Supplementary data

Transformation of Nanoparticles into Hydrogel for Long-acting and Sensitized Apoptosis Therapy of Triple Negative Breast Cancer

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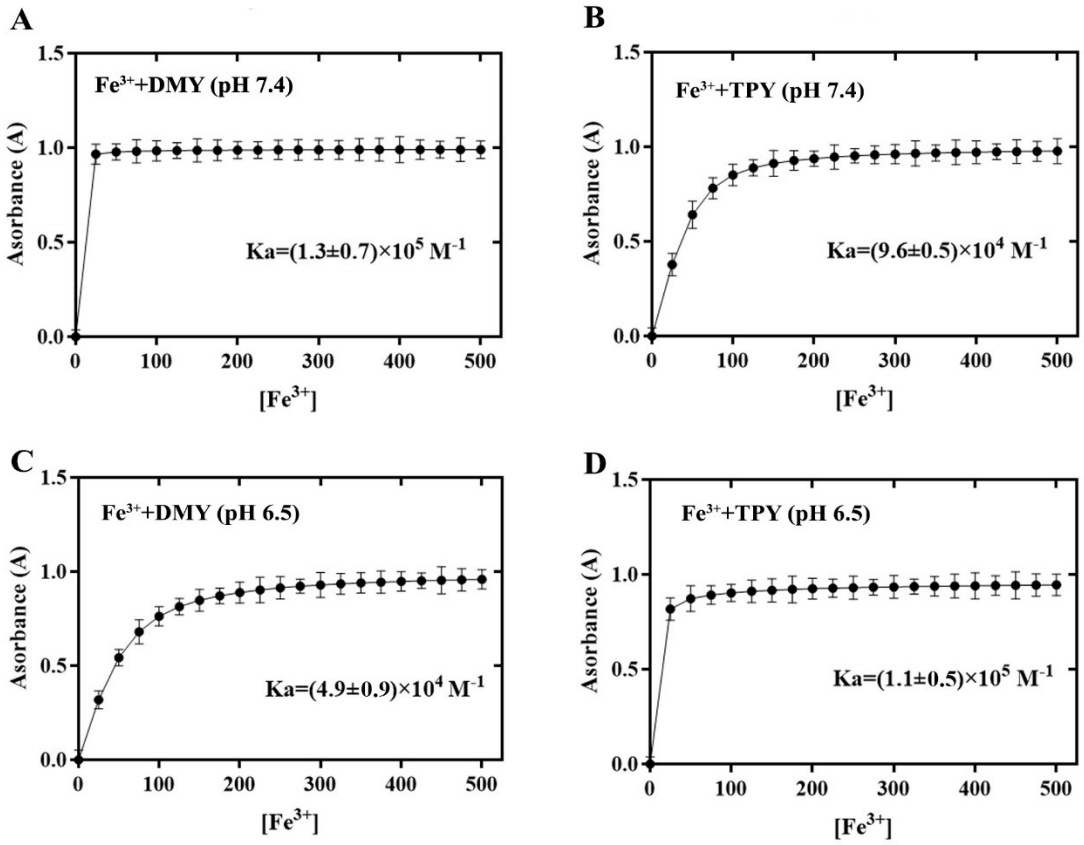

Figure S1. The affinity curve of Fe^{3+} with DMY at pH 7.4 (A), Fe^{3+} with TPY at pH 7.4 (B), Fe^{3+} with DMY at pH 6.5 (C) and Fe^{3+} with TPY at pH 6.5 (D).

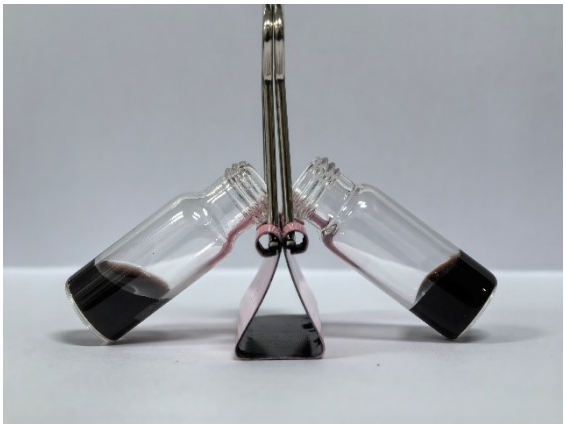

Figure S2. SF_{sTRAIL}@MPN gelation transition from pH 7.4 (L) to pH 6.5 (R).

