

SUPPLEMENTARY MATERIAL

FOR

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

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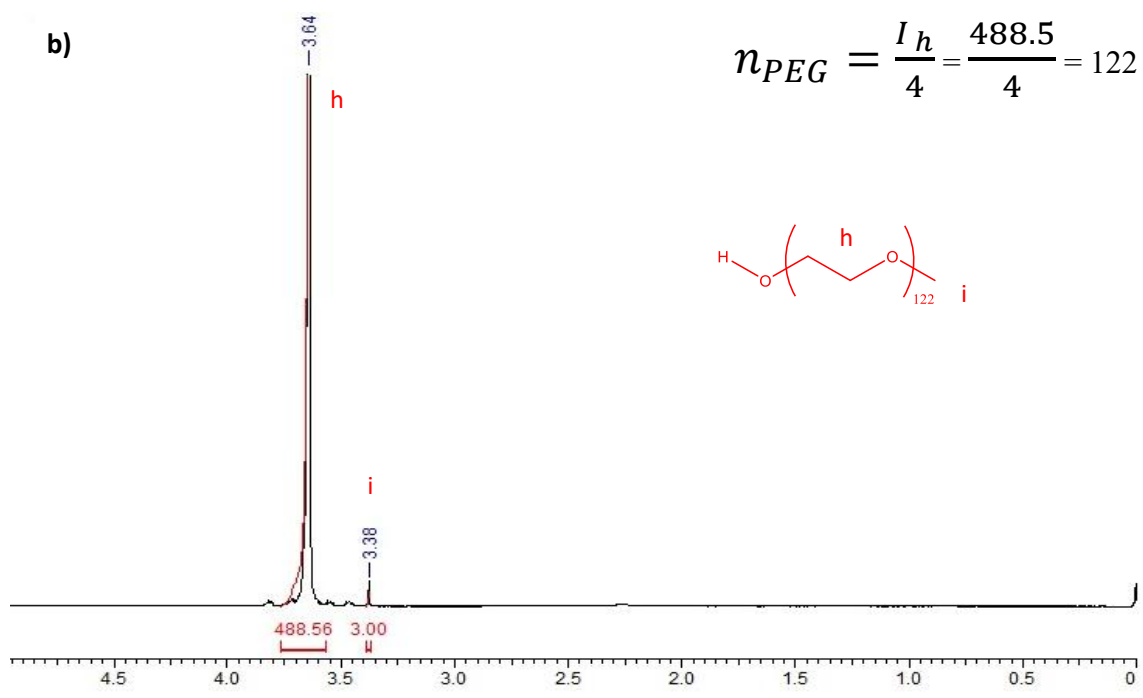
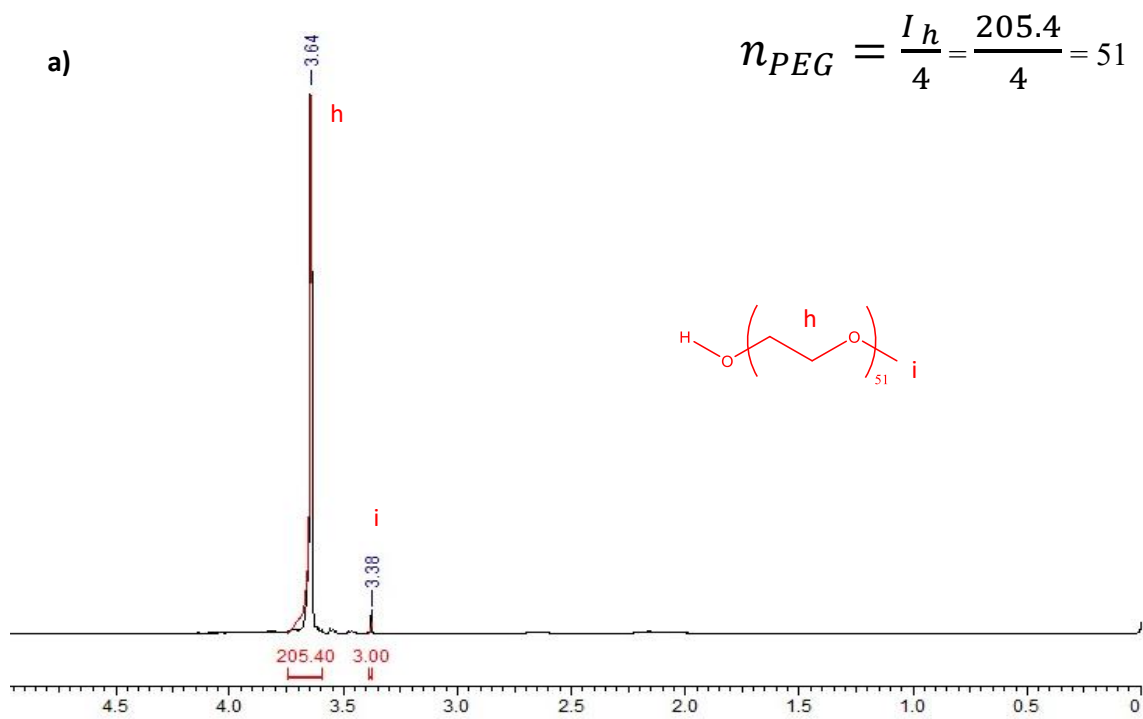


Figure S1. $^1\text{H-NMR}$ spectra for Sigma Aldrich® methoxy-Polyethyleneglycol of a) 2000 Da and b) 5000 Da.

