# Supplementary Information

## Active targeting co-delivery of therapeutic *Sur* siRNA and antineoplastic drug via epidermal growth factor receptor mediated magnetic nanoparticles for synergistic programmed cell death in glioblastoma stem cells

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This supporting information provides all of the additional information as noted in the manuscript and more detailed discussion of the current study.

**Synthesis of γ-$Fe_2O_3$ magnetic nanoparticles**

γ-$Fe_2O_3$ magnetic nanoparticles used in this study were synthetized from magnetite ($Fe_3O_4$) according to methods proposed elsewhere[1,2]. First, 4.5 mL $FeCl_3$ (2 M dissolved in 2 M HCl) was added to 15.5 mL DI water, and then 3 mL $Na_2SO_3$ (1 M) was added dropwise into the mixture within 1 min with stirring. When the color of the solution changed from red to light yellow, it was added to 120 mL of $NH_4OH$ solution (0.85 M) with vigorous stirring. A black precipitate quickly formed and was allowed to crystallize completely for another 40 min. After washed with deoxygenated water, the black precipitate was diluted to 252 mL (with a mass concentration of 3 mg/mL) and was adjusted to pH 3.0 with HCl (0.1 M). The suspension was then heated to 90 ˚C in 5 min, and was stirred under aeration (with air) for 90 min at 110 ˚C. The color of the suspension slowly changed from black to reddish-brown. After washing with DI water by magnetic decantation, the reddish-brown precipitate was dried to a powder of γ-$Fe_2O_3$.

**The PEI content coupled with the MNNS analysis** The amount of PEI coupled with the MNNS was measured with the ninhydrin chromogenic method as previously described [3]. The standard curve was first established, and the absorbance at 570 nm was determined by ultraviolet-visible spectrophotometer (NanoDrop 2000, themro) and PEI content was calculated three times after adding 0.1% indene 1 mL of indene in 95 ℃ water bath for 5 min.

**Stability and magnetic response analysis of eMNNS**

The dispersion stability and magnetic response to an external magnetic field of the fabricated eMNNS was evaluated with transmittance in RPMI-1640 medium, PBS solution (pH7.4), and DI water at different time points using ultraviolet-visible spectrophotometer (NanoDrop 2000, themro).

