

## Supporting Information

### Transferrin receptor-targeted PEG-PLA Polymeric Micelles for Chemotherapy against Glioblastoma multiforme

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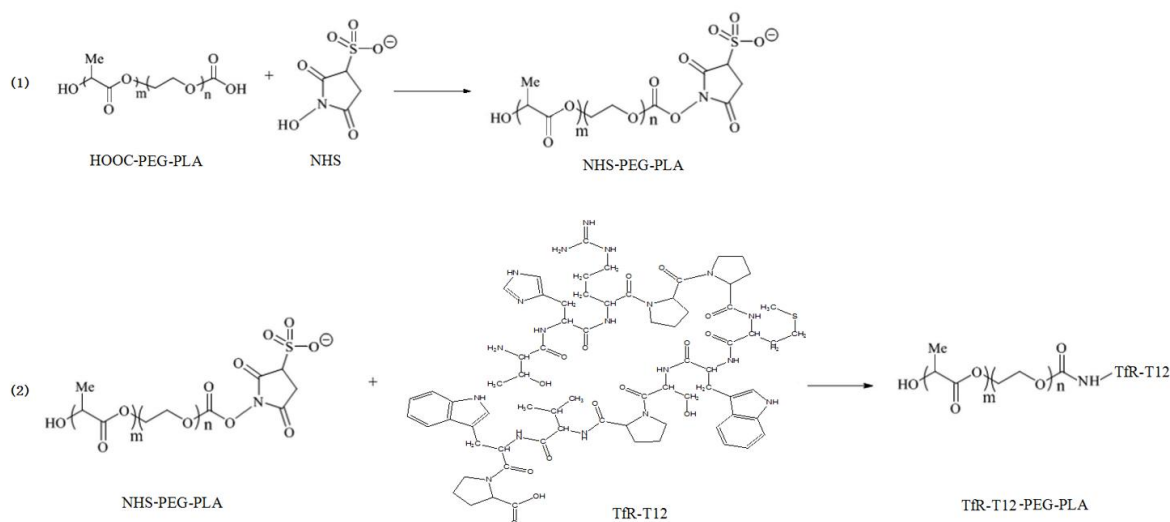


Figure S1: The synthetic route of TfR-T12-PEG-PLA copolymer, EDC/NHS was used to activator for reaction 24h.

**Abbreviations:** EDC, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide-2-hydrochloride; NHS, N-Hydroxysuccinimide.

