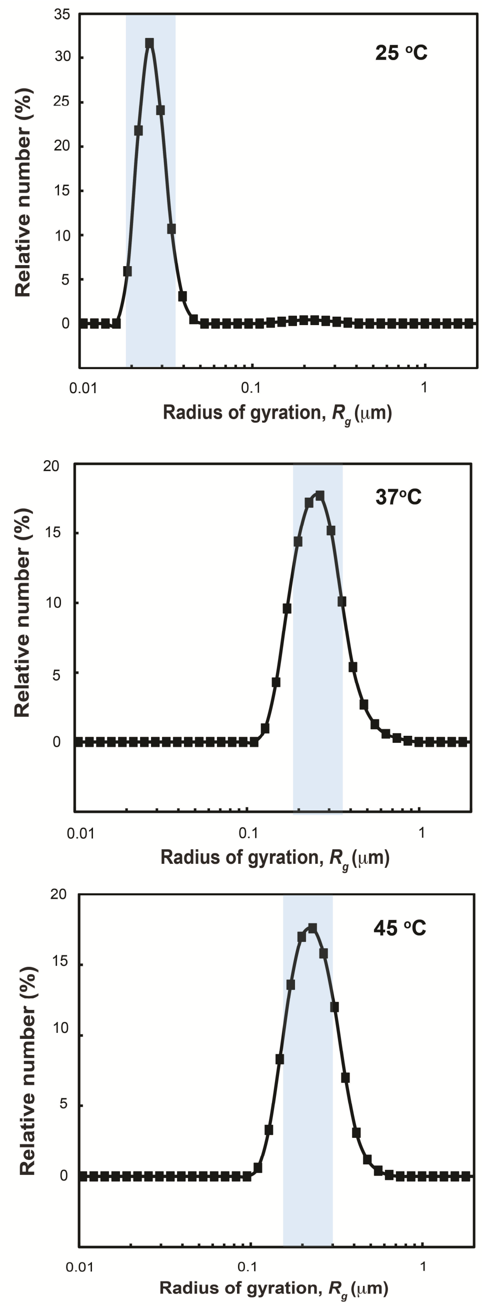

Figure S6. Size distribution of pristine PLGA-PEG-PLGA micelles was measured by dynamic light scattering at 25, 37, and 45 °C.