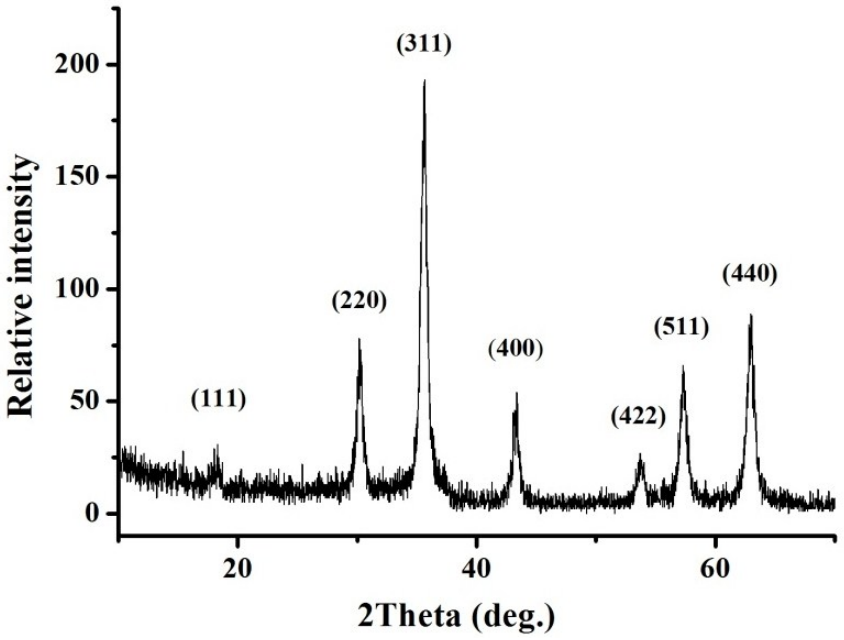


**Figure S1.** XRD pattern of SPIO NPs.

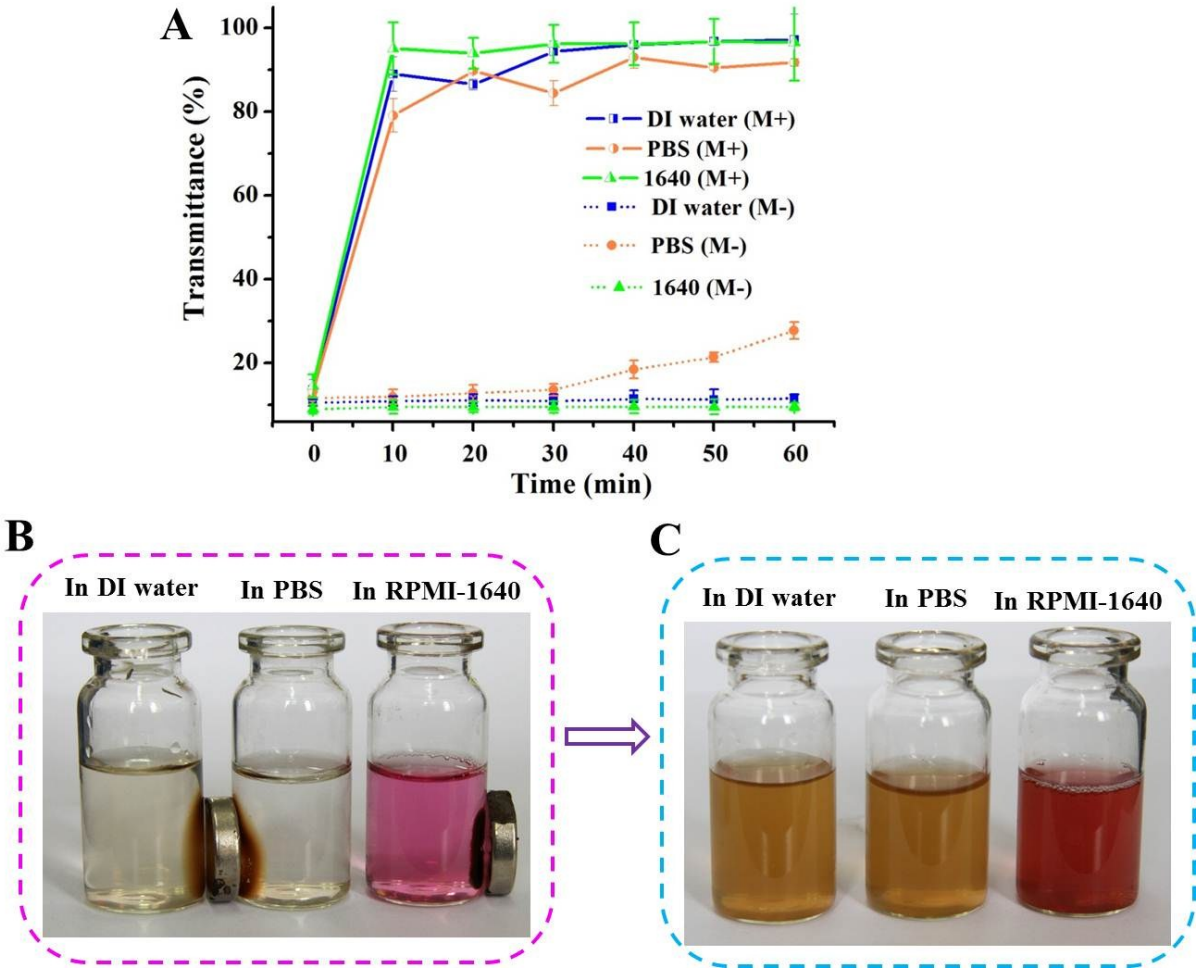


**Figure S2.** (A) The stability and magnetic responsiveness of eMNNS to an external magnetic field in different media, including DI water, PBS (pH 7.4), and RPMI-1640 culture medium. Magnetic field (M+), without applied magnetic field (M-). Optical photos of the magnetic-responsive aggregation and redispersion of the prepared eMNNS in an aqueous suspension by adding and removing an external magnetic field (B&C).