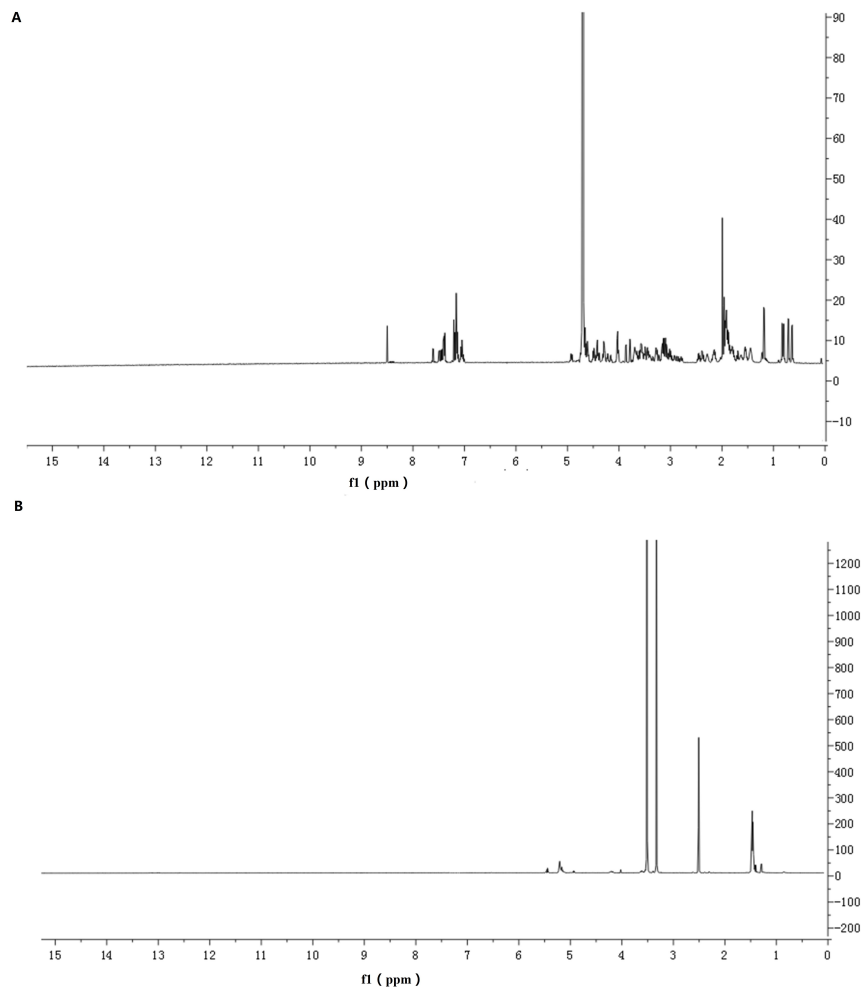


Figure S2:  $^1\text{H-NMR}$  spectroscopy of TfR-T12 peptide (A) and PEG-PLA (B).  
Abbreviations: TfR-T12, Transferrin Receptor-T12 peptide; PEG-PLA, Poly(ethylene glycol)-b-poly(L-lactide-co-glycolide).

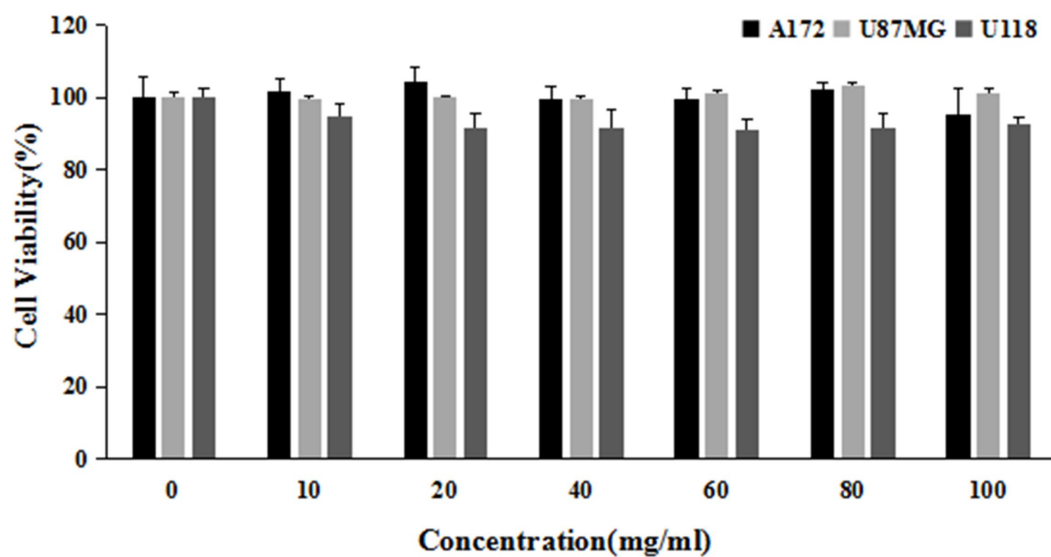


Figure S3: Toxicity evaluation of TfR-T12-PEG-PLA copolymer within 0-100mg/ml concentration in A172, U87MG and U118 cells, the cell viability was above 90% in every group.

