Supporting Information

Enzyme-instructed self-aggregation of Fe_3O_4 nanoparticles for enhanced MRI T_2 imaging and photothermal therapy of tumor

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1. Syntheses of compounds

Compound of Acetyl-Arg-Val-Arg-Arg-Cys (StBu)-Lys (compound A) was synthesized with solid phase peptide synthesis (SPPS). Isobutyl chloroformate (IBCF, 8.7 μL, 0.12 mmol) was added to a mixture of compound A (180 mg, 0.1 mmol) and 4-methylmorpholine (MMP, 8.5 μL, 0.15 mmol) in THF (1.5 mL) at 0℃ under N_2. The reaction mixture was stirred for 30 min. The solution of 2-cyano-6-aminobenzothiazole (CBT, 18 mg, 0.1 mmol) was added to the reaction mixture and further stirred at 0℃ for 1 h. Then the mixture was stirred overnight at room temperature. After the compound B (70mg, yield: 30%) was purified with HPLC, The Pbf and Boc protecting groups were removed with 95% TFA in CH_2Cl_2 for 3h. The pure product compound 1 (20 mg, 50%) was obtained after HPLC purification.

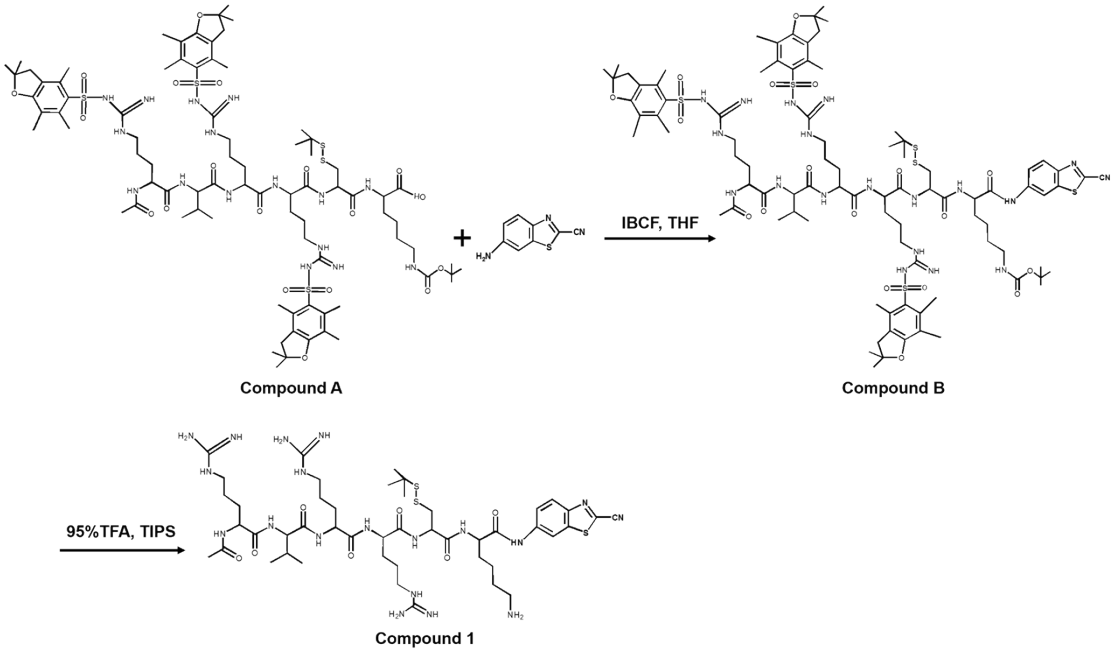
2. Calculation of the photothermal conversion efficiency

The photothermal conversion efficiency of SPIO@1NPs before and after the aggregation were determined according to previous method [1]. Detailed calculation was given as following:

$$\eta = \frac{m \cdot c\,(T_{max} - T_{max,\,H2O})}{I(1-10^{-A_\lambda}) \cdot \tau_s}$$

where m is the solution mass (pure water), c is the heat capacity of solvent (4.2 J/g), T_{max} and $T_{max,\,H2O}$ are the temperature change of the NPs and solution suspensions at the maximum steady-state temperature, respectively, I is the laser power density (5W/cm^2), A_λ is the absorbance of the NPs solution at 808 nm, and τ_s is sample system time constant (Figure S7).