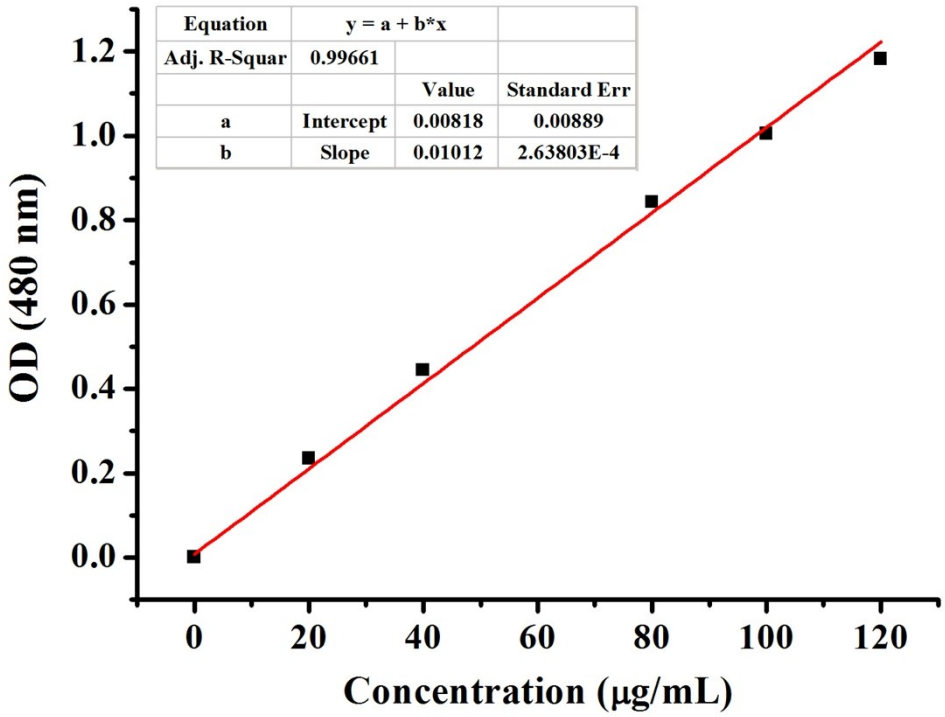


**Figure S3.** The calibration curve of DOX content.

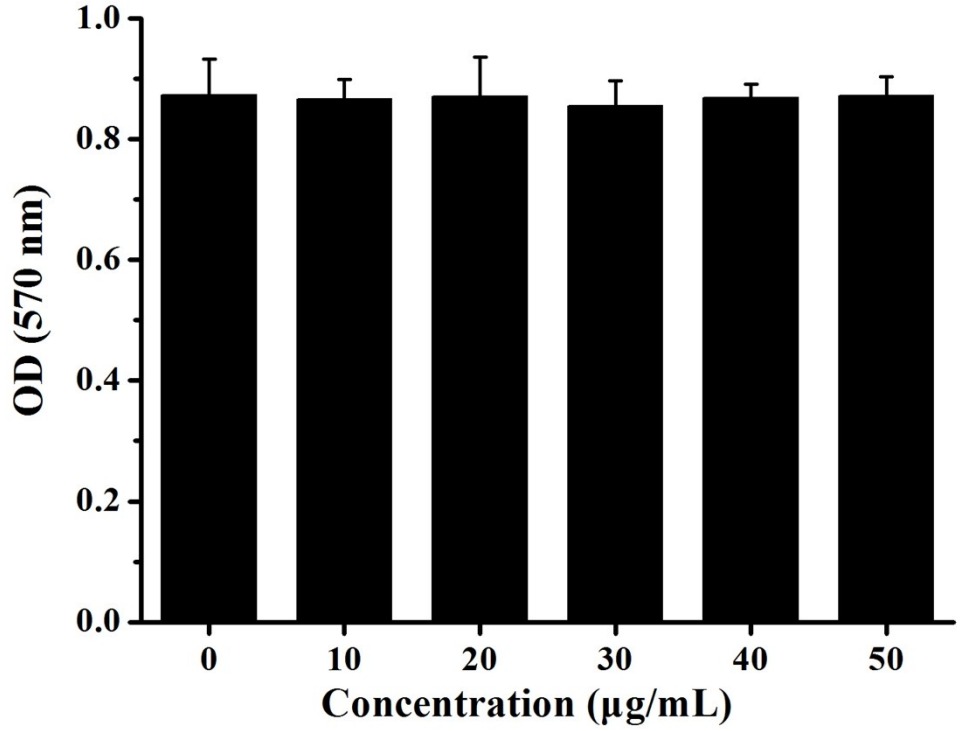


**Figure S4.** The growth of GSCs after treatment with different concentration eMNNS from 0 to 50 μg/mL, and were measured by MTT assay after incubation for 24 h.

**References**

[1] S. Qu, H. Yang, D. Ren, S. Kan, G. Zou, D. Li, M. Li, Magnetite nanoparticles prepared by precipitation from partially reduced ferric chloride aqueous solutions, J. Colloid Interface Sci. 215 (1999) 190–192.

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[3] Friedman M, Applications of the ninhydrin reaction for analysis of amino acids, peptides, and proteins to agricultural and biomedical sciences, J. Agric. Food Chem. 52 (2004) 385–406.