**Abbreviations:** TfR-T12, Transferrin Receptor-T12 peptide.

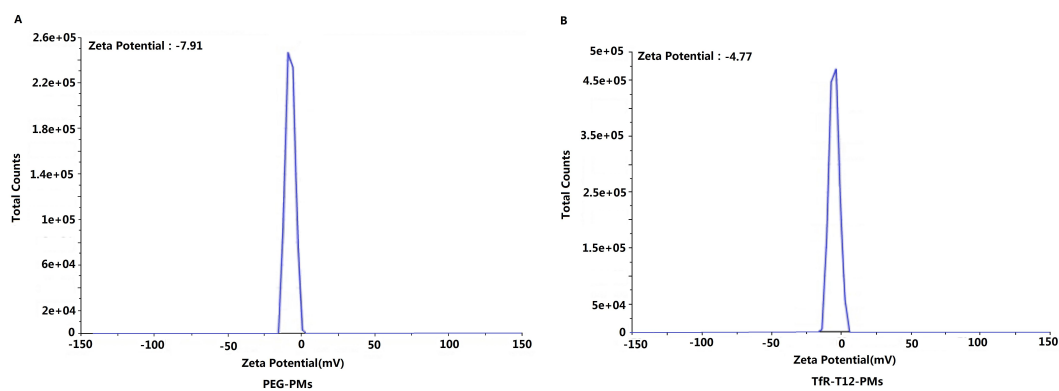


Figure S4: The zeta potential distribution of PEG-PMs (A) and TfR-T12-PMs (B).

**Abbreviations:** PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.

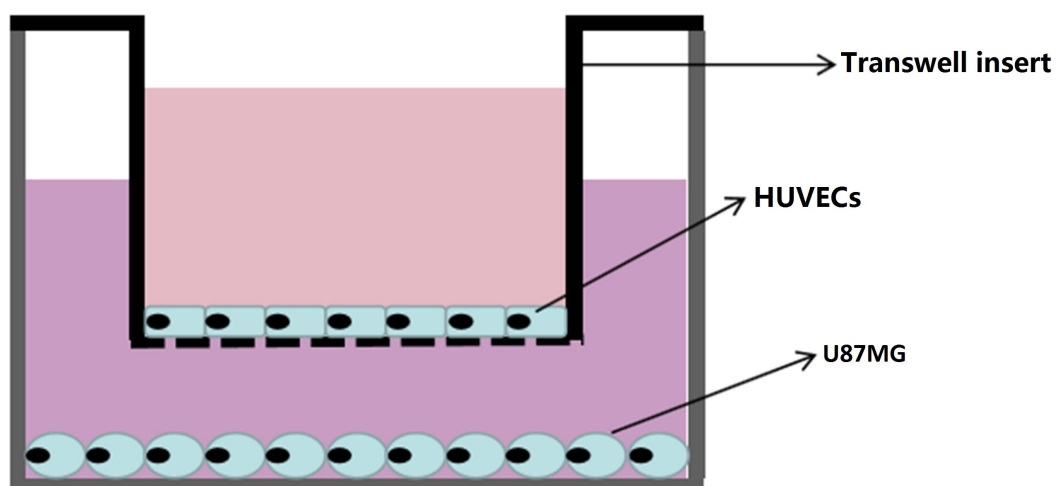


Figure S5: Schematic of the *in vitro* BBB/BBTB model, which is formed by HUVECs /U87MG cells co-culture over the transwell insert for 3days.