3. Supporting figures and tables



Scheme S1. Chemical syntheses of compound 1.

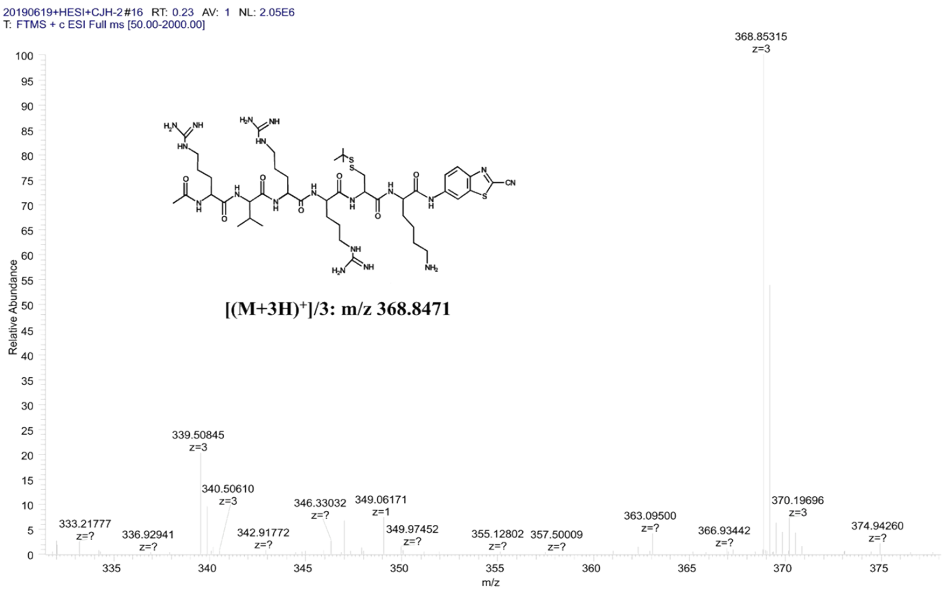


Figure S1. HR-ESI/MS spectrum of compound 1.

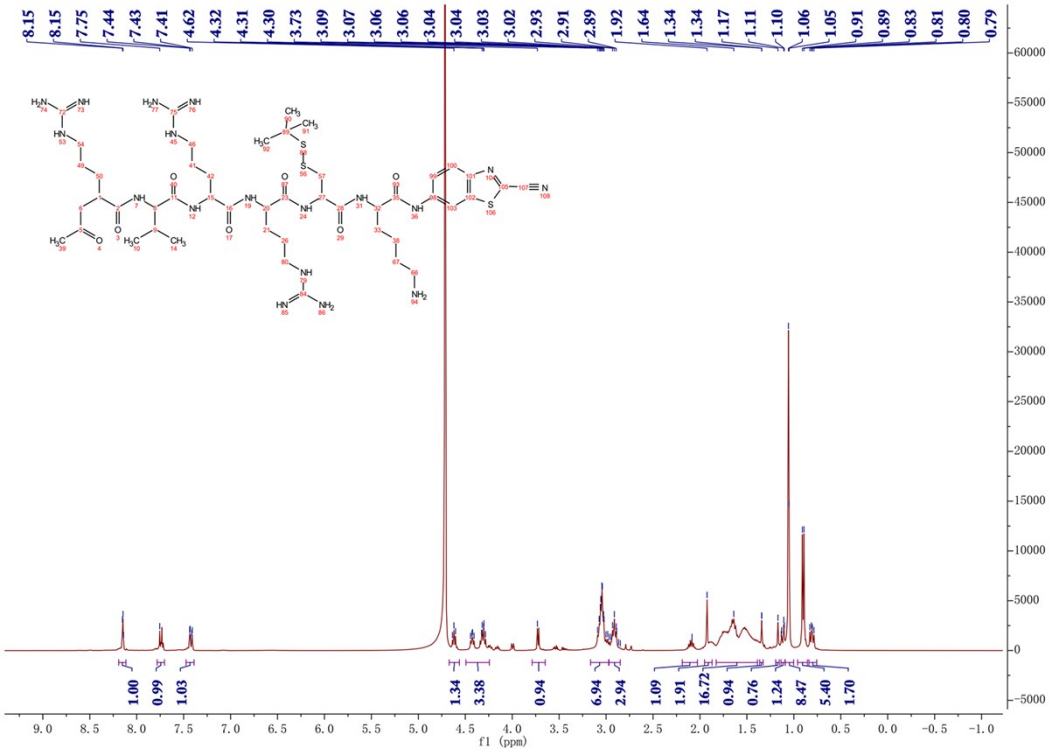


Figure S2. ^{1}H NMR spectrum of compound 1.

