Supplementary information

T_1-weighted and T_2-weighted MRI probe based on Gd-DTPA surface conjugated SPIO nanomicelles

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Synthesis of FA-PASPD

Synthesis of poly(succinimide) (PSI)

PSI was synthesized as our previously report.[20] The resulting PSI (23 reapeating units) was obtained, with Mn(GPC)= 2.2×10^3 g/mol and Mn/Mw=1.21. The ^{1}H-NMR (DMSO-d_6, δ/ppm) spectra contained the following peaks: 2.6-3.5 (-C**H**$_2$-CO-), 5.3 (-C**H**-CO-).

Synthesis of poly(succinimide)-grafted-(p(ethylene glycol)-folic acid) (PSI-g-(PEG-FA))

Amino-p(ethylene glycol)-folic acid (NH_2-PEG-FA) was prepared in our previous work.[20] PSI (0.50 g, 0.23 mmol) was dissolved in DMF (10 mL), and NH_2-PEG$_{2000}$-FA (3.78 g, 1.55 mmol) was added to the DMF solution. The reaction mixture was stirred at 60 ℃ for 48 h under nitrogen atomosphere. Then the reaction mixture was precipitated in ether. The precipitate was dialyzed against deionized water for 5 days to remove the unreacted NH_2-PEG-FA (dialysis tube Mw cut-off 8000 Da) and freeze-drized. The product was obtained at 88% yield. with Mn(GPC)=1.89×10^4 g/mol and Mw/Mn=1.43. ^{1}H-NMR (DMSO-d_6, δ/ppm) spectra contained the following peaks: 8.0 (-CO-N**H**-), 3.60 (-O-C**H**$_2$-C**H**$_2$-), 4.6 (-C**H**-CO-NH-), 5.3 (-N-CO-C**H**-), 3.3 (-C**H**$_2$-CO-N-) 6.85-8.59 (FA) in Fig. S1A.

Synthesis of poly(succinimide)-grafted-(p(ethylene glycol)-folic acid)-dodecylamine (PSI-g-(PEG-FA)-DDA)

PSI-g-(PEG-FA) (500 mg , 0.026 mmol) was dissolved in DMF (5 mL), and DDA (33.8 mg, 0.183 mmol) was added to the DMF solution. The reaction mixture was stirred at 110 ℃ for 24 h under nitrogen atomosphere. Then the reaction mixture was precipitated in ether. The precipitate was dialyzed against deionized water for 2 days (dialysis tube Mw cut-off 8000 Da) and freeze-dried. The product PSI-g-(PEG-FA)-DDA (PEG and DDA with 30% and 30% mol substitution with respect to aspartate units, respectively) was obtained at 92% yield. with Mn(GPC)=1.99×10^4 g/mol and Mw/Mn=1.38. ^{1}H-NMR (DMSO-d6, δ/ppm) spectra contained the following peaks: 8.0 (-CO-N**H**-), 3.60 (-O-C**H**$_2$-C**H**$_2$-), 4.6 (-C**H**-CO-NH-), 5.3 (-N-CO-C**H**-), 3.3 (-C**H**$_2$-CO-N-), 6.85-8.59 (FA), 0.88 (-(CH$_2$)$_{11}$-C**H**$_3$), 1.25 (-(C**H**$_2$)$_{11}$-CH$_3$) in Fig. S1B.

Synthesis of poly(aspartate)-grafted-((p(ethylene glycol)-folic acid))-dodecylamine-ethylenediamine (PASP-g-(PEG-FA)-DDA-EDA)

PSI-g-(PEG-FA)-DDA (200 mg, 0.010 mmol) was dissolved in DMSO (2 mL), and Excess EDA (165 mg, 2.75 mmol) was added to the DMSO solution above. The reaction mixture was stirred at room temperature for 12 h under argon atomosphere. After the reaction, the solution was trasferred into a dialysis tube (Mw cut-off 3500 Da) and dialyzed against water 3 times, and freeze-dried. The yeild of product was 78%. ^{1}H-NMR (DMSO-d6, δ/ppm) spectra contained the following peaks: 8.0 (-CO-N**H**-), 3.60 (-O-C**H**$_2$-C**H**$_2$-), 4.6 (-C**H**-CO-NH-), 3.3 (-C**H**$_2$-CO-N-), 6.85-8.59 (FA), 0.88 (-(CH$_2$)$_{11}$-C**H**$_3$), 1.25 (-(C**H**$_2$)$_{11}$-CH$_3$), 3.1 (-C**H**$_2$-C**H**$_2$-NH$_2$) in Fig. S1C.

