Supporting information

Hierarchically designed hybrid nanoparticles for combinational photochemotherapy of pancreatic cancer

F. Joubert [a] and G. Pasparakis *[a]

[a] UCL School of Pharmacy, 29-39 Brunswick square, WC1N 1AX London, UK

* corresponding author: g.pasparakis@ucl.ac.uk

Calculation of the amount of GEM per particles

The calculation have been made for the Hybrid NPs of sample S7' where the loading in GNPs was maximal. From the TEM images, the average size diameter of the hybrid NPs was found to be 144 nm. We hypothesise the hybrid NPs can be seen as one large spherical GNPs with a volume (V_{GNPs}) being 1.563×10^{-15} cm^3 (i.e. $4\Pi/3R^3$). The Gold has a density of 19.320 g/cm^3 and the amount of GNPs used was 0.4 mg, hence the amount of place taken by the Gold is defined by the ratio of the amount of Gold to its density and was found to be 2.070×10^{-5} cm^{-3}. The number of hybrid NPs is obtained from the ratio of the amount of place taken by Gold to the V_{GNPs} and was found to be 1.324×10^{19} particles. For the hybrid NPs of sample S7', the amount of GEM-polymer conjugate was 15.625 µg. The total amount of GEM-polymer conjugate per particles is found to be 1.177×10^{-18} µg. Finally, the amount of GEM per hybrid NPs is estimated to be 0.588×10^{-18} µg.

Calculation of the photothermal conversion efficiency

The photothermal conversion efficiency (η) of hybrid NPs was calculated according to Hu's report.[1]

$$\eta = \frac{hS\left(T_{max} - T_s\right) - Q_{Dis}}{I(1 - 10^{-A_{640}})}$$

where h is the heat transfer coefficient, S the surface area of the container and the value hS is obtained from Eq. 4 and Fig. 5c. The maximum steady temperature (T_{max}) of the aqueous solution of the hybrid NPs was 46.4 ˚C and surrounding temperature was 34.2 ˚C. So the temperature change (T_{max}-T_s) of the solution of hybrid NPs was 12.2 ˚C. The laser power I is 0.9 W. The absorbance of the hybrid NPs at 640 nm is 0.72. Q_{Dis} defines the heat dissipated from the light absorbed by the solvent and the container and is 29 mW.

In order to gain hS, a dimensionless parameter θ is introduced as follows (Eq. 1):

$$\theta = \frac{T - T_S}{T_{max} - T_s}$$

A sample system time constant τ_s can be calculated as follows (Eq. 2):

$$t = -\tau_s \mathrm{Ln}(\theta)$$

According to Fig. 5c, τ_s was determined and found to be 104.08.

$$hS = \frac{m_D C_D}{\tau_s}$$

where m_D and C_D are the the mass and heat capacity of the solvent. Here, m_D is 1 g and C_D is 4.2 J/g. ˚C, hence hS is 0.04 W/˚C.

Substituting hS value into Eq. 1, the photothermal conversion efficiency (η) of hybrid NPs was calculated to be 63%.