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 ($M_n=5400$ 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).

¹H NMR (400 MHz, CDCl₃, δ ppm): 3.64 (CH₂CH₂O of the PEG chain), 3.38 (OCH₃, chain end of the PEG), 3.33 (SCH₂CH₂ of the CTA), 2.66-2.47 (CH₂CH₂OCO of the CTA), 2.51-2.16 (CH₂CH₂OCO), 1.87 (SCH₂CH₂ of the CTA) 1.70 (CH₃CN), 1.26 (SCH₂(CH₂)₉-CH₃ of the CTA), 0.88 (CH₃ of the CTA).

References

[1] G. Moad, Y.K. Chong, A. Postma, E. Rizzardo, S.H. Thang, Advances in RAFT polymerization: the synthesis of polymers with defined end-groups, *Polymer*, 46 (2005) 8458-8468. <https://doi.org/10.1016/j.polymer.2004.12.061>

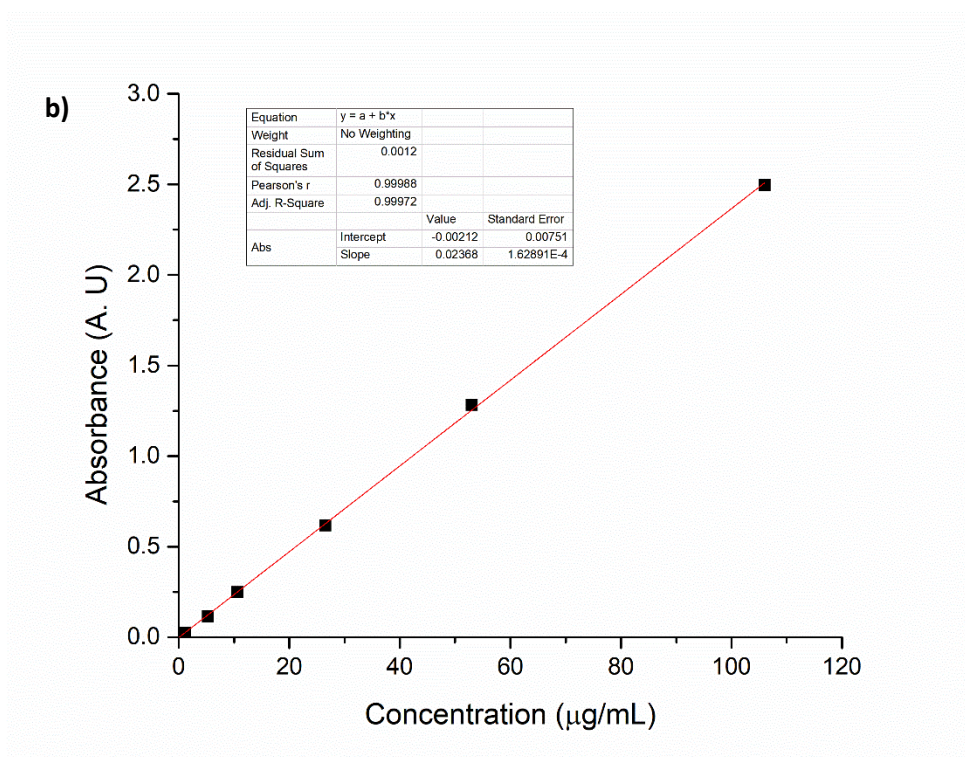
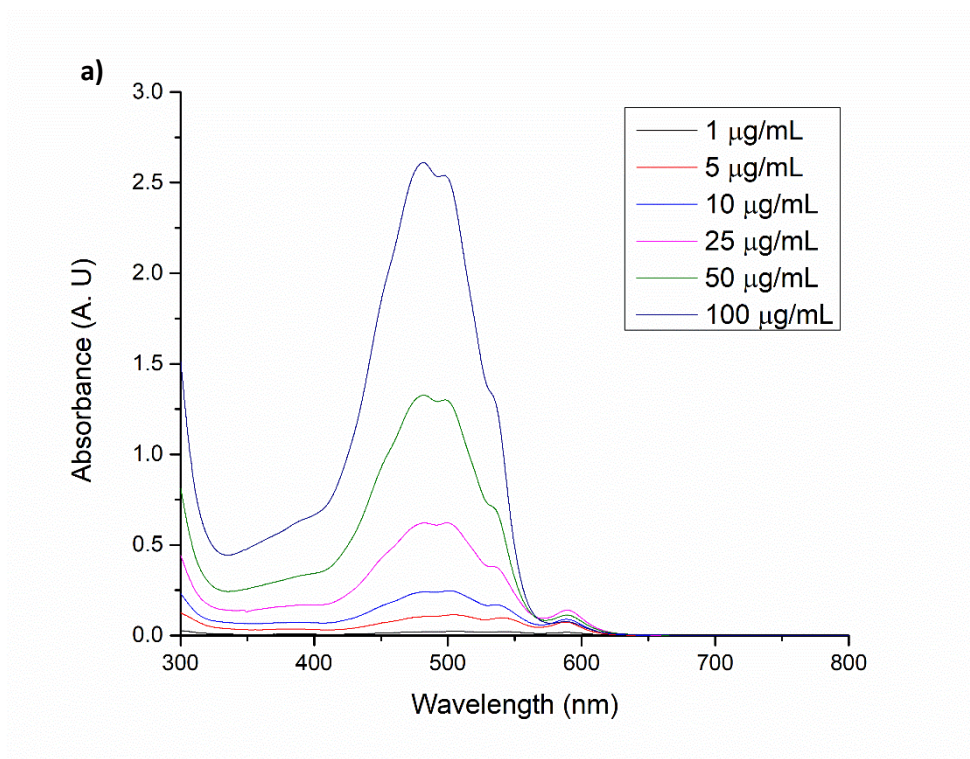


Figure S3. a) UV-Vis spectra of DOX in DMSO at different concentrations (0-100 µg/mL) and b) Calibration curve of DOX in DMSO at 484 nm.