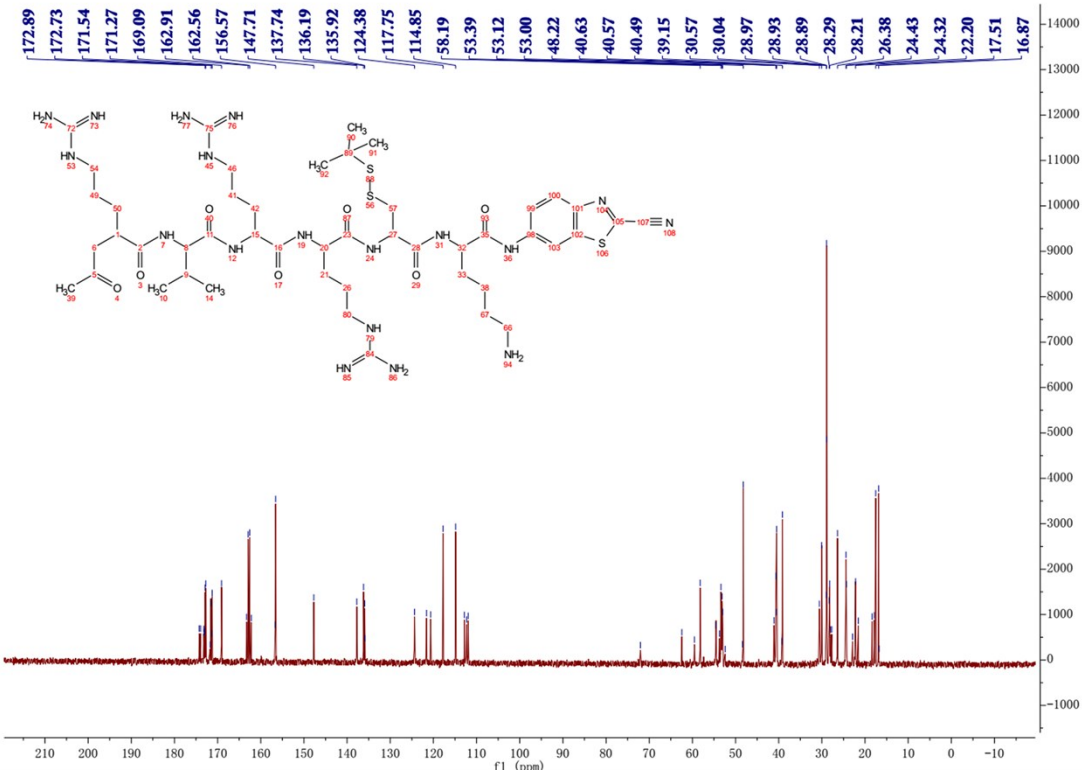


Figure S3. ^{13}C NMR spectrum of compound 1.

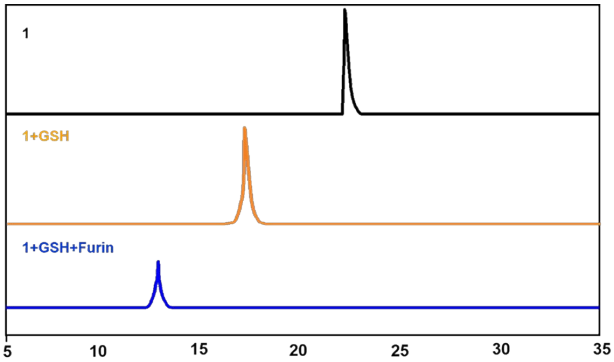


Figure S4. HPLC traces of 100 μM compound 1 (black), 100 μM compound 1 treated with 1 mM GSH for 2 h (orange), 100 μM compound 1 treated with 1 mM GSH and 1 n mol/U of furin at 37 °C for 6 h (blue).