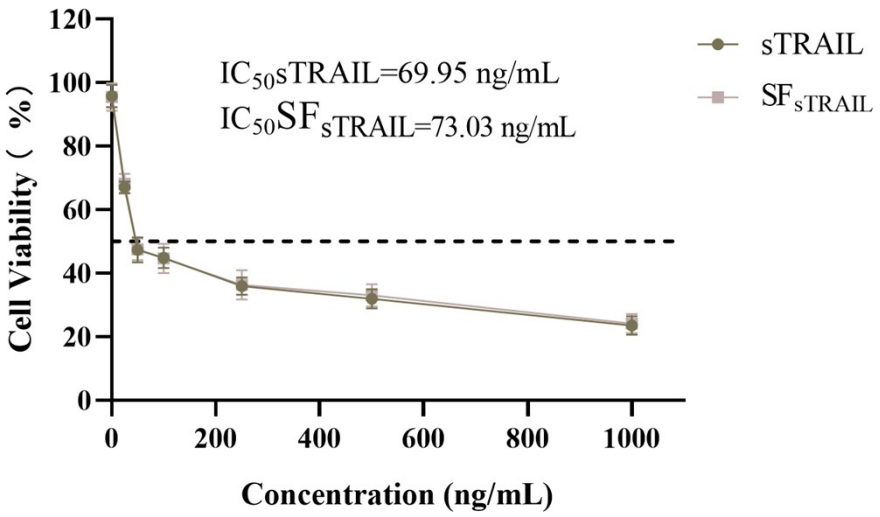

Figure S3. Cell viability and IC_{50} of sTRAIL. (n=5).

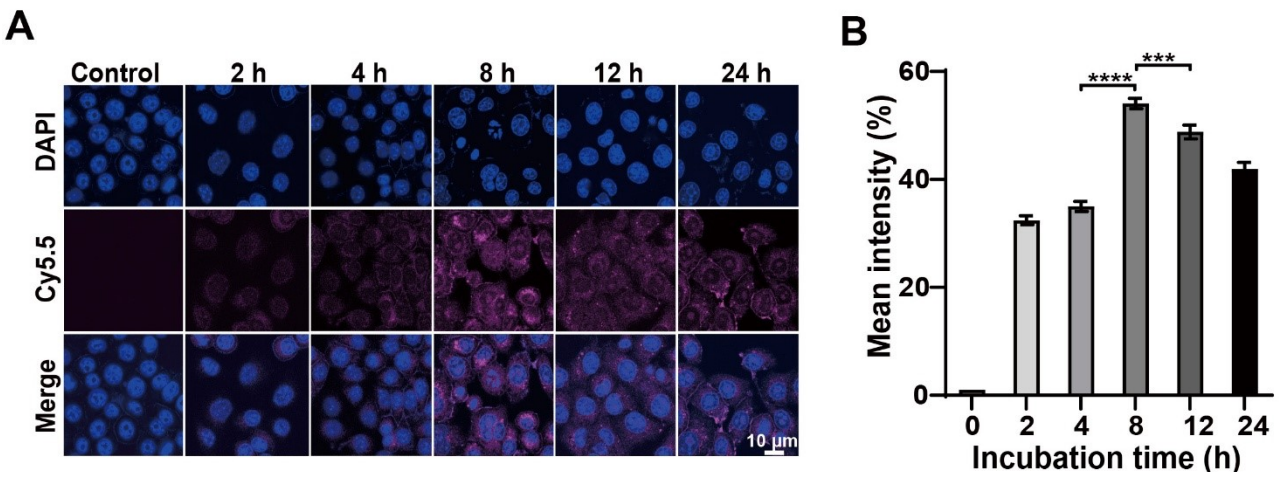

Figure S4. (A) Examination of binding ability of sTRAIL in SF_{sTRAIL}@MPN by 4T1 cells at pH7.4; (B) Fluorescence quantification analysis of binding ability at pH 7.4. Bar = 10 μm.

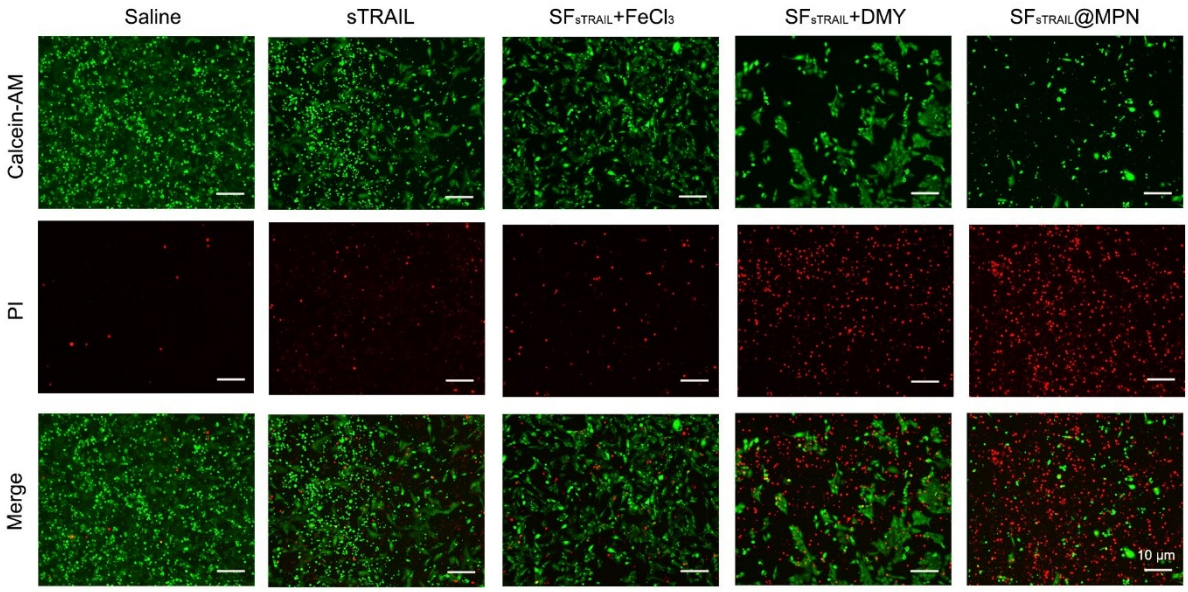

Figure S5. Live/dead viability staining of SF_{sTRAIL}@MPN. Bar = 10 μm.