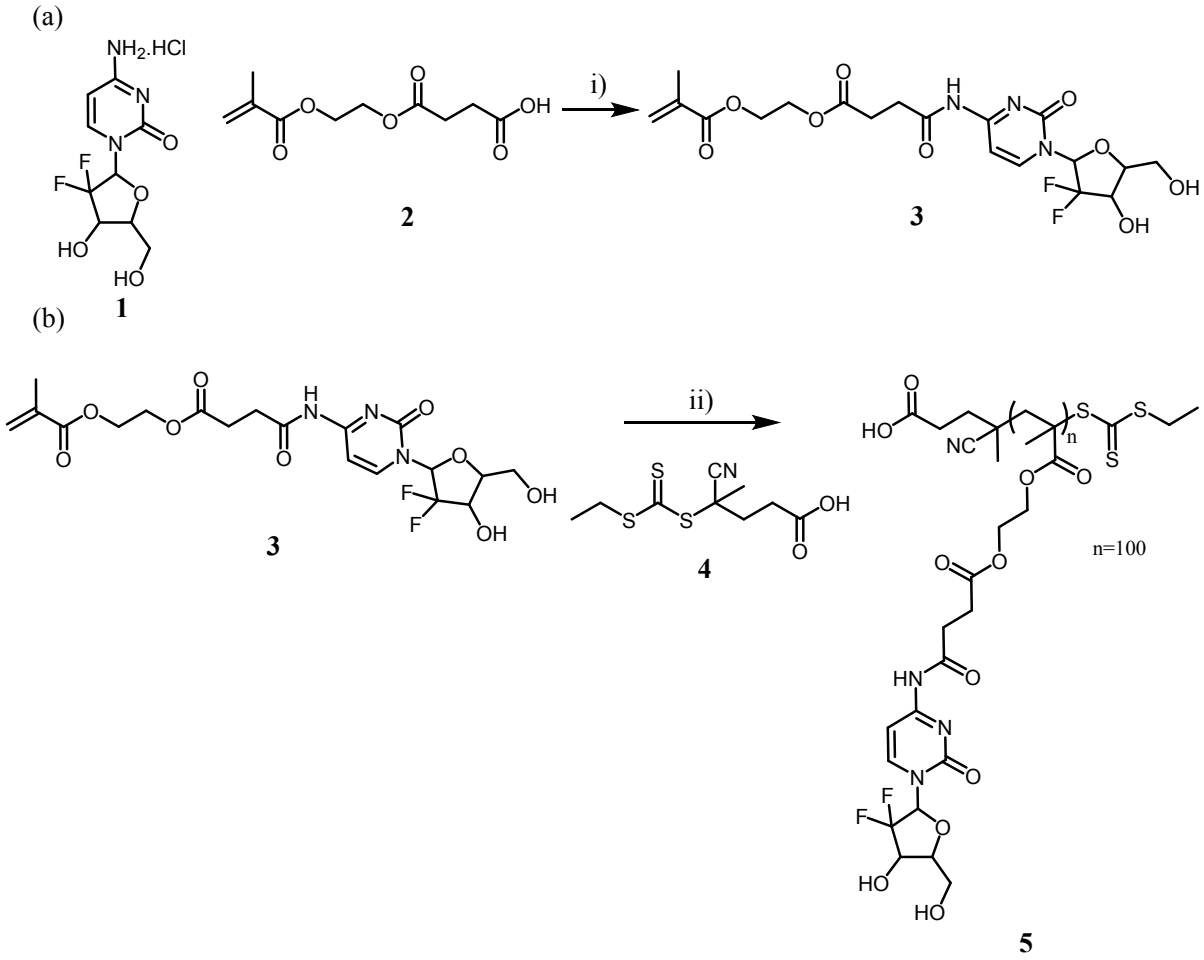
The τ_S of the GNPs was determined and was found to be 81.62 (Fig. S4), hS is deducted to be 0.05 W/˚C. The absorbance of the GNPs at 640 nm is 0.10, finally the photothermal effect of the GNPs was found to be 54%.

Calculation of the combination index (CI)

The combination index (CI) was calculated using the following equation.[2]

$$CI = \frac{C_{A,X}}{IC_{X,A}} + \frac{C_{B,X}}{IC_{X,B}}$$

where $C_{A,X}$ and $C_{B,X}$ are the concentration of A and B used in combination to achieve x % drug effect. $IC_{X,A}$ and $IC_{X,B}$ are the concentration for single agents to achieve the same effect. In our case, A and B represent GEM-polymer conjugate NPs and GNPs respectively and the IC_{50} is the drug effect which is look at to determine the CI.