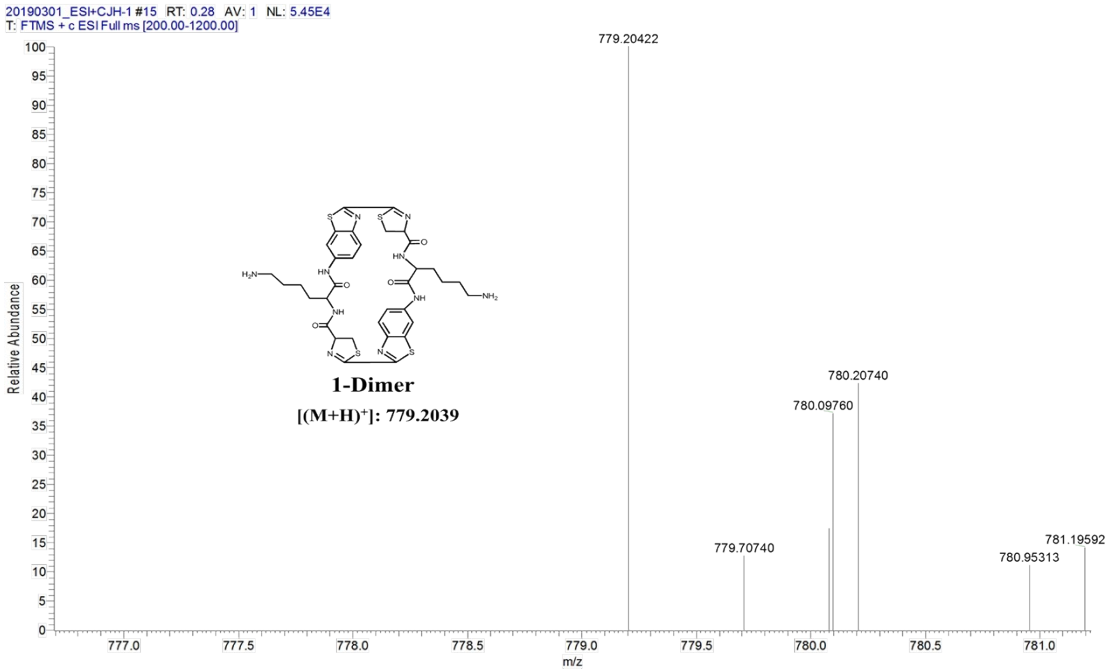


Figure S5. HR-ESI/MS spectrum of HPLC peaks of HPLC peak at 15 min in figure S4.

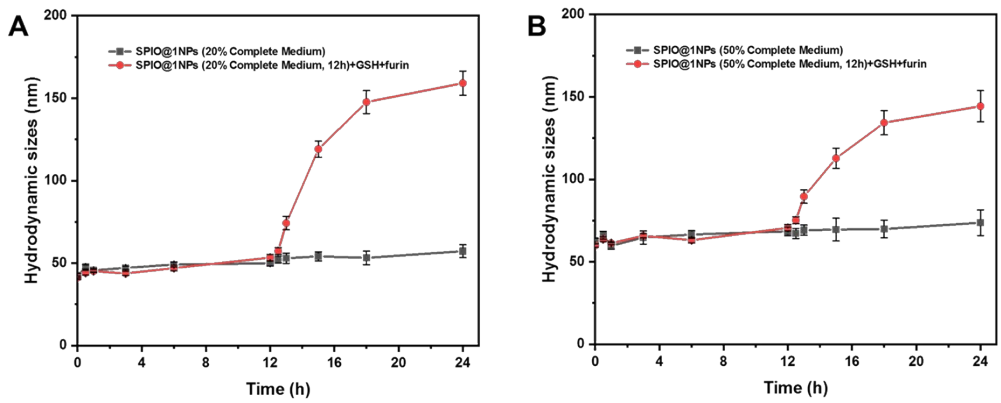


Figure S6. Hydrodynamic diameter of SPIO@1NPs pre-incubated in PBS buffer containing 20% complete medium (A), 50% complete medium (B) for 12h, then incubated with GSH (1 mM) and of furin (1 nmol/U) and without for another 12 h.

