Injectable zwitterionic thermosensitive hydrogels with low-protein adsorption and combined effect of photothermal-chemotherapy†

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Chemical structure characterization of PNS nanogels

Fig. S1 (a) FT-IR spectrum and (b) 1H NMR spectrum of PNS nanogels.

The copolymerization of SBMA, NIPAM and MBA was confirmed by FTIR and 1H NMR spectrum. In Fig. S1a, the peak at 2924 cm⁻¹ (peak a) is assigned to C–H stretching vibrations of methyl or methylene in polymer. The peak at 1649 cm⁻¹ (peak b) is assigned to C=O stretching of amide and 1462 cm⁻¹ (peak c) is assigned to C–N bond of amine. The stretching bands of S=O in SBMA appears at 1044 cm⁻¹ (peak e). 1H NMR spectrum was shown in Fig. S1b. The peaks at δ=1.48~1.60 (a) and δ=1.91~2.01 (b) were assigned to methylene (a) and methyldyne (b) produced from the polymerization of carbon-carbon double bonds, respectively. The others are assigned as follows: δ=1.1 (g, CH(CH₃)₂), 2.2 (m, CH₂CH₂SO₃⁻), 2.89 (n, CH₂CH₂SO₃⁻), 3.16 (k, N⁺(CH₃)₂), 3.52 (l, N⁺CH₂CH₂CH₂SO₃⁻), 3.71 (j, COOCH₂CH₂), 3.79 (f, CH(CH₃)₂), 4.41 (i, COOCH₂; h, CONHCH₂NHCO).
Fig. S2 Diameters of PNA nanogels versus temperature.

Fig. S3 (a) FT-IR spectra of PDA NPs. (b) Hydrodynamic diameter of PDA NPs and its distribution measured by DLS. (c) TEM image of PDA NPs and (d) UV-Vis-NIR spectra of PDA NPs aqueous suspension and DA aqueous solution (both the concentration of DA and PDA NPs were 200 μg/mL).
Fig. S4 (a) Photographs and (b) rheology behavior of the sol-gel transition of PNS dispersion (25 wt%).

Photothermal conversion efficiency of PDA NPs

![Temperature change curve and linear relationship](image)

Fig. S5 (a) Temperature change curve of PDA NPs dispersion (200 μg/mL) under NIR laser irradiation (808 nm, 1.0 W/cm²) for 15 min and then shutting off the laser, and (b) linear relationship of time versus –\(\ln \theta\) obtained from the cooling curve in (a).

The photothermal conversion efficiency (\(\eta\)) of PDA NPs can be calculated according to Eq. S1 as reported\(^1\,^2\) and the experimental data.

\[
\eta = \frac{hA\Delta T_{\text{max}} - Q_s}{I(1 - 10^{-A \lambda})} \quad (\text{Eq. S1})
\]

Wherein \(h\) is the heat transfer coefficient, \(A\) is the surface area of the container, \(\Delta T_{\text{max}}\) is the maximum temperature change of PDA NPs suspension at the steady-state temperature, \(I\) is the laser power density used, \(A \lambda\) is the absorbance of the PDA NPs suspension at 808 nm, and \(Q_s\) is the heat of the solvent (water) produced by the laser irradiation.

In this system, \(\Delta T_{\text{max}}\) was 38.0 °C (Fig. S5a), \(A \lambda\) was 0.237 (Fig. S3d, \(l=1\) cm) and \(I\) was 1.0 W/cm². \(Q_s\) could be calculated from \(Q_s = C_{\text{water}} m \Delta T / t = 4.2 \text{ J/(g·°C)} \times 0.30 \text{ g} \times 5.8 \text{ °C/900 s} = 8.12 \text{ mW.}\) \(hA\) was obtained by applying the linear time data from the cooling period vs \(-\ln \theta\) (Fig. S5b) and Eq. S2. Herein, \(\theta\) is defined in Eq. S3, \(m\) and \(C_p\) are the mass (0.30 g) and heat capacity of water (4.2 J/(g·°C)).

\[
\tau_s = \frac{\sum m_i C_{p,i}}{hA} \quad (\text{Eq. S2})
\]
\[
\theta = \frac{\Delta T}{\Delta T_{\text{max}}} = \frac{T - T_{\text{air}}}{T_{\text{max}} - T_{\text{air}}}
\]  

(Eq. S3)

According to the data in Fig. S5a and Eq. 3, \(-ln\theta\) at different time could be calculated out. In addition, the slope of the fitted line in Fig. S5b was the time constant \(\tau_s\) (281.01). Therefore, \(hA\) equaled to 4.48 mW/°C according to Eq. S2 and \(\eta\) was 38.5% based on Eq. S1.

**Fig. S6** In vitro DOX release profiles of D/PNS and D/PNA hydrogels. (a) Without and (b) with FBS adsorbed on the DOX-loaded hydrogel (n=3). Note: ** \(P<0.01\), with significant difference.

**Fig. S7** Body weight of mice *versus* time.
Fig. S8 *In vivo* anti-tumor effect. (a) Tumour volumes change of D/PNS compared with D/PNA versus time. (b) Tumour volumes change of D-PDA/PNS compared with D-PDA/PNA versus time and (c) the corresponding photographs of the peeled tumours after intratumoral injection for 14 days. (d) Fluorescence
images of tumour tissue slice stained by Tunel. **\( p<0.01 \), *\( p<0.05 \).

References