Scheme S1 (a) Synthesis of methacrylate-based GEM-monomer conjugate **3**: i) HOBT/EDC, pyridine, 72 h, at room temperature, DMF, under positive Ar (b) RAFT polymerization conditions of **3** using a trithiocarbonate **4** as CTA: ii) 4 h at 70 ˚C in DMF under positive N_2.

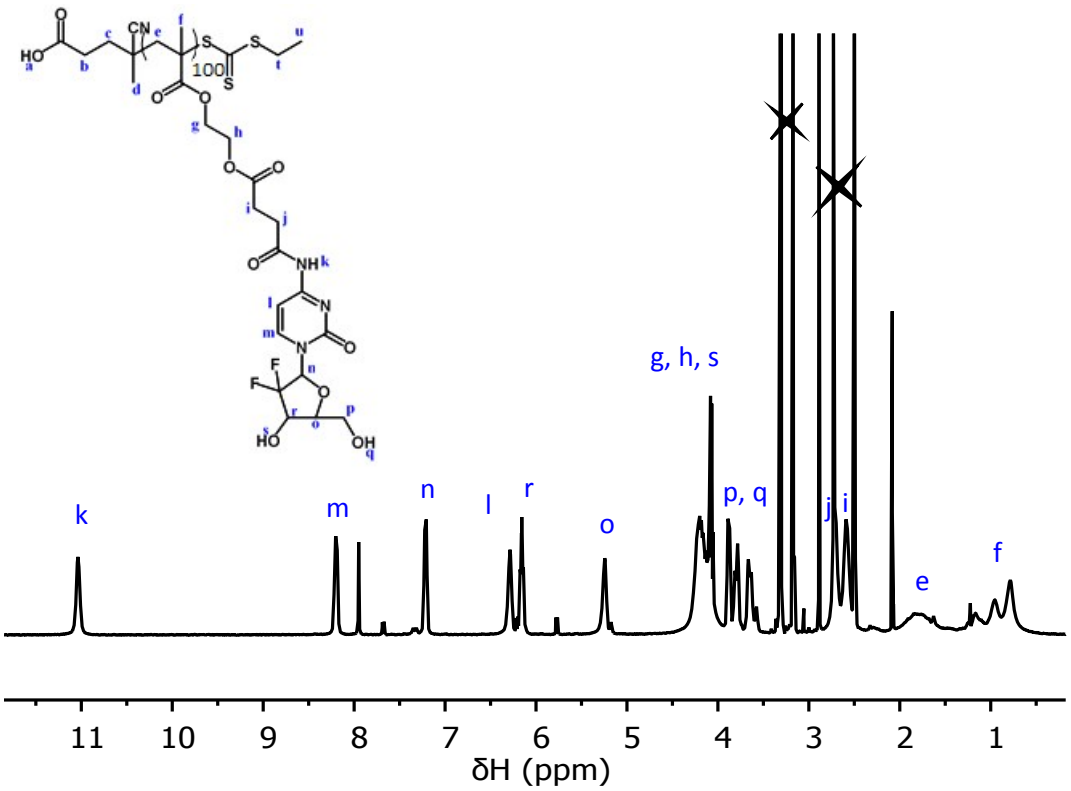


Fig. S1 ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of the GEM-polymer conjugate **5**; DP 100 (× designates the NMR and residual solvents peaks).