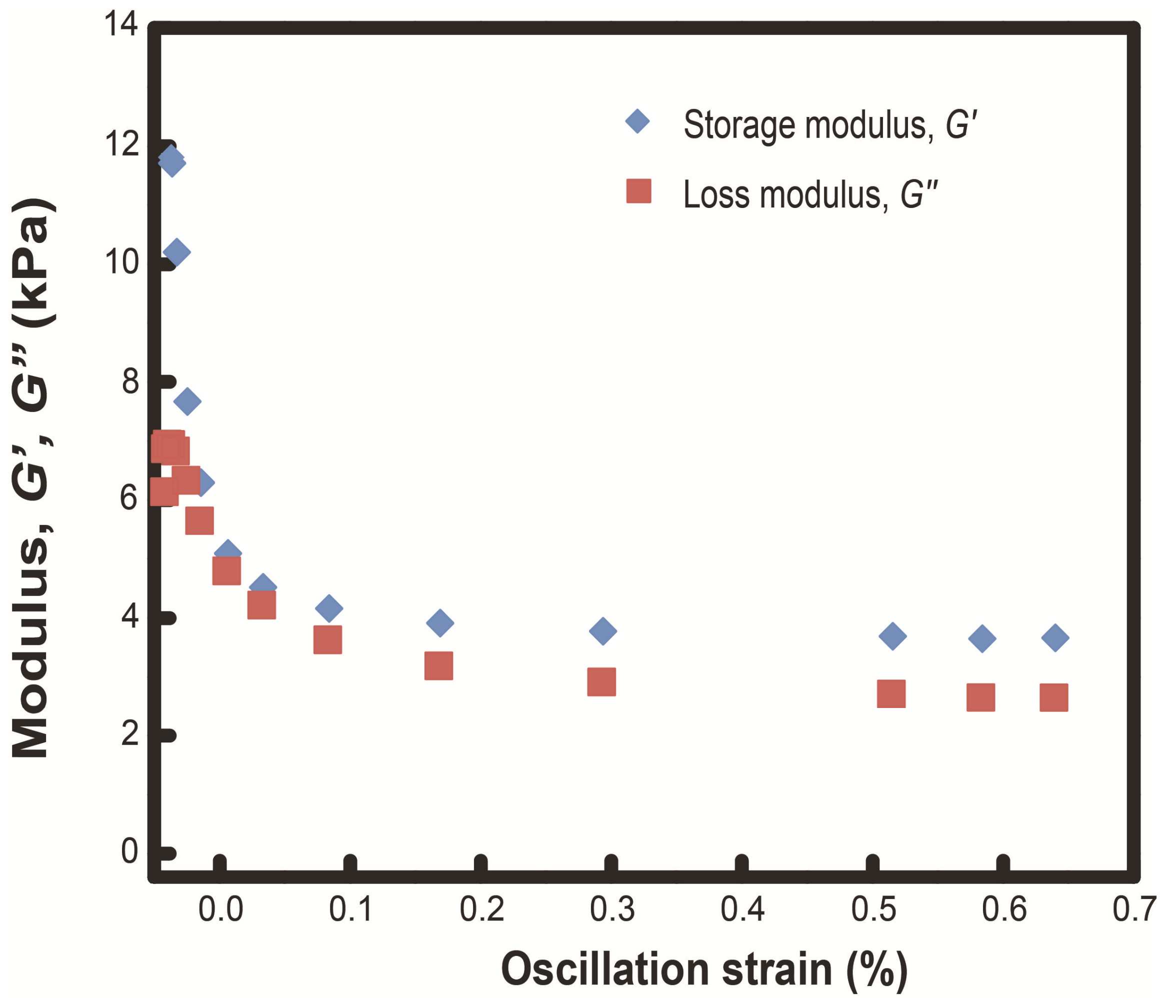

Figure S7. Amplitude sweep of hydrogel PLGA-PEG-PLGA doped with 1mg-mL^{-1} MelNP at ω = 5rad/s shows that the parameter chosen (0.5% strain) is in the linear viscoelastic regime.