Synthesis of poly(aspartate)-grafted-p(ethylene glycol)-dodecylamine-ethylenediamine (PASP-g-PEG-DDA-EDA)

PSI-g-PEG-DDA was synthesized as our previously report.[21] The synthesis process of PASP-g-PEG-DDA-EDA was similar as that of PASP-g-(PEG-FA)-DDA-EDA. ^{1}H-NMR (DMSO-d6, δ/ppm) spectra contained the following peaks: 8.0 (-CO-N**H**-), 3.60 (-O-C**H**$_2$-C**H**$_2$-), 4.6 (-C**H**-CO-NH-), 3.3 (-C**H**$_2$-CO-N-), 0.88 (-(CH$_2$)$_{11}$-C**H**$_3$), 1.25 (-(C**H**$_2$)$_{11}$-CH$_3$), 3.1 (-C**H**$_2$-C**H**$_2$-NH$_2$) in Fig. S1D.

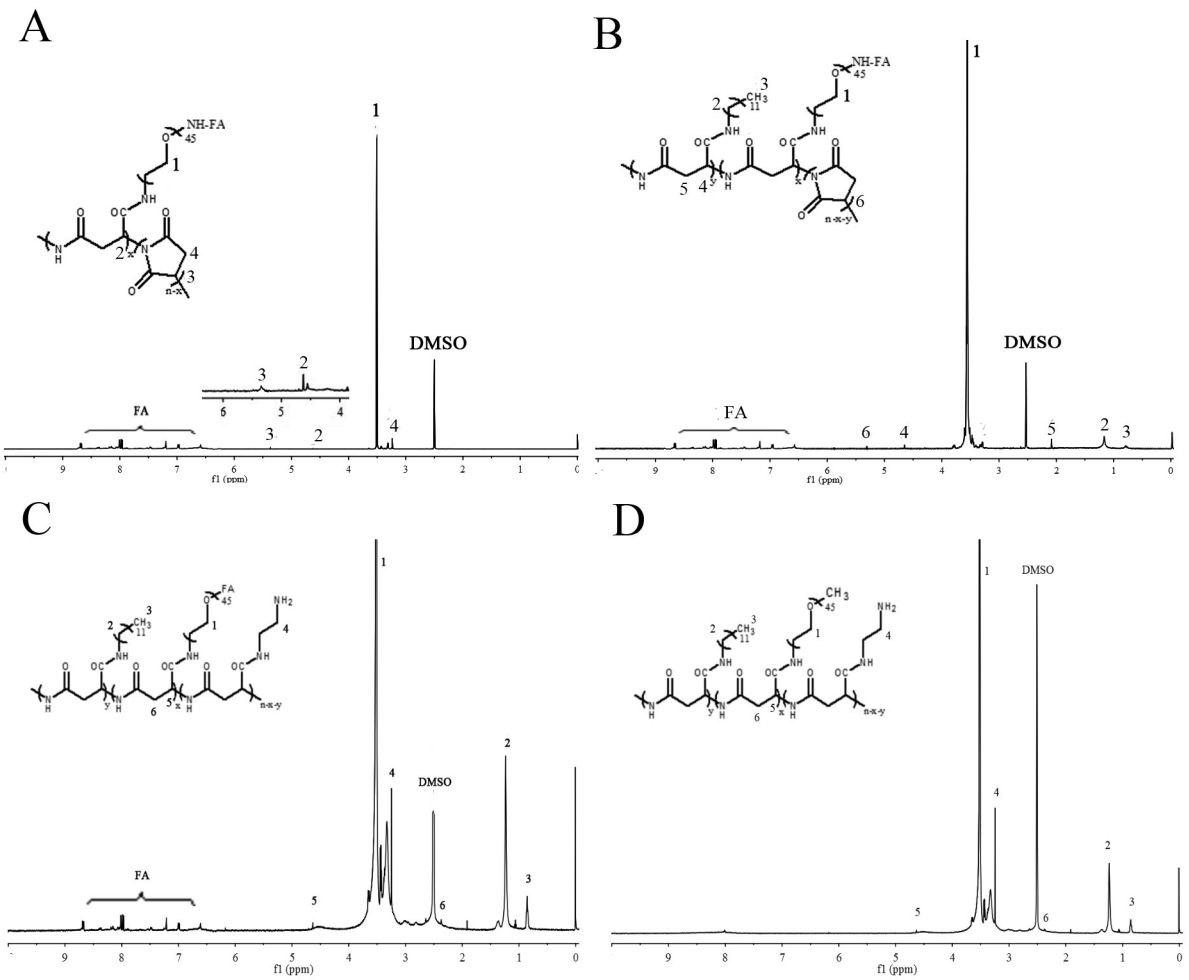

Fig. S1 ^{1}H-NMR spectra of (A) PSI-g-(PEG-FA) in DMSO-d_6 (B) PSI-g-(PEG-FA)-DDA in DMSO-d_6 (C) PASP-g-(PEG-FA)-DDA-EDA in DMSO-d_6 (D) PASP-g-PEG-DDA-EDA in DMSO-d_6