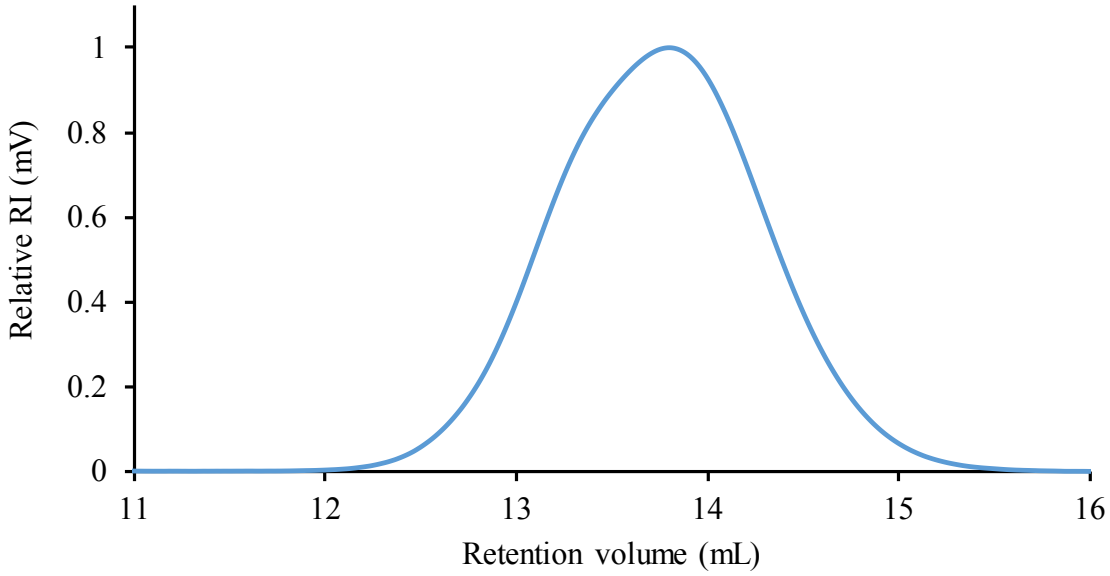


Fig. S2 SEC trace of GEM-polymer conjugate in DMF.