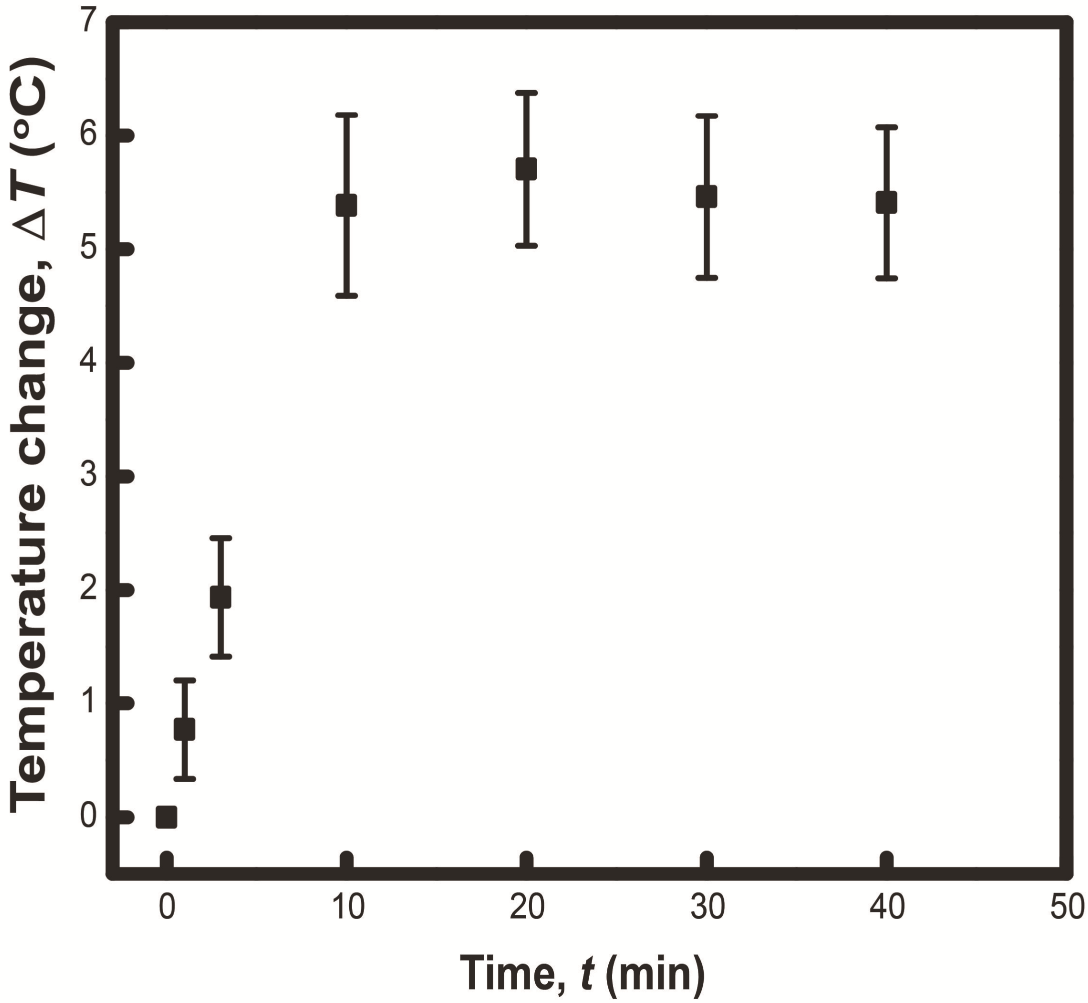

Figure S8. Photothermal response of hydrogel formed from 200 mg-mL^{-1} PLGA-PEG-PLGA to UV irradiation shows an increase of 5.4 ± 0.6 ^{o}C. This temperature increase is significantly smaller compared to the increase of 20.4 ± 0.1 ^{o}C that is achievable with aqueous dispersions of 1 mg-mL^{-1} MelNP (Fig.3).

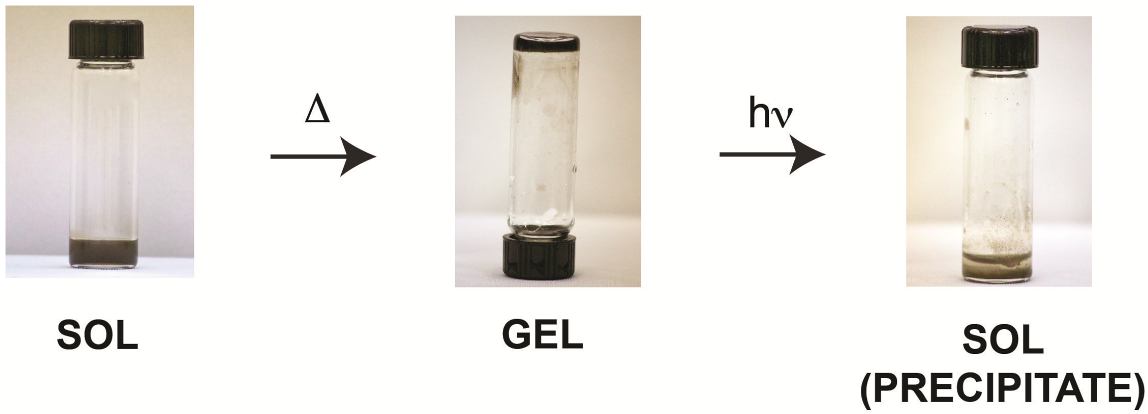

Figure S9. Photographic images of hydrogel formed from 200 mg-mL^{-1} PLGA-PEG-PLGA doped with 1 mg-mL^{-1} MelNP undergoing phase transitions from SOL to GEL to PRECIPITATE after UV irradiation for 30 minutes.

Table S2. The total free energy of adsorption of PLGA-PEG-PLGA to MelNP ($\Delta G_{ads,vol}$) was calculated and compared to the competing process of gelation (ΔG_{gel}). This calculation is consistent with the trends in gelation versus MelNP concentration (See Text).

MelNP Concentration c_{MelNP} (mg-mL^{-1})	$\Delta G_{ads,vol}$ (J-mL^{-1})[a]	ΔG_{gel} (J-mL^{-1})[b]	Gel formation
0.05	-0.05	-6.1	Yes
0.1	-0.11	”	Yes
0.2	-0.22	”	Yes
1	-1.08	”	Yes
5	-5.34	”	Yes
10	-16.1	”	No
20	-32.3	”	No

[a]Calculated from Eqns. 5 and 6 of main text.
[b]Constant value for all compositions. Taken from reference 45 of main text.

Additional References

1. W. J. Wiscombe, *Applied optics*, 1980, 19, 1505-1509.
2. N. P. Bansal and R. H. Doremus, *Handbook of glass properties*, 1986.