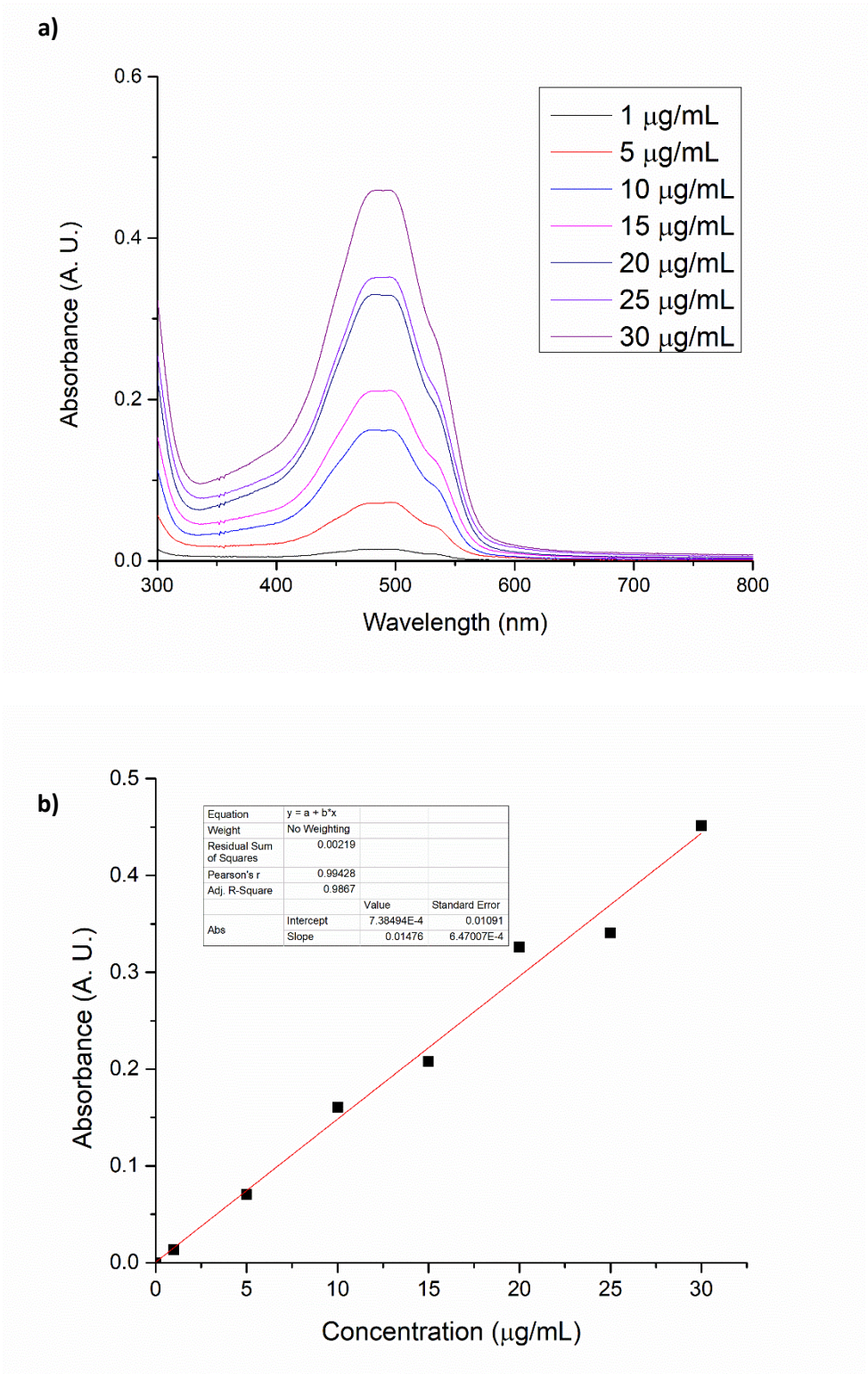


Figure S4. a) UV-Vis spectra of DOX in PBS at different concentrations (0-30 $\mu\text{g/mL}$) and b) Calibration curve of DOX in DMSO at 484 nm.