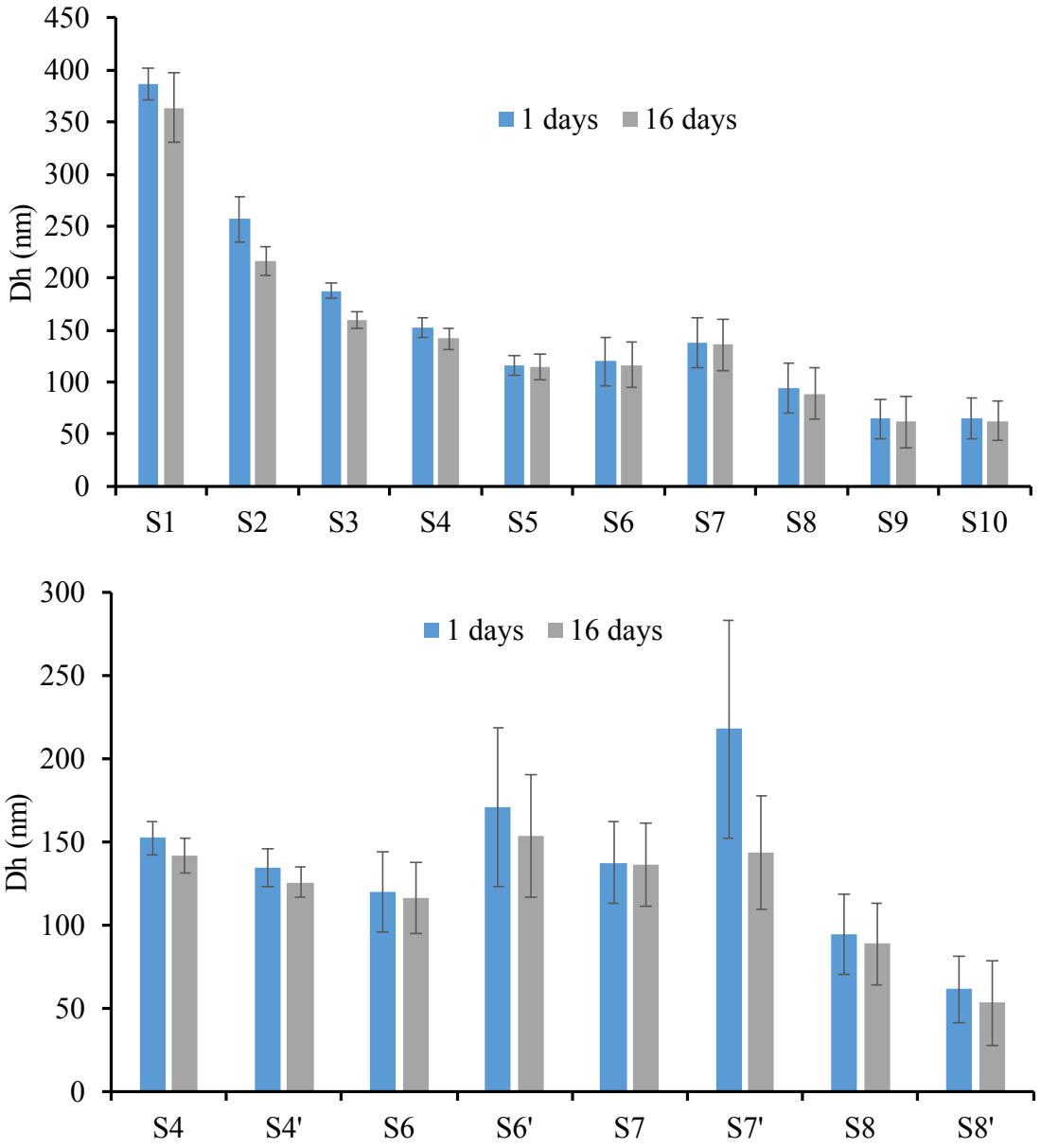


Fig. S3 DLS measurements of hybrids NPs after 16 days.

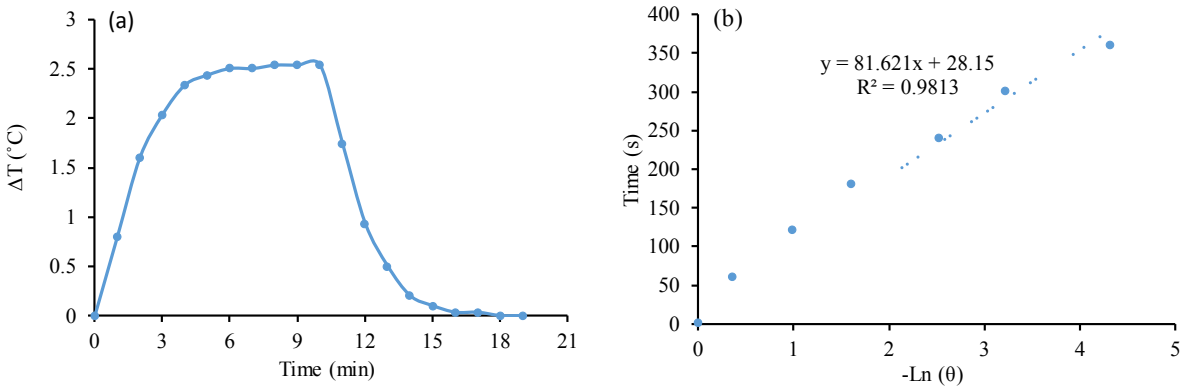


Fig. S4 (a) photothermal effect of the irradiation of the aqueous dispersion of GNPs for 10 min with a red laser (640 nm, 0.8 W/cm^2) and then the laser was turned off and (b) linear time data from the cooling period versus negative natural logarithm of driving force temperature which was obtained from the cooling phase.

