Surface modification of nanoparticles enhances drug delivery to the brain and improves survival in a glioblastoma multiforme murine model.

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Supporting information

Synthesis of PLGA-b-PEG-COOH copolymers

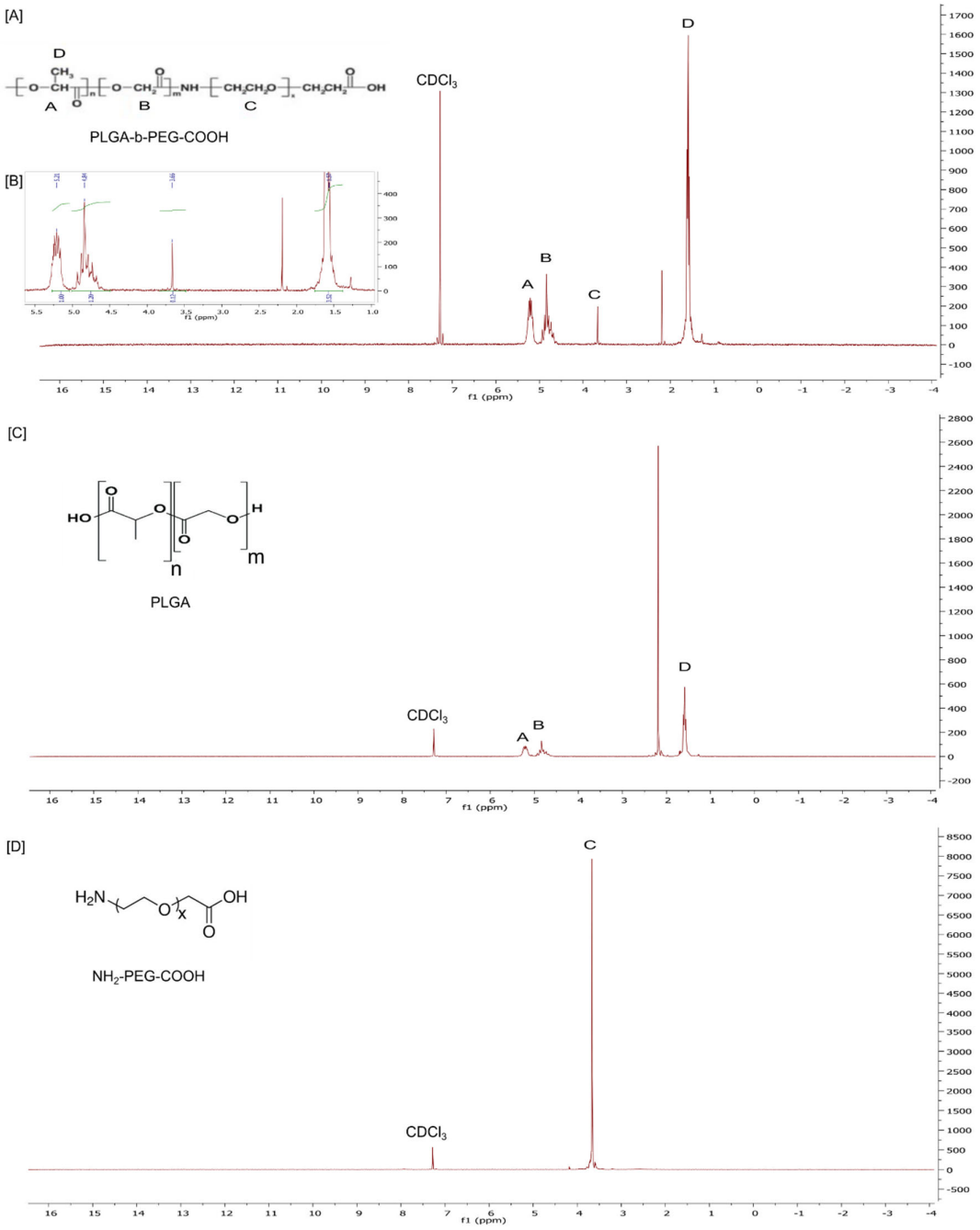

Figure S1. PLGA-b-PEG-COOH copolymers were successfully synthesized and characterized using $CDCl_3$ as a solvent and ^1H NMR spectrometry. (**A**) The peaks appeared at δ 1.56 ppm, δ 3.66 ppm, δ 4.81 ppm and δ 5.21 ppm which corresponded with the ^1H NMR spectrum of (**C**) PLGA (at δ 1.63 ppm, δ 4.83 ppm and δ 5.18 ppm) and the ^1H NMR spectrum of (**D**) NH_2-PEG-COOH (at δ 3.67 ppm). Integral ratios between PLGA (-C<u>H</u>C<u>H</u>$_3$-)-(-O-C<u>H</u>$_2$-) and PEG (-CH_2C<u>H</u>$_2$O-) peaks (**B**) are shown in the figure.