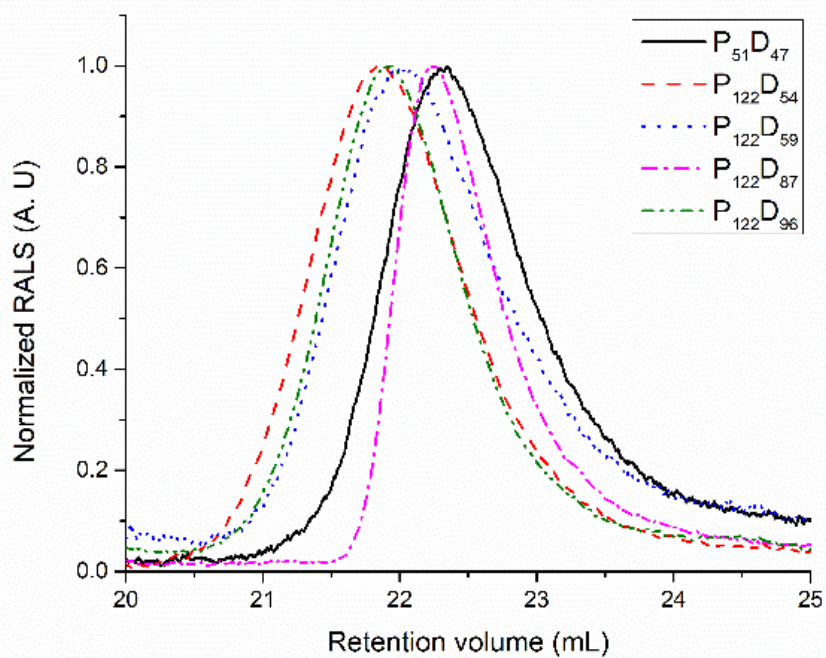
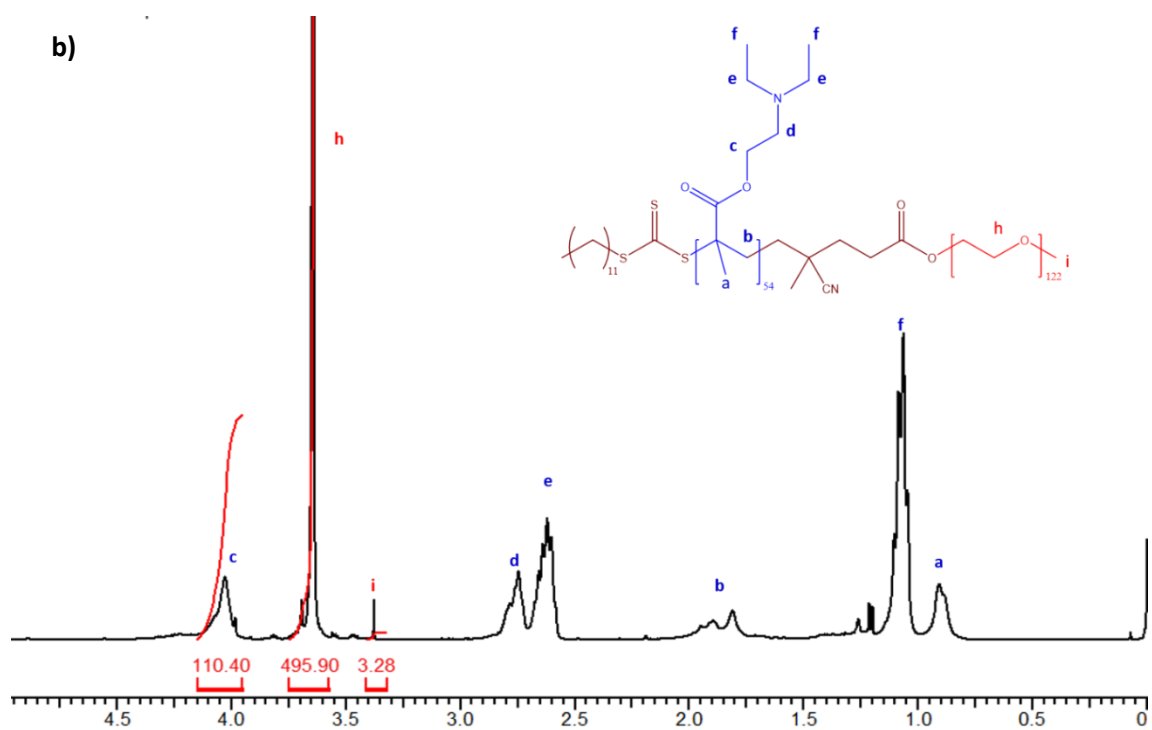
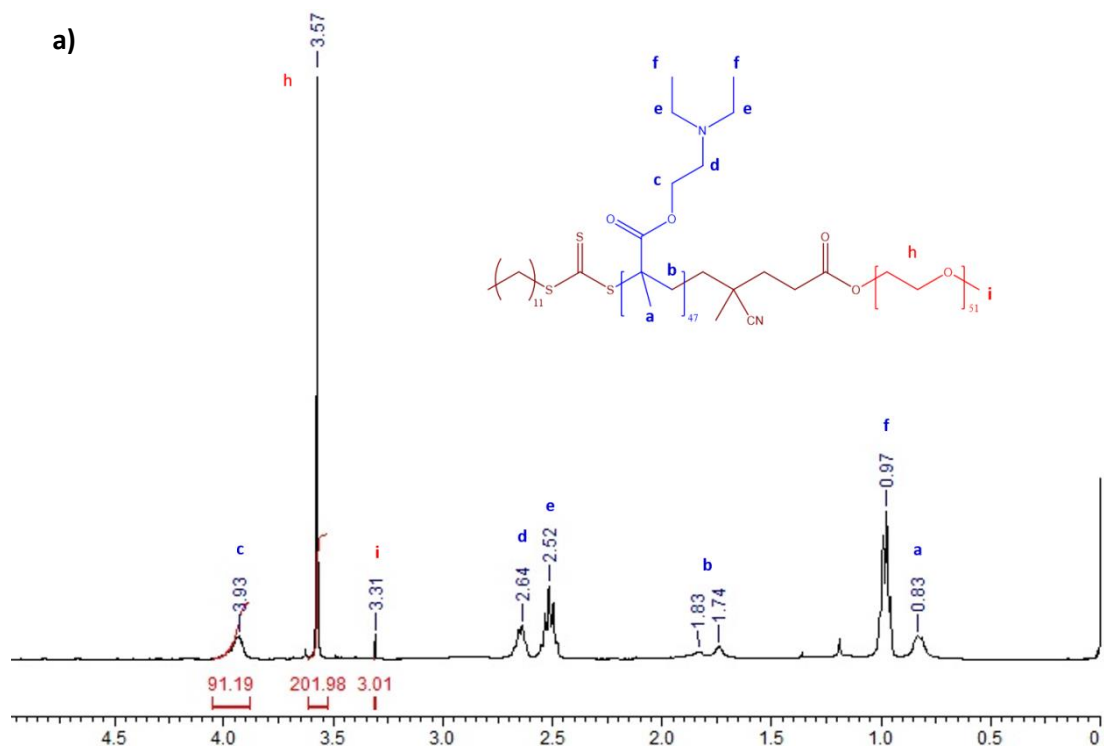


