SUPPLEMENTARY MATERIAL

FOR

Dual-responsive polymersomes for gold nanorod and doxorubicin encapsulation: Nanomaterials with potential use as smart drug delivery systems

Melissa DiazDuarte-Rodríguez¹, Norma A. Cortez-Lemus¹, Angel Licea-Claverie¹*, Jacob Licea-Rodriguez²,³, Eugenio Méndez-Méndez².


3. Cátedras Conacyt, Centro de Investigación Científica y de Educación Superior de Ensenada.
Figure S1. $^1$H-NMR spectra for Sigma Aldrich® methoxy-Polyethyleneglycol of a) 2000 Da and b) 5000 Da.

The number of EG repetitive units was determined dividing the integration value of the signal $h$ by the corresponding 4 Hydrogens.
Synthesis of the PEG122-macroCTA

In a three necked flask, equipped with a magnetic stir bar, thermometer, and a Dean-Stark trap with a reflux condenser, methoxy-poly(ethylene glycol)5000 (M<sub>n</sub>=5400 g/mol, 10.02 g, 1.86 mmol) was dissolved in toluene and refluxed for 48 h to eliminate water residues. Then, 4-cyano-4(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (1.6 g, 5.7 mmol), synthesized as described in the literature,[1] was dissolved in DCM (50 mL) and DMAP (0.24 g) was added to the three necked flask. The reaction mixture was cooled in an ice-bath and dicyclohexylcarbodiimide (0.82 g, 3.97 mmol) dissolved in DCM (6.0 mL) was added dropwise over 15 min. The reaction was allowed to proceed in an ice-cold bath for about 1 h, and then allowed to warm up to room temperature and stirred for 48 h. The solution was filtered to remove the precipitate. The solution was concentrated, and precipitated into ice-cold diethylether (x3). The yellow product was dried in vacuum oven at 25 °C for 24 h (43.2% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, δ ppm): 3.64 (CH<sub>2</sub>CH<sub>2</sub>O of the PEG chain), 3.38 (OCH<sub>3</sub>, chain end of the PEG), 3.33 (SCH<sub>2</sub>CH<sub>2</sub> of the CTA), 2.66-2.47 (CH<sub>2</sub>CH<sub>2</sub>OCO of the CTA), 2.51-2.16 (CH<sub>2</sub>CH<sub>2</sub>OCO), 1.87 (SCH<sub>2</sub>CH<sub>2</sub> of the CTA) 1.70 (CH<sub>3</sub>CN), 1.26 (SCH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>-CH<sub>3</sub> of the CTA), 0.88 (CH3 of the CTA).

References

Figure S2. $^1$H-NMR (400 MHz, CDCl$_3$) spectra for a) CTA: 4-cyano-4-(dodecylsulfanylthiocarbonyl) sulfanyl pentanoic acid, b) PEG$_{51}$-macroCTA, and c) PEG$_{122}$-macroCTA.
Figure S3. a) UV-Vis spectra of DOX in DMSO at different concentrations (0-100 \( \mu \)g/mL) and b) Calibration curve of DOX in DMSO at 484 nm.
Figure S4. a) UV-Vis spectra of DOX in PBS at different concentrations (0-30 µg/mL) and b) Calibration curve of DOX in DMSO at 484 nm.
Figure S5. GPC traces (RALS-detector) of the copolymers $P_{51}D_{47}$ (PEG$_{51}$-b-PDEAEM$_{47}$), $P_{122}D_{54}$ (PEG$_{122}$-b-PDEAEM$_{54}$), $P_{122}D_{59}$ (PEG$_{122}$-b-PDEAEM$_{59}$), $P_{122}D_{87}$ (PEG$_{122}$-b-PDEAEM$_{87}$) and $P_{122}D_{96}$ (PEG$_{122}$-b-PDEAEM$_{96}$).
Figure S6. $^1$H-NMR spectra (400 MHz, CDCl$_3$) of synthetized block copolymers: a)P$_{51}$D$_{47}$, b)P$_{122}$D$_{54}$, c)P$_{122}$D$_{59}$, d)P$_{122}$D$_{87}$
Figure S7. Statistics of TEM measurements of polymer aggregates: a) P_{51}D_{47}, b) P_{122}D_{54}, c) P_{122}D_{96}. 
Figure S8. DLS distribution of sizes for the $P_{122}D_{96}$ polymer aggregates obtained by nanoprecipitation in water at different pH values.
Figure S9. TGA-thermograms of synthetized block copolymers: a) $P_{51}D_{47}$, b) $P_{122}D_{54}$, c) $P_{122}D_{96}$
Figure S10. pH sensitive behavior for polymersomes encapsulating gold nanorod AuNR-761: a) encapsulated with P$_{51}$D$_{47}$; b) encapsulated with P$_{122}$D$_{54}$; c) encapsulated with from P$_{122}$D$_{96}$. 