Table S1. Physicochemical characterization of NP formulations.

Samples	Particle size (nm ± S.D.)	PDI ± S.D.	Zeta potential (mV ± S.D.)	Loading (µg/1mg particles)	% Encapsulation
PGM NPs	177.1 ± 2.9	0.086 ± 0.011	28.4 ± 10.4	-	-
DiR-PG NPs	149.4 ± 6.0	0.083 ± 0.008	(-) 39.0 ± 1.8	1.66 ± 0.34	49.86 ± 10.20
DiR-PGM NPs	173.1 ± 5.6	0.069 ± 0.005	31.2 ± 9.5	1.63 ± 0.12	49.03 ± 3.55
DiR-PGI NPs	161.9 ± 23.9	0.086 ± 0.014	37.5 ± 5.4	1.42 ± 0.09	42.65 ± 2.69
Coumarin-6-PG NPs	135.6 ± 0.7	0.120 ± 0.019	(-) 20.7 ± 1.5	1.29 ± 0.02	35.42 ± 6.12
Coumarin-6-PGM NPs	159.1 ± 1.2	0.102 ± 0.008	11.7 ± 0.1	0.78 ± 0.08	23.30 ± 2.62
Coumarin-6-PGI NPs	172.0 ± 2.7	0.043 ± 0.038	13.2 ± 0.2	0.82 ± 0.10	24.69 ± 2.97

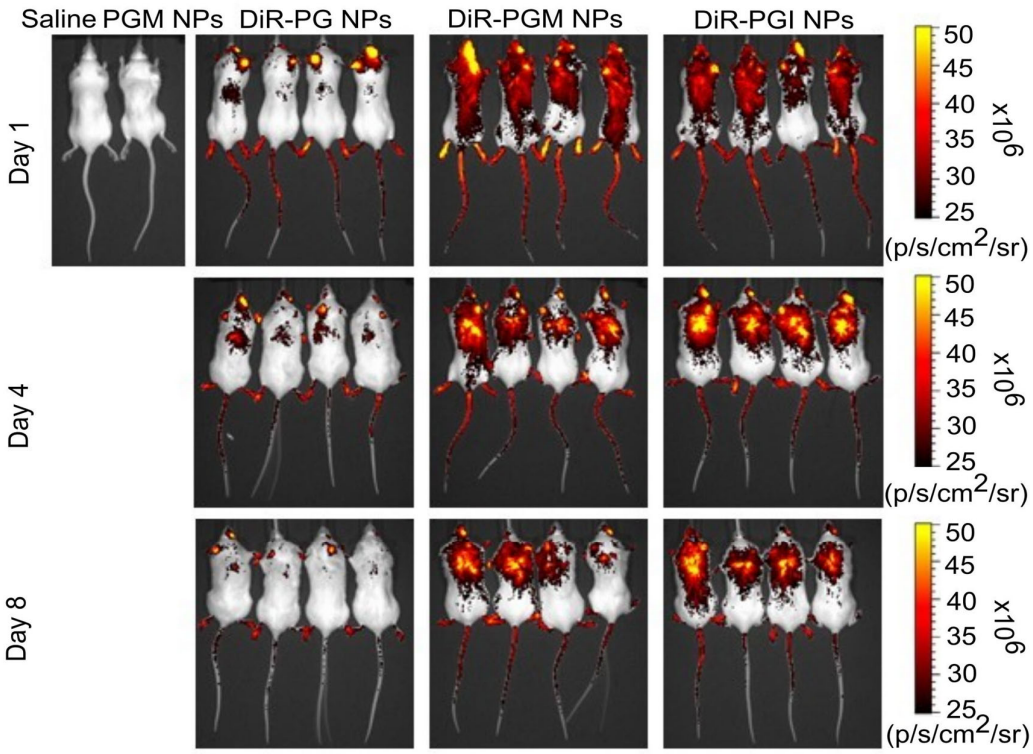

Figure S2. Fluorescence intensity of mice injected IV with either saline, blank PGM, DiR-PG, DiR-PGM or DiR-PGI NPs. The mice were injected with 5 mg of DiR-loaded NP formulations equal to 8.5 µg of DiR or 5 mg of blank PGM NPs by retro-orbital injection to observe biodistribution. On days 1, 4, and 8 after injection, the mice were anesthetized and whole body fluorescence was measured using an IVIS-200 after (n = 4/group).