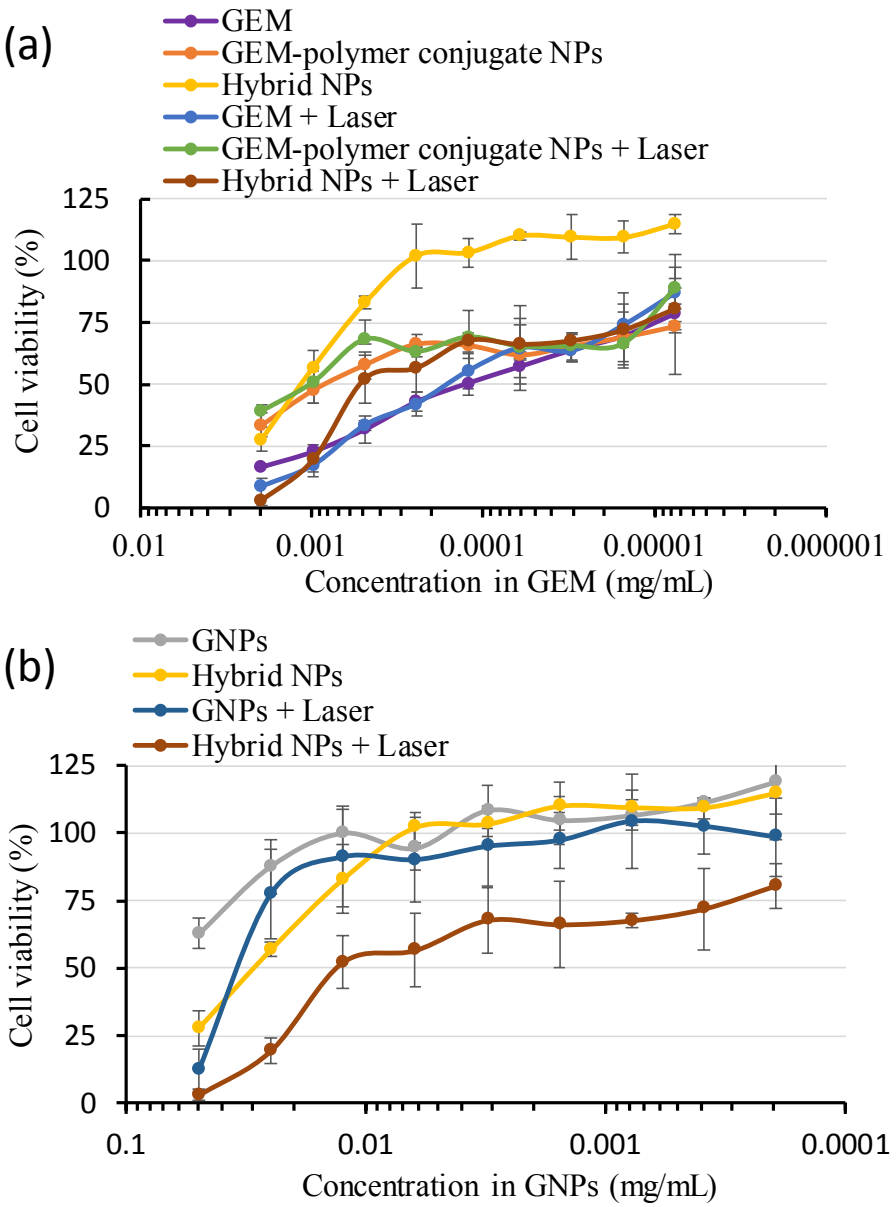


Fig. S5 Evolution of the cell viability as a function of the concentration of (a) GEM and (b) GNPs.

1 X. Liu, B. Li, F. Fu, K. Xu, R. Zou, Q. Wang, B. Zhang, Z. Chen and J. Hu, *Dalton Trans.*, 2014, **43**, 11709-11715.

2 S. Manni, A. Brancalion, L. Quotti Tubi, A. Colpo, L. Pavan, A. Cabrelle, E. Ave, F. Zaffino, G. Di Maira, M. Ruzzene, F. Adami, R. zambello, M. R. Pitari, P. Tassone, L. A. Pinna, C. Gurrieri, G. Semenzato and F. Piazza, *Clin. Cancer Res.*, 2012, DOI: 10.1158/1078-0432.ccr-11-1789.