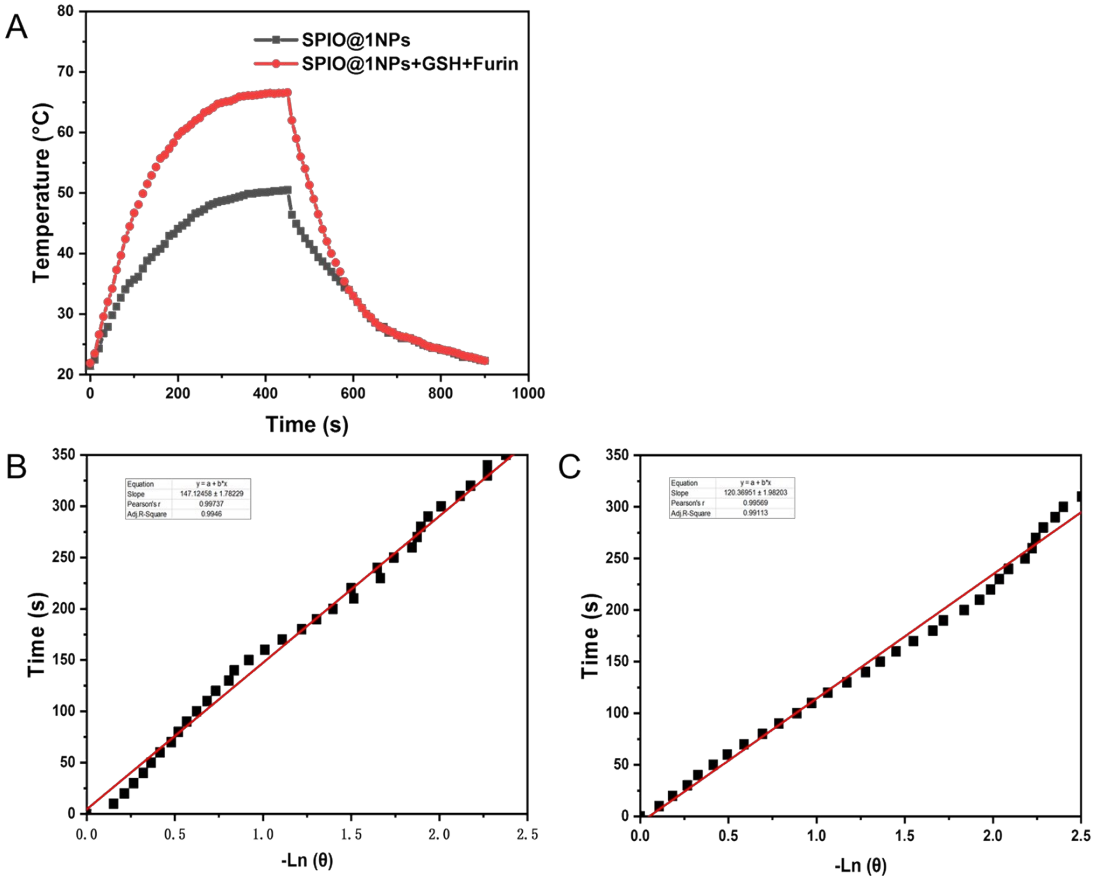


Figure S7. (A)The photothermal heating curves of SPIO@1NPs and SPIO@1NPs treated with GSH and furin under laser irradiation. Linear fitting of the cooling time data (after 450 s) of the curves of the SPIO@1NPs (B) and SPIO@1NPs treated with GSH and furin (C) versus the responding negative natural logarithm of the temperature driving force (θ) to obtain their system time constant (τ_s).

Table S1. HPLC condition for the purification of compound 1

Time (min)	Flow (ml/min)	H_2O% (0.1%TFA)	CH_3OH% (0.1%TFA)
0	12.0	80	20
3	12.0	80	20
35	12.0	20	80
37	12.0	20	80
38	12.0	80	20
40	12.0	80	20

References

1. Ding, X., Liow, C.H., Zhang, M., Huang, R., Li, C., Shen, H., Liu, M., Zou, Y., Gao, N., Zhang, Z., Li, Y., Wang, Q., Li, S. and Jiang, J., *J AM CHEM SOC*, 2014, **136**, 15684-15693.