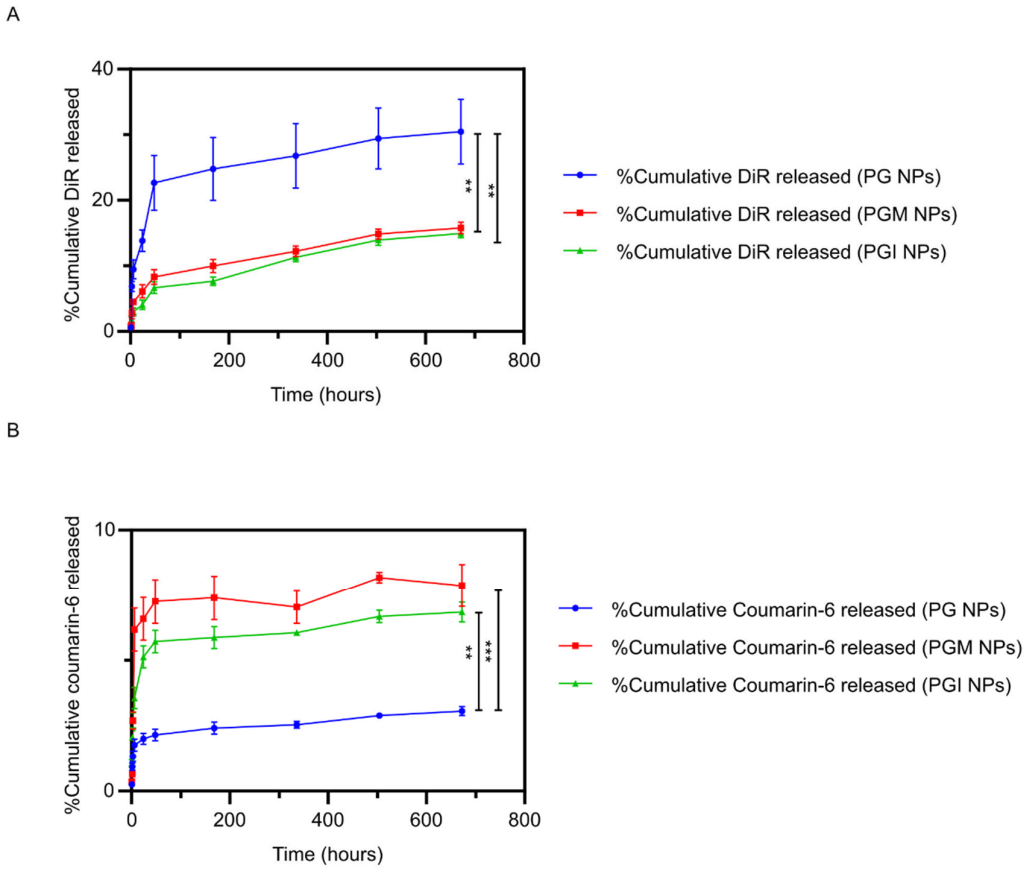

Figure S3. In vitro release profile of DiR from NP formulations over 672 hours reported as mean ± S.D. (n = 3) (A). In vitro release profile of coumarin-6 from NP formulations over 672 hours reported as mean ± S.D. (n = 3) (B). Results were analyzed using repeated measures ANOVA (Tukey's post-hoc test); ** $p < 0.01$ and *** $p < 0.001$.

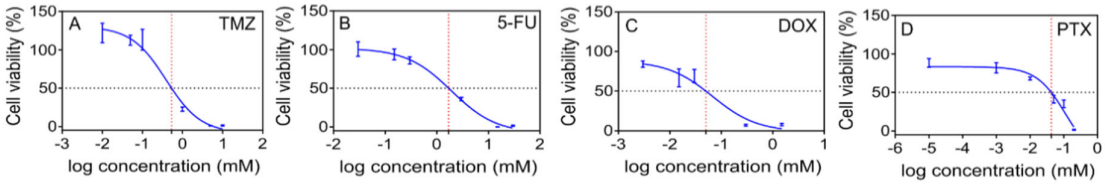

Figure S4. In vitro cytotoxicity results from MTS assays performed using U87MG-Red-Fluc cells incubated with (a) TMZ, (b) 5-FU, (c) DOX, or (d) PTX solutions at various concentrations for 24 h. The media alone and untreated cells were used as negative controls. Results are reported as mean ± S.D. (n = 3/group).