Figure S5. GPC traces (RALS-detector) of the copolymers $P_{51}D_{47}$ (PEG₅₁-*b*-PDEAEM₄₇), $P_{122}D_{54}$ (PEG₁₂₂-*b*-PDEAEM₅₄), $P_{122}D_{59}$ (PEG₁₂₂-*b*-PDEAEM₅₉), $P_{122}D_{87}$ (PEG₁₂₂-*b*-PDEAEM₈₇) and $P_{122}D_{96}$ (PEG₁₂₂-*b*-PDEAEM₉₆).



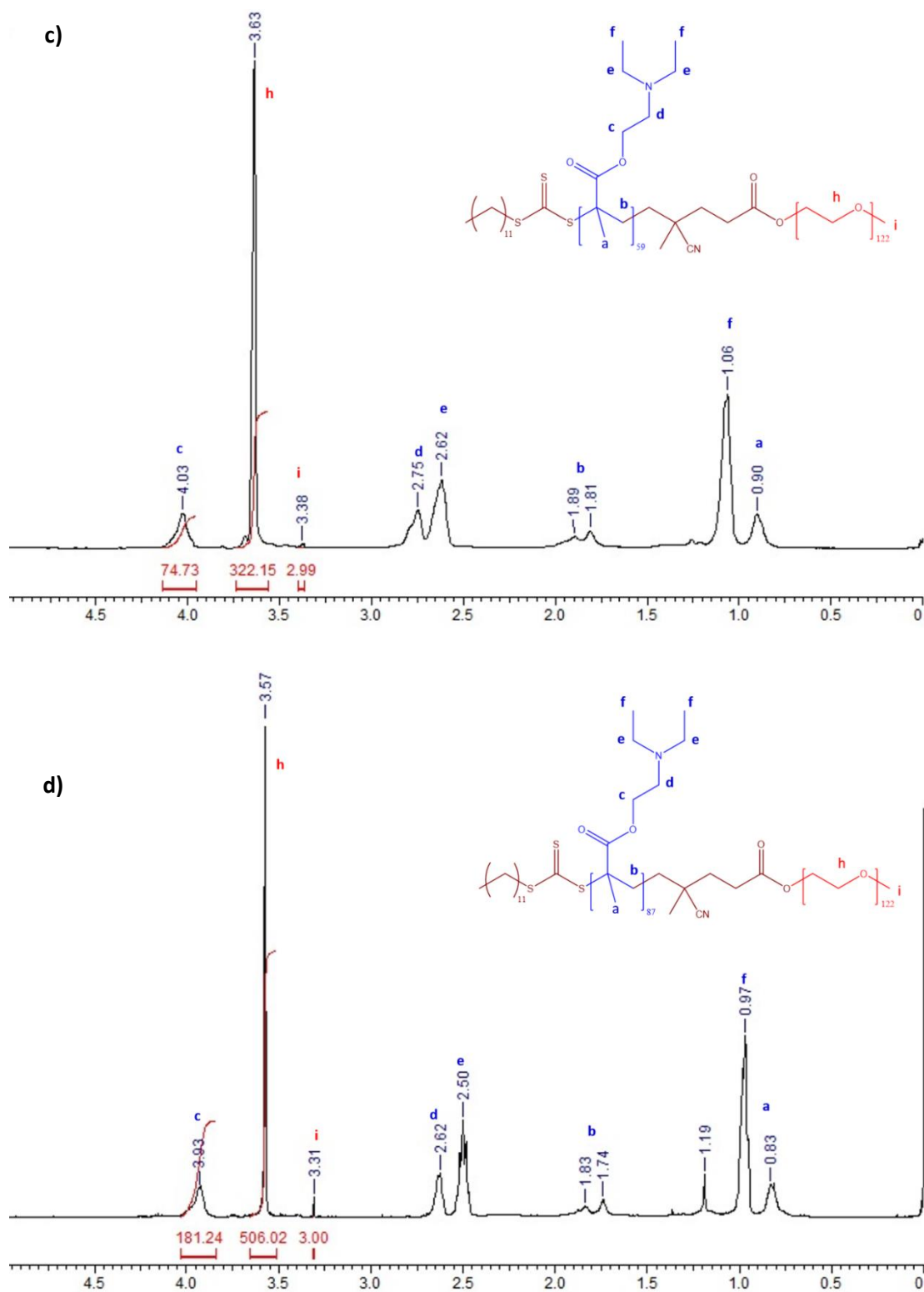


Figure S6. ¹H-NMR spectra (400 MHz, CDCl₃) of synthesized block copolymers: a)P₅₁D₄₇, b)P₁₂₂D₅₄, c)P₁₂₂D₅₉, d)P₁₂₂D₈₇