**Abbreviations:** BBB, Blood–Brain Barrier; BBTB, Blood–Brain Tumor Barrier

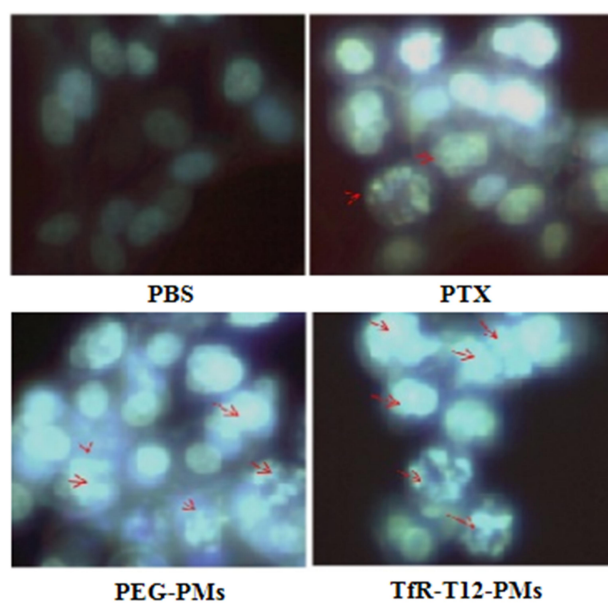


Figure S6: The hoechst staining observation of U87MG cells treated with different PTX formulations after HUVEC/U87MG co-culture, PBS was as control group, and the red arrow represents U87MG apoptosis.

**Abbreviations:** PTX, Paclitaxel; PEG-PMs, PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.

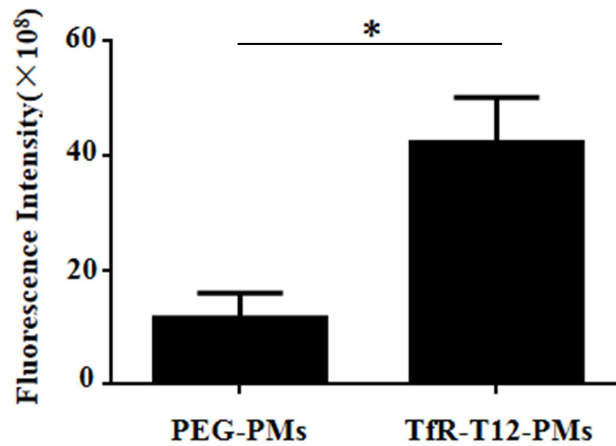


Figure S7: Fluorescence distribution of brain tissue in health mice, DiR was loaded in PEG-PMs and TfR-T12-PMs in this study, data are depicted as means  $\pm$  SD, n = 3, \*P < 0.05.

**Abbreviations:** PEG-PMs, PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.

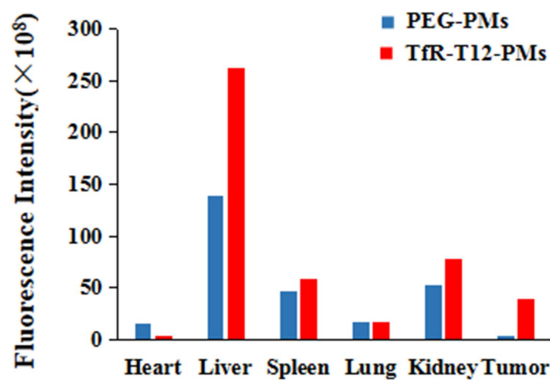


Figure S8: Fluorescence distribution of heart, liver, spleen, lung, kidney and tumor in subcutaneous tumor model, n = 3.