Figure S6. Individual tumor growth of Saline, SF_{sTRAIL}, SF_{sTRAIL} + $FeCl_3$, SF_{sTRAIL} + DMY and SF_{sTRAIL}@MPN in 4T1 tumor-bearing mice. (n = 3). **** $p < 0.000\ 1$, ** $p < 0.01$.

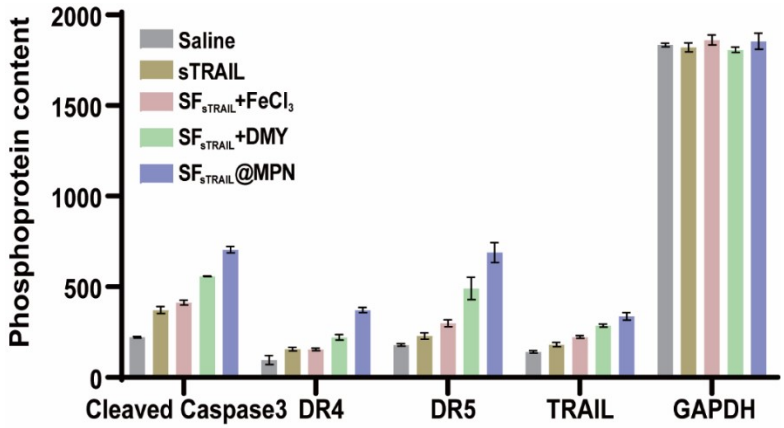

Figure S7. (A) Quantitative analysis of expression of Cleaved Caspase-3, TRAIL, DR4 and DR5 in tumor tissues collected from different groups (n = 3).

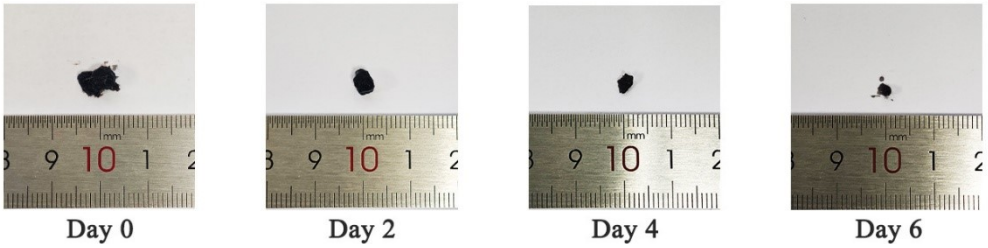

Figure S8. Biodegradation of SF_{sTRAIL}@MPN for 0, 2, 4, 6 days.

Table S1. Interaction sites of Silk Fibroin and TRAIL

Silk fibroin interface residue	TRAIL interface residue	Hydrogen Bonds(Å)
ASP 181A	LEU 243D	2.923
GLN 224A	TYR 187D	2.911
GLN 224A	TYR 189D	2.941
GLN 224A	TYR 247D	3.071
TYR 252A	LEU 251D	3.079
GLN 255A	ILE 284D	2.941

Table S2. Interaction sites of Dihydromyricetin with Silk Fibroin and TRAIL

Ligand	Target	Binding Energy (Kcal/mol)	Ki (μM)
Dihydromyricetin	Silk fibroin	-7.5	3.1
Dihydromyricetin	TRAIL	-6.9	8.6

Table S3. Binding constants (Ka) of Fe^{3+} with DMY and TPY at different pH values

Ligands	pH value	Ka (10^4 M^{-1})
DMY	7.4	13±7
DMY	6.5	4.93±0.86
TPY	7.4	9.6±0.513
TPY	6.5	11.5±4.6

Table S4. Interaction sites of Dihydromyricetin with Silk Fibroin and TRAIL

Test indicators	pH 6.8	pH 6.0
Viscosity (cP)	2.55	32.85
Torque (%)	1.7	21.9
Shear stress (dyne/cm2)	1.73	22.34

Table S4. qPCR primer design for Cleaved Caspase-3, TRAIL, DR4 and DR5.

Gene	Forward Primer	Reward Primer
Cleaved Caspase-3	CTGGCGTGTGCGAGATGAG	CTTAGCGTTCCAAGCTCCCC
TRAIL	CCTCTCGGAAAGGGCATTCA	CTGCACCAGCTGTTTGGTTC
DR4	TGCTCATCGGCTTGGTGTTG	AGTAGTTGGTGGGTGTCTGC
DR5	GCGAACTCTGTGCATTCGTC	TCGTCAGCTGAGTCGTTTCC