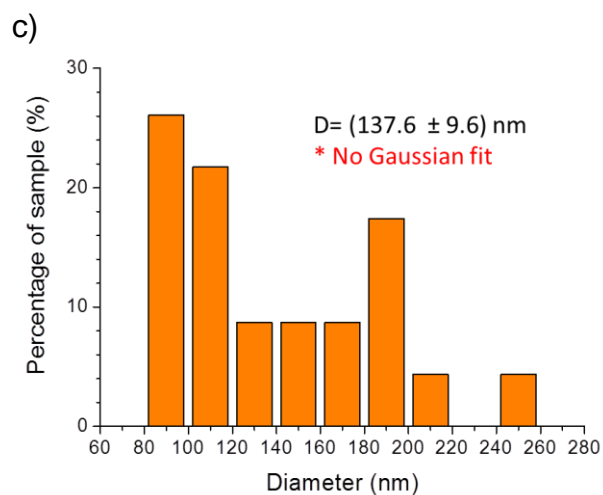
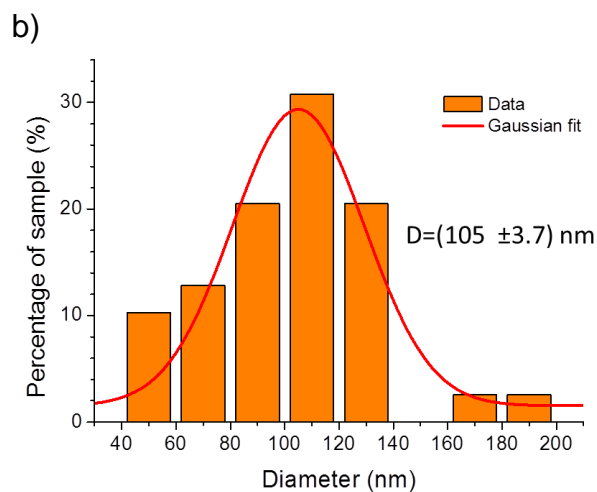
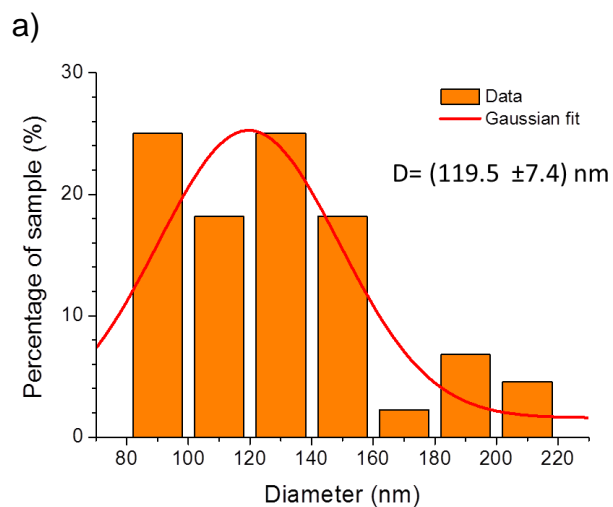


Figure S7. Statistics of TEM measurements of polymer aggregates: a) $P_{51}D_{47}$, b) $P_{122}D_{54}$, c) $P_{122}D_{96}$.