**Abbreviations:** PEG-PMs, PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.

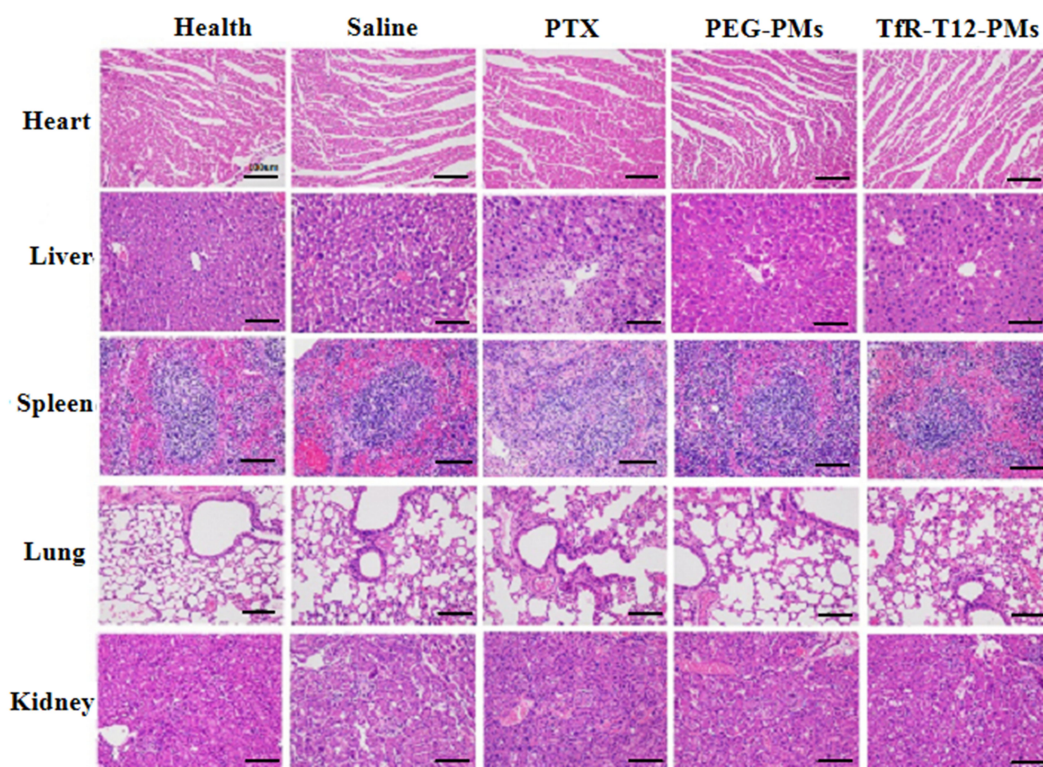


Figure S9: H&E stained for heart, liver, spleen, lung and kidney sections of U87MG subcutaneous bearing mice treated with saline, PTX, PEG-PMs and TfR-T12-PMs. Health mice were taken as control; scale bar =100 $\mu$ m.

**Abbreviations:** H&E, Hematoxylin and Eosin; PTX, Paclitaxel; PEG-PMs, PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.

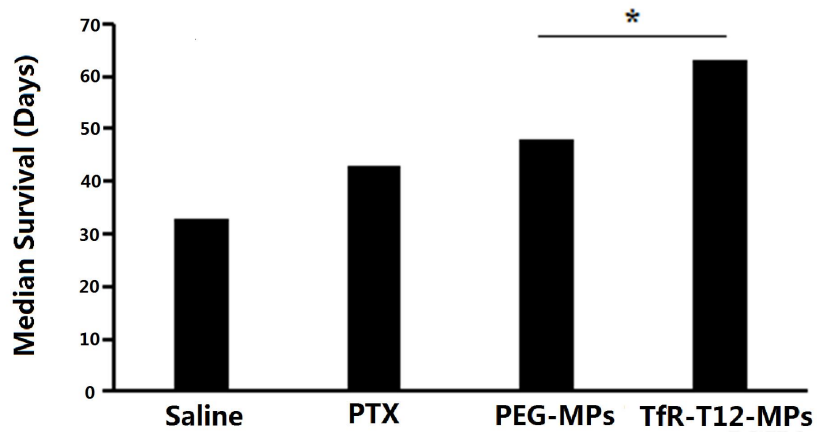


Figure S10: Median survival of orthotopic U87MG bearing mice treated with saline, PTX, PEG-PMs and TfR-T12-PMs, n=7, \*P < 0.05.

**Abbreviations:** PTX, Paclitaxel; PEG-PMs, PEG-PLA/PTX Polymer Micelles; TfR-T12-PMs, TfR-T12-PEG-PLA/PTX Polymer Micelles.