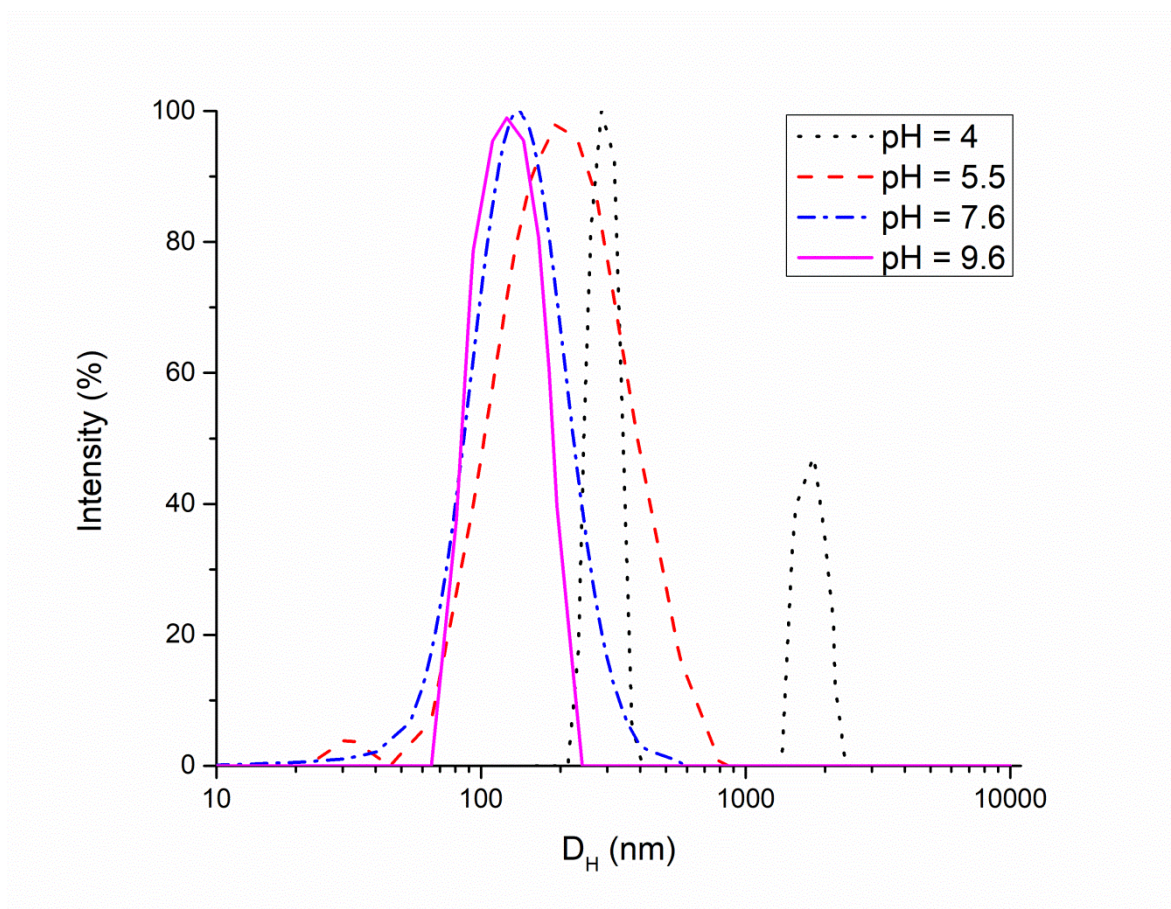


Figure S8. DLS distribution of sizes for the P₁₂₂D₉₆ polymer aggregates obtained by nanoprecipitation in water at different pH values.

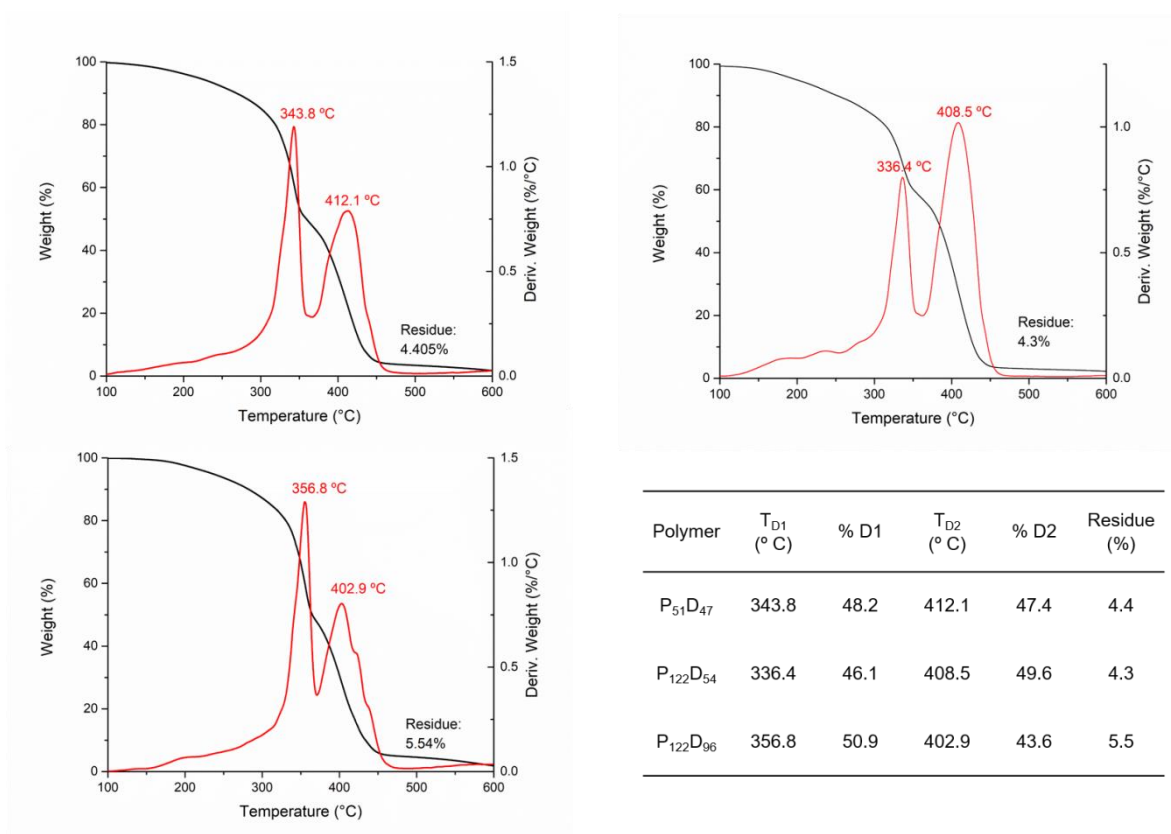
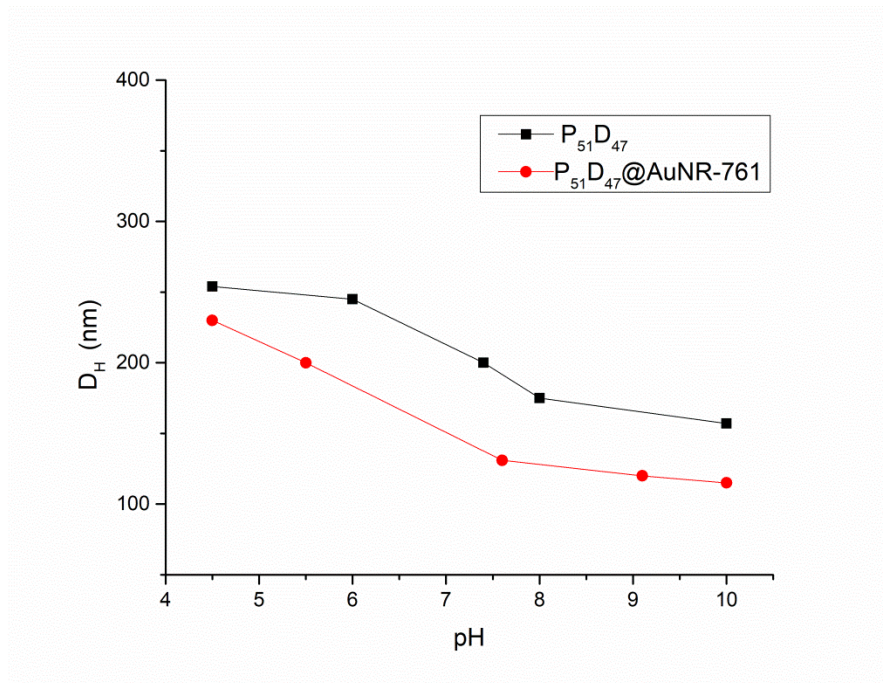
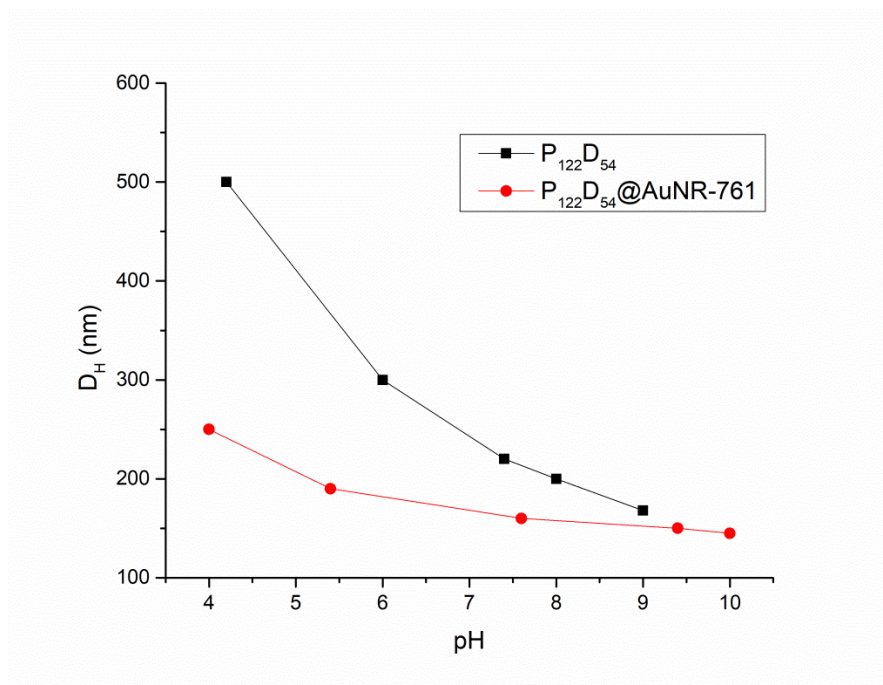


Figure S9. TGA-thermograms of synthesized block copolymers: a) P₅₁D₄₇, b) P₁₂₂D₅₄, c) P₁₂₂D₉₆

a)



b)



c)

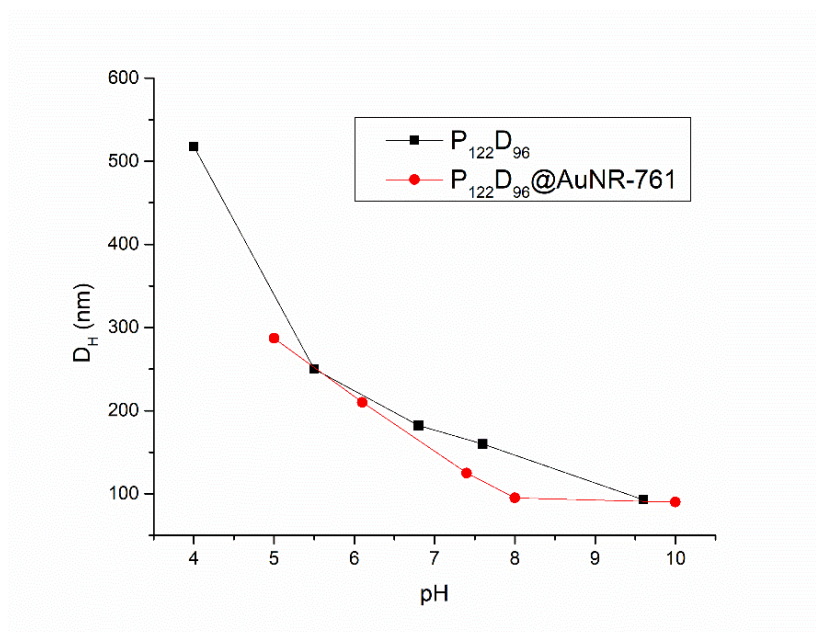


Figure S10. pH sensitive behavior for polymersomes encapsulating gold nanorod AuNR-761: a) encapsulated with $P_{51}D_{47}$; b) encapsulated with $P_{122}D_{54}$; c) encapsulated with from $P_